Dossier zur Nutzenbewertung gemäß § 35a SGB V

Selumetinib (Koselugo®)

AstraZeneca GmbH

Modul 4A, Anhang 4-G1

Behandlung von symptomatischen, inoperablen plexiformen Neurofibromen bei Kindern ab 3 Jahren und Jugendlichen mit Neurofibromatose Typ 1

Vollständige Darstellung der für das vorliegende Dossier relevanten Ergebnisse als unveränderte Ausgabe der Statistik-Software

Stand: 12.08.2021

Table 1.1.1 Progression-free survival (PFS - Investigator), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=50)			Natural History (N=92)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	50	3 (6.0)	NE (NE, NE)	92	80 (87.0)	1.3 (1.1, 1.6)	0.23	0.14, 0.37	<0.0001

NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Table 1.1.1.1 Progression-free survival (PFS - Investigator), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
Gender = Male, Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=30)			Natural History (N=56)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	30	2 (6.7)	NE (NE, NE)	56	50 (89.3)	1.3 (1.0, 1.9)	0.24	0.13, 0.43	<0.0001

NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Table 1.1.1.2 Progression-free survival (PFS - Investigator), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
Gender = Female, Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=20)			Natural History (N=36)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	20	1 (5.0)	NE (NE, NE)	36	30 (83.3)	1.4 (1.0, 1.9)	0.22	0.10, 0.48	0.0002

NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Table 1.1.1.3 Progression-free survival (PFS - Investigator), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Progressive, Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=21)			Natural History (N=34)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	21	3 (14.3)	NE (NE, NE)	34	33 (97.1)	0.7 (0.6, 0.9)	0.11	0.06, 0.22	<0.0001

NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Table 1.1.1.4 Progression-free survival (PFS - Investigator), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Not progressive, Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=15)			Natural History (N=49)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	15	0	NE (NE, NE)	49	41 (83.7)	2.0 (1.6, 2.7)	0.28	0.11, 0.70	0.0064

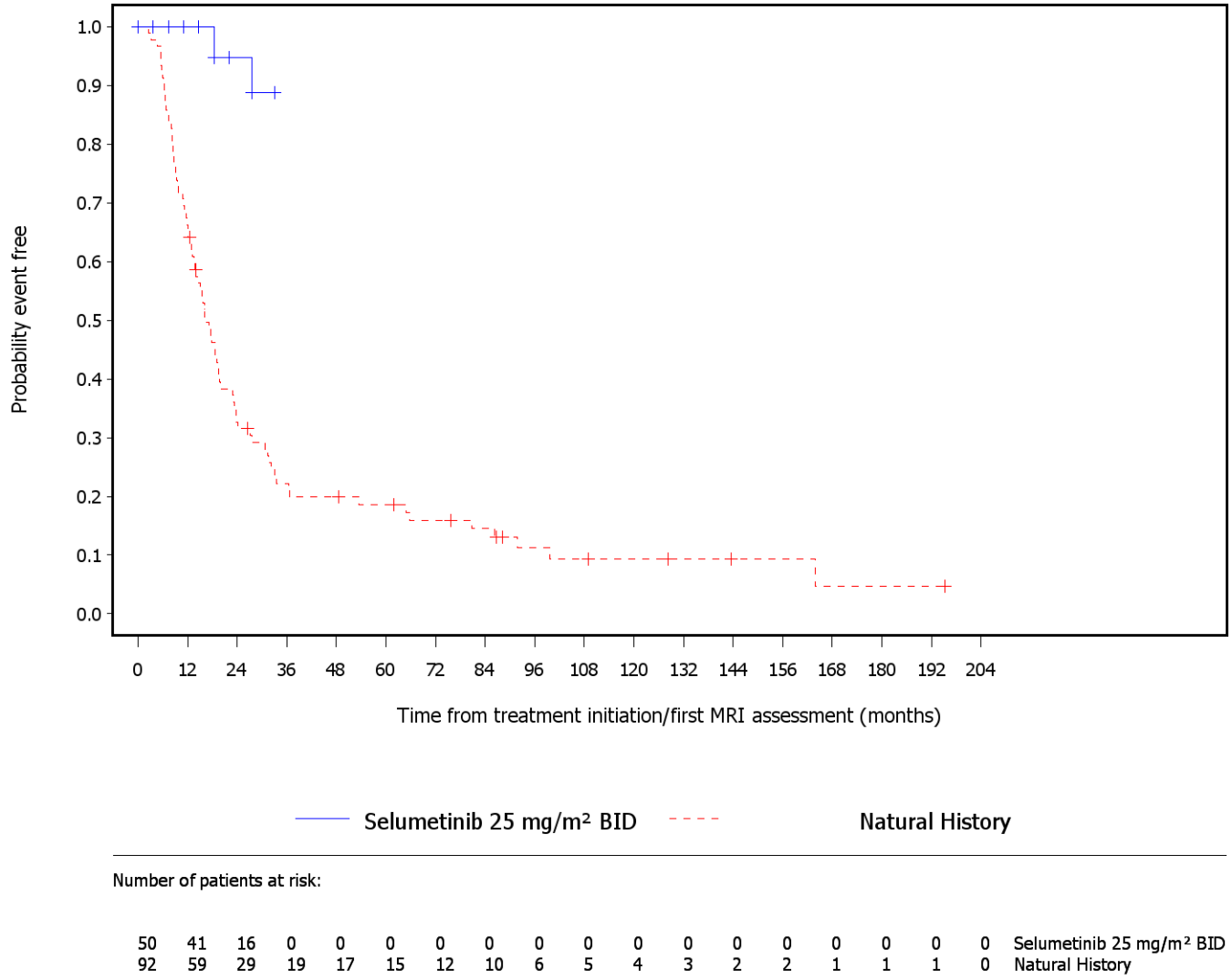
NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Table 1.1.1.5 Progression-free survival (PFS - Investigator), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Unknown, Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=14)			Natural History (N=9)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	14	0	NE (NE, NE)	9	6 (66.7)	2.0 (0.5,13.7)	0.09	0.01, 0.56	0.0097

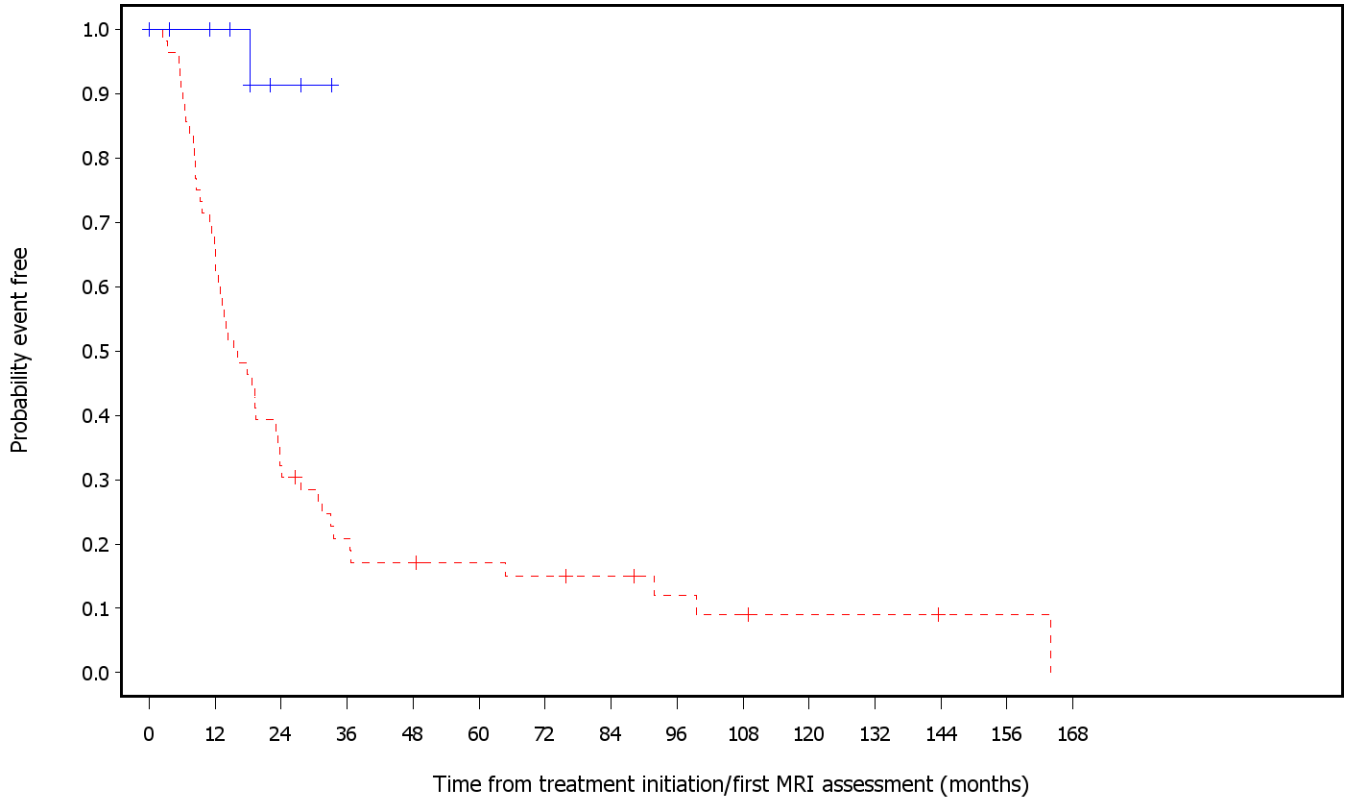
NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Figure 1.1.2 Kaplan-Meier plot for PFS - Investigator, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I Phase II Stratum 1, Data cut-off: 29th June 2018



Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Figure 1.1.2.1 Kaplan-Meier plot for PFS - Investigator, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
Gender = Male, Phase II Stratum 1, Data cut-off: 29th June 2018

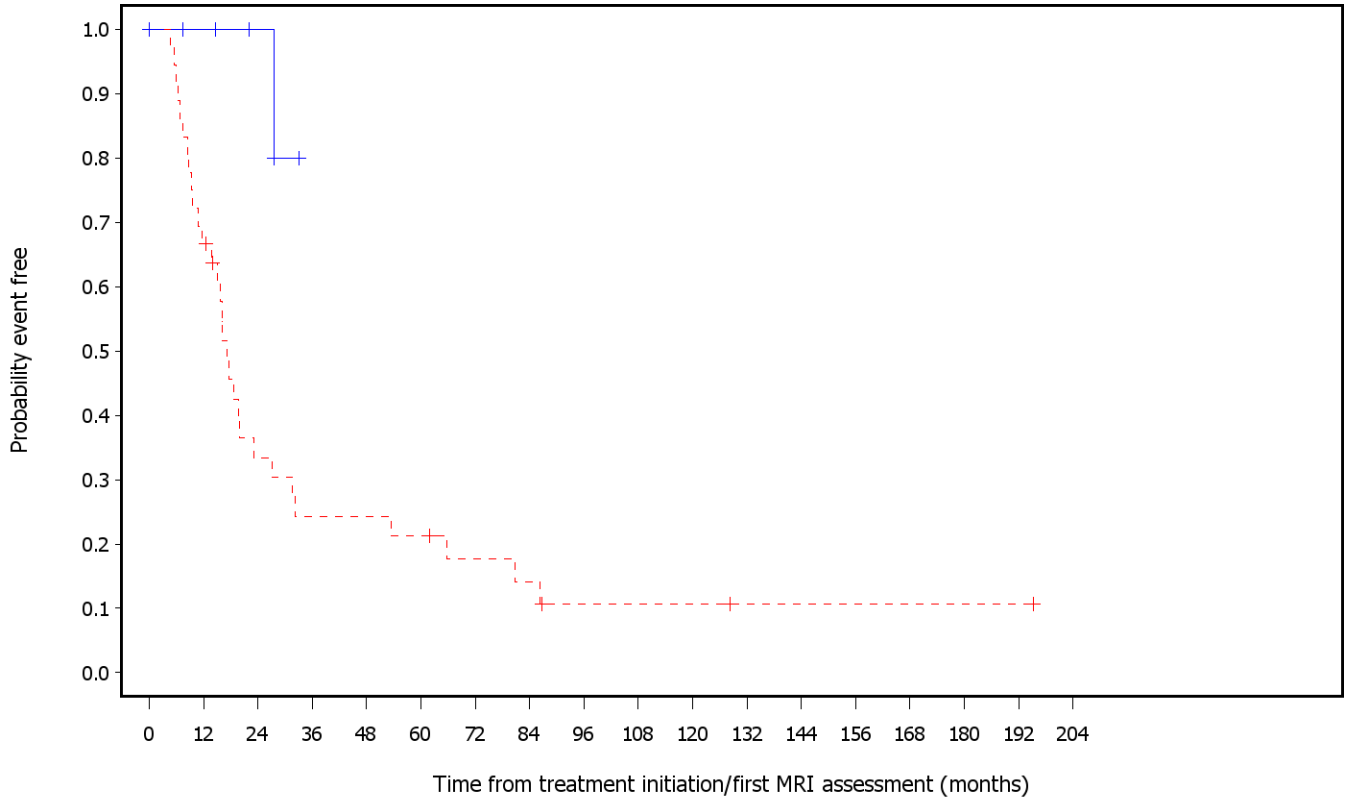


Number of patients at risk:

30	24	11	0	0	0	0	0	0	0	0	0	0	0	0	Selumetinib 25 mg/m² BID
56	35	18	11	9	8	7	6	4	3	2	2	1	1	0	Natural History

Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Figure 1.1.2.2 Kaplan-Meier plot for PFS - Investigator, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I Gender = Female, Phase II Stratum 1, Data cut-off: 29th June 2018

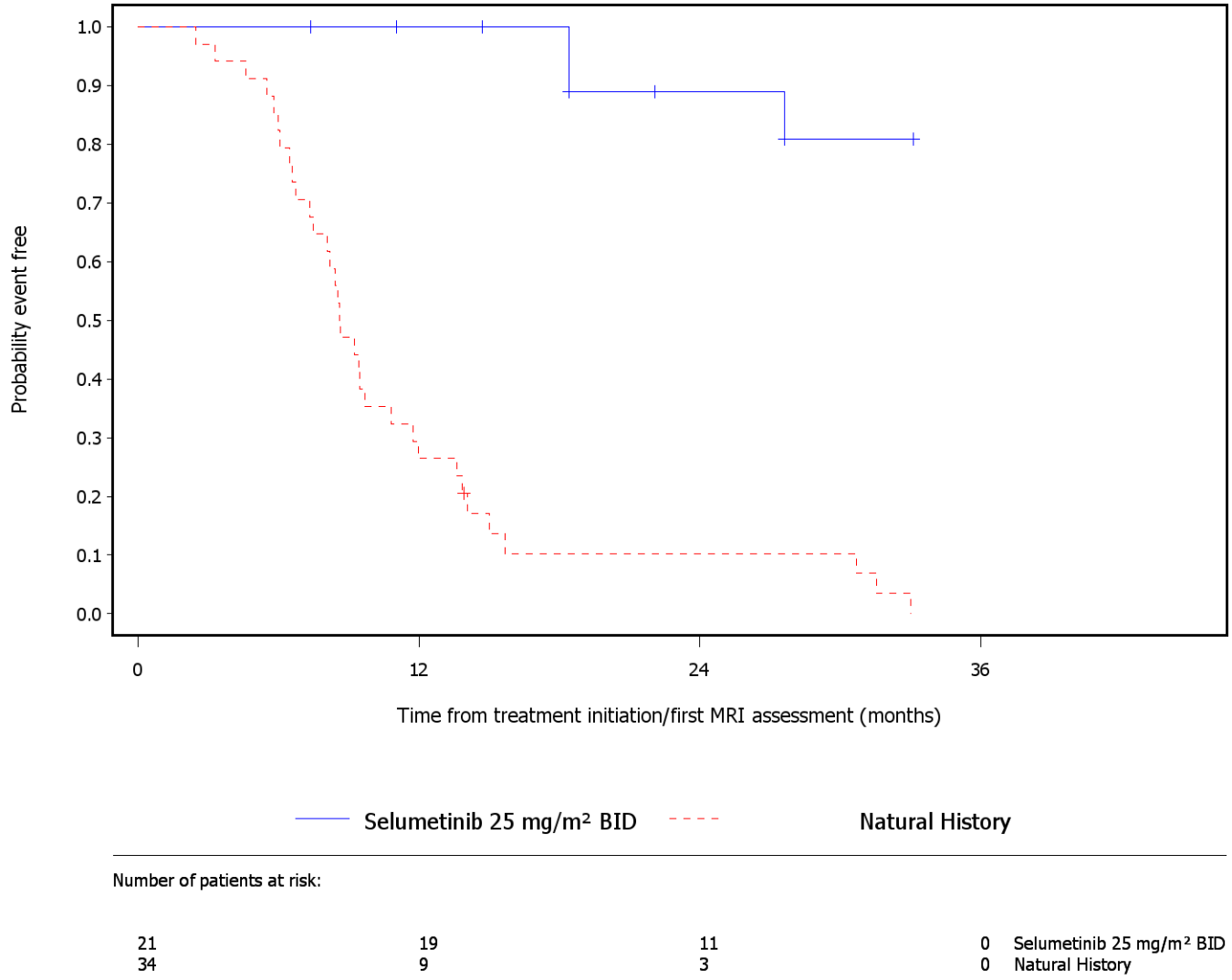


Number of patients at risk:

20	17	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Selumetinib 25 mg/m² BID
36	24	11	8	8	7	5	4	2	2	2	1	1	1	1	1	1	0	Natural History

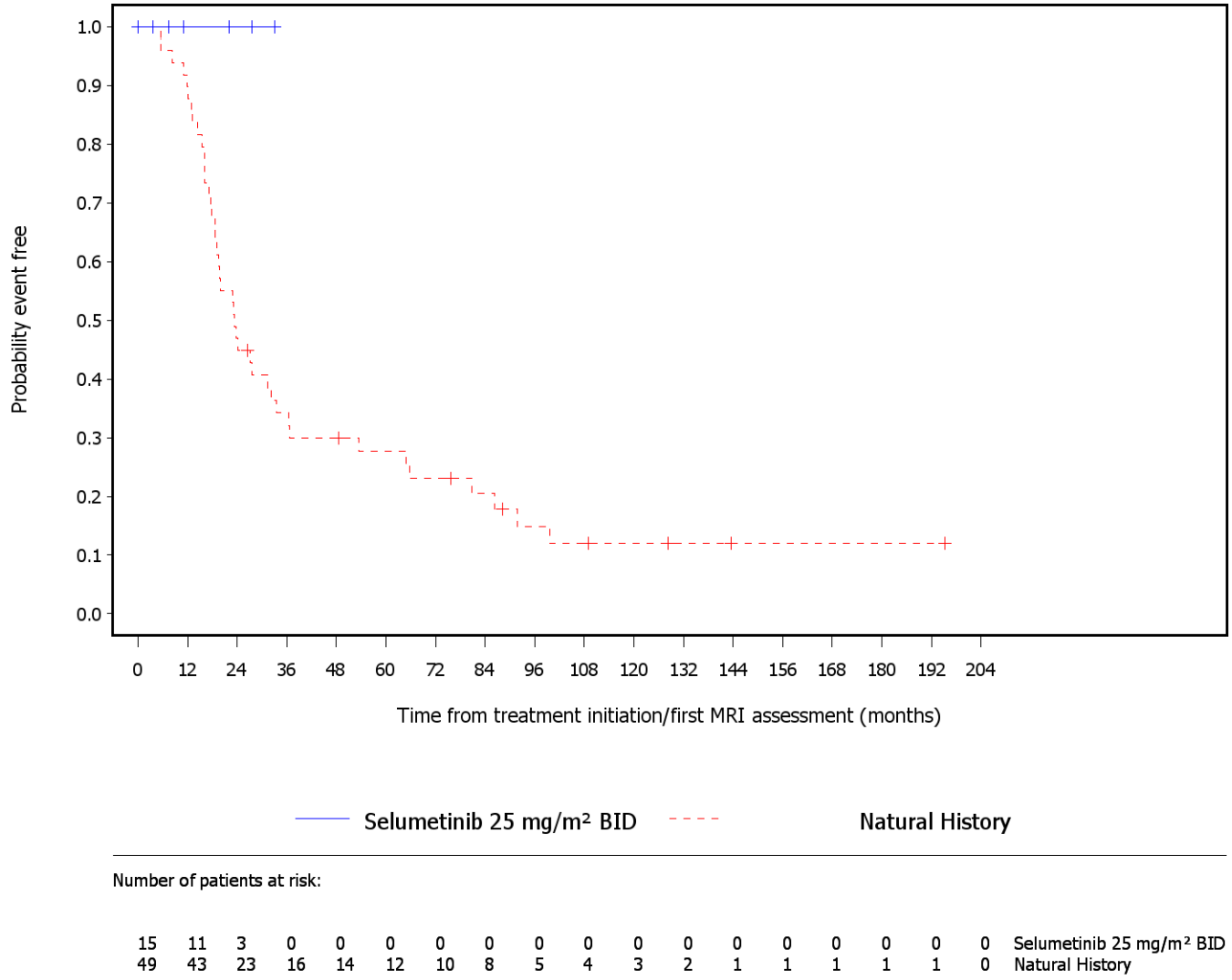
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Figure 1.1.2.3 Kaplan-Meier plot for PFS - Investigator, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Progressive, Phase II Stratum 1, Data cut-off: 29th June 2018



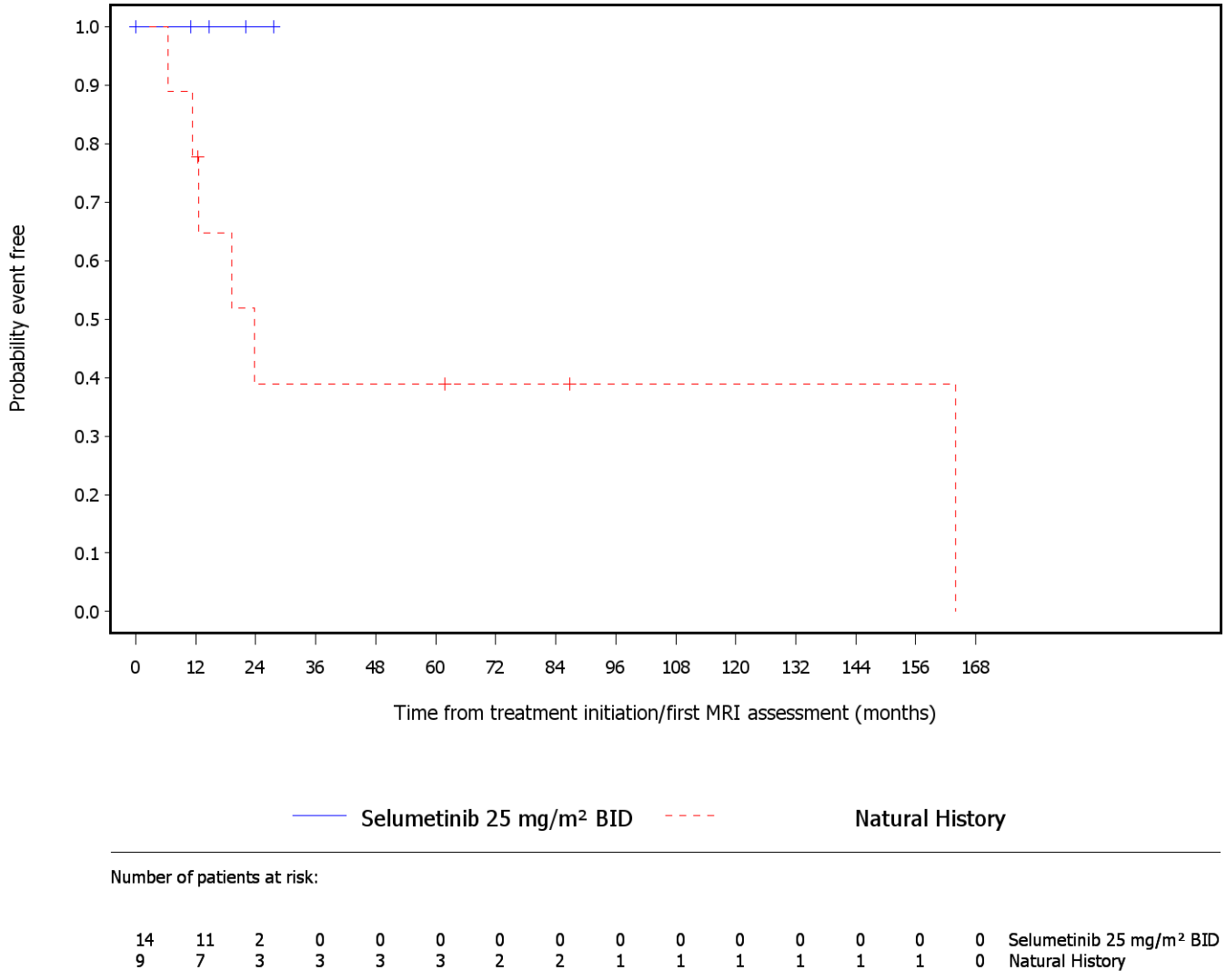
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Figure 1.1.2.4 Kaplan-Meier plot for PFS - Investigator, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Not progressive, Phase II Stratum 1, Data cut-off: 29th June 2018



Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Figure 1.1.2.5 Kaplan-Meier plot for PFS - Investigator, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Unknown, Phase II Stratum 1, Data cut-off: 29th June 2018



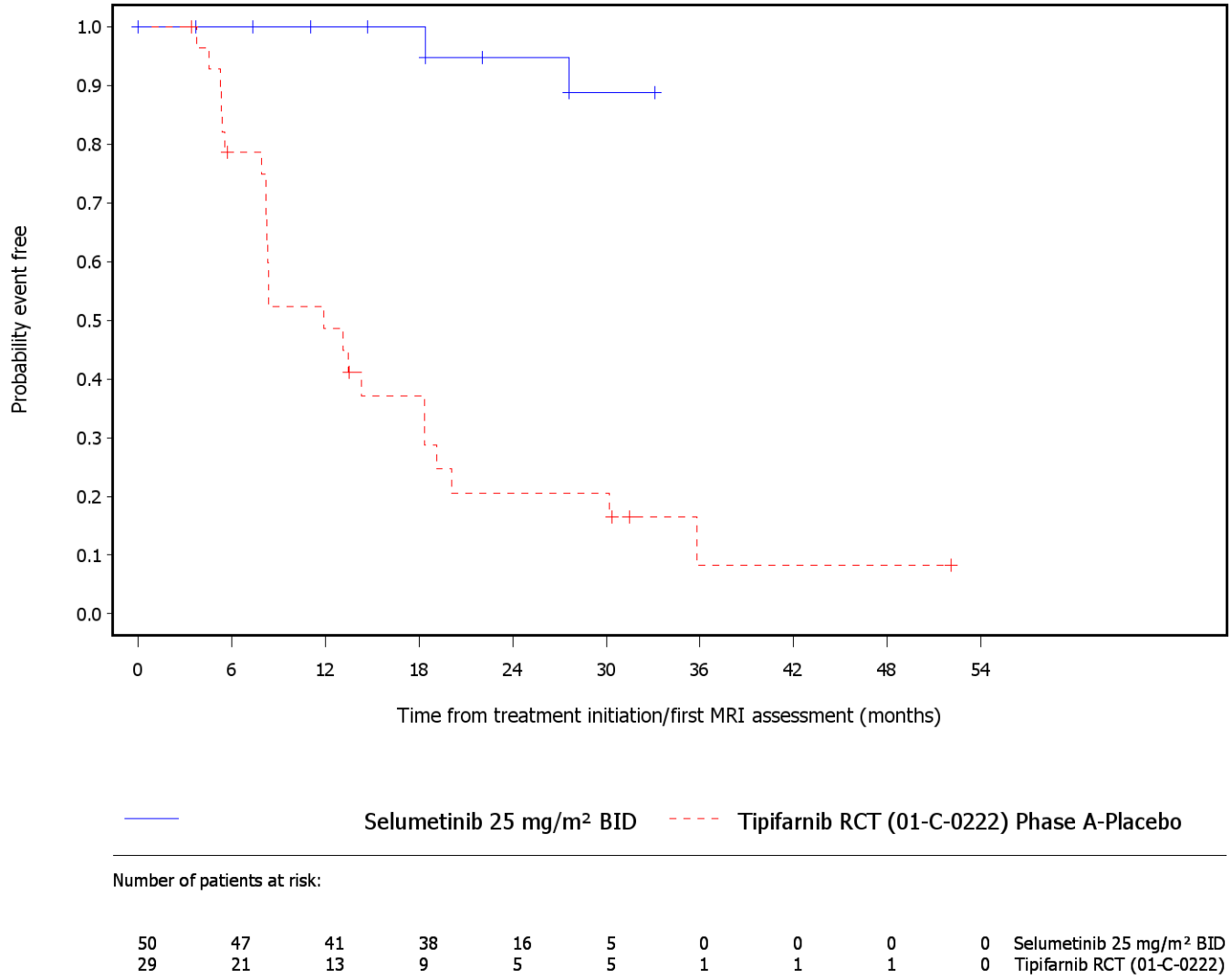
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Table 1.1.3 Progression-free survival (PFS - Investigator), Tipifarnib RCT (01-C-0222) Phase A-Placebo vs. SPRINT Phase II Strat. I Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=50)			Tipifarnib RCT (01-C-0222) Phase A-Placebo (N=29)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	50	3 (6.0)	NE (NE, NE)	29	23 (79.3)	1.0 (0.7, 1.5)	0.04	0.02, 0.10	<0.0001

NC = Not calculated.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
Hazard ratio <1 favours Selumetinib.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Figure 1.1.4 Kaplan-Meier plot for PFS - Investigator, Tipifarnib RCT (01-C-0222) Phase A-Placebo vs. SPRINT Phase II Stratum I Phase II Stratum 1, Data cut-off: 29th June 2018



Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Table 1.1.5 Progression-free survival (PFS - ICR), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=50)			Natural History (N=92)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	50	11 (22.0)	NE (NE, NE)	92	80 (87.0)	1.3 (1.1, 1.6)	0.35	0.22, 0.55	<0.0001

NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
Hazard ratio <1 favours Selumetinib.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Table 1.1.5.1 Progression-free survival (PFS - ICR), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
Gender = Male, Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=30)			Natural History (N=56)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	30	5 (16.7)	NE (NE, NE)	56	50 (89.3)	1.3 (1.0, 1.9)	0.30	0.17, 0.54	<0.0001

NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Table 1.1.5.2 Progression-free survival (PFS - ICR), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
Gender = Female, Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=20)			Natural History (N=36)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	20	6 (30.0)	NE (NE, NE)	36	30 (83.3)	1.4 (1.0, 1.9)	0.45	0.22, 0.94	0.0340

NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Table 1.1.5.3 Progression-free survival (PFS - ICR), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Progressive, Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=21)			Natural History (N=34)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	21	4 (19.0)	NE (NE, NE)	34	33 (97.1)	0.7 (0.6, 0.9)	0.12	0.06, 0.23	<0.0001

NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Table 1.1.5.4 Progression-free survival (PFS - ICR), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Not progressive, Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=15)			Natural History (N=49)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	15	4 (26.7)	NE (NE, NE)	49	41 (83.7)	2.0 (1.6, 2.7)	0.59	0.25, 1.38	0.2214

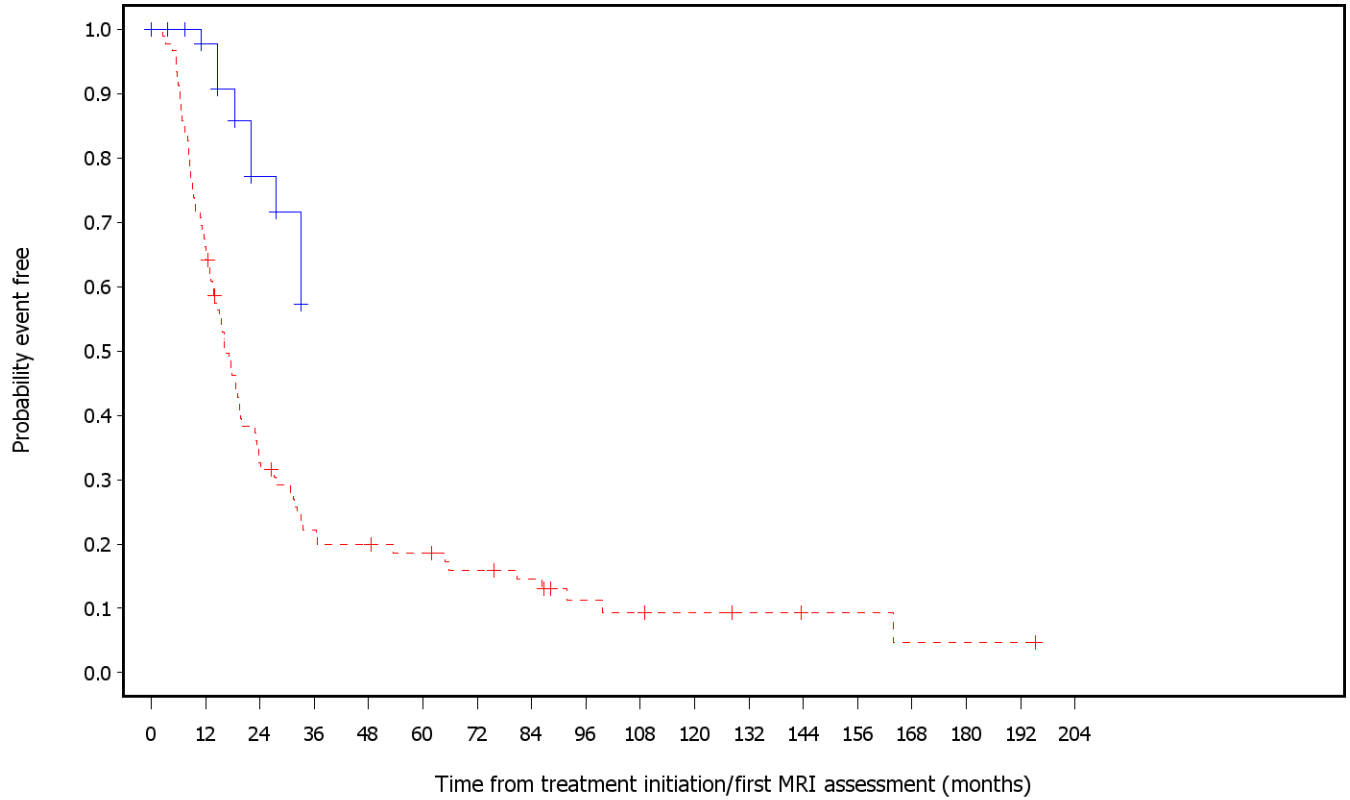
NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Table 1.1.5.5 Progression-free survival (PFS - ICR), Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Unknown, Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=14)			Natural History (N=9)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	14	3 (21.4)	NE (NE, NE)	9	6 (66.7)	2.0 (0.5,13.7)	0.39	0.09, 1.65	0.2006

NC = Not calculated.
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Hazard ratio <1 favours Selumetinib.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Figure 1.1.6 Kaplan-Meier plot for PFS - ICR, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
Phase II Stratum 1, Data cut-off: 29th June 2018

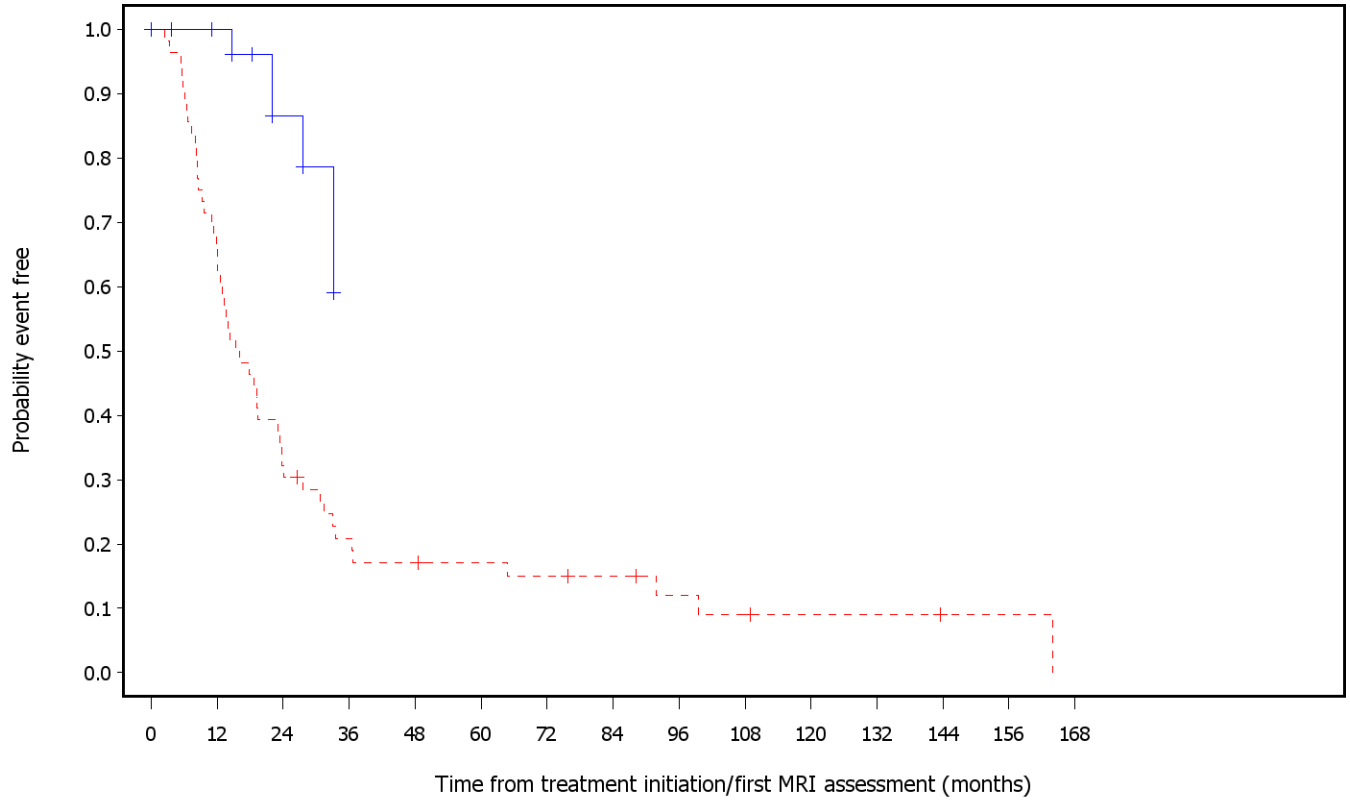


Number of patients at risk:

50	42	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Selumetinib 25 mg/m² BID
92	59	29	19	17	15	12	10	6	5	4	3	2	2	1	1	1	0	Natural History

Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Figure 1.1.6.1 Kaplan-Meier plot for PFS - ICR, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
Gender = Male, Phase II Stratum 1, Data cut-off: 29th June 2018

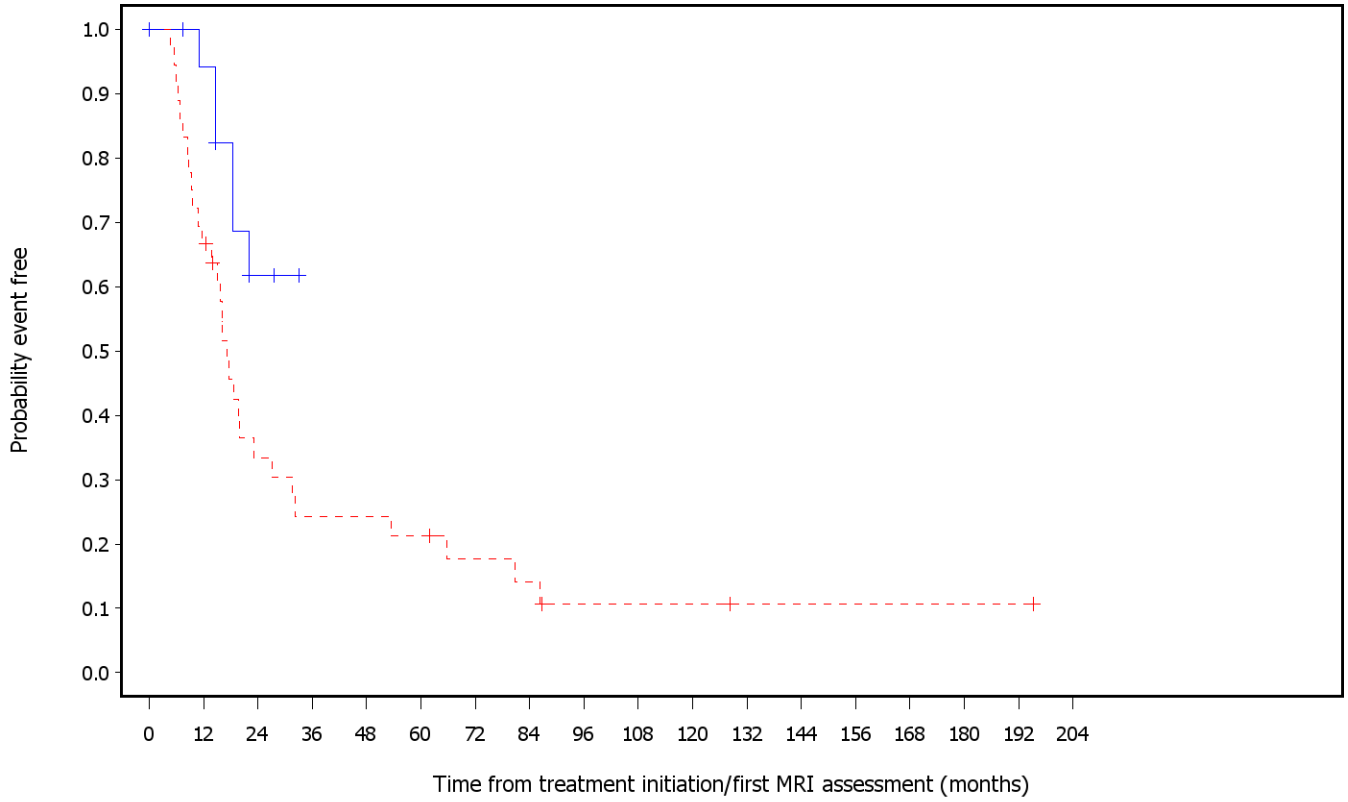


Number of patients at risk:

30	26	11	0	0	0	0	0	0	0	0	0	0	0	0	Selumetinib 25 mg/m² BID
56	35	18	11	9	8	7	6	4	3	2	2	1	1	0	Natural History

Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Figure 1.1.6.2 Kaplan-Meier plot for PFS - ICR, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
Gender = Female, Phase II Stratum 1, Data cut-off: 29th June 2018

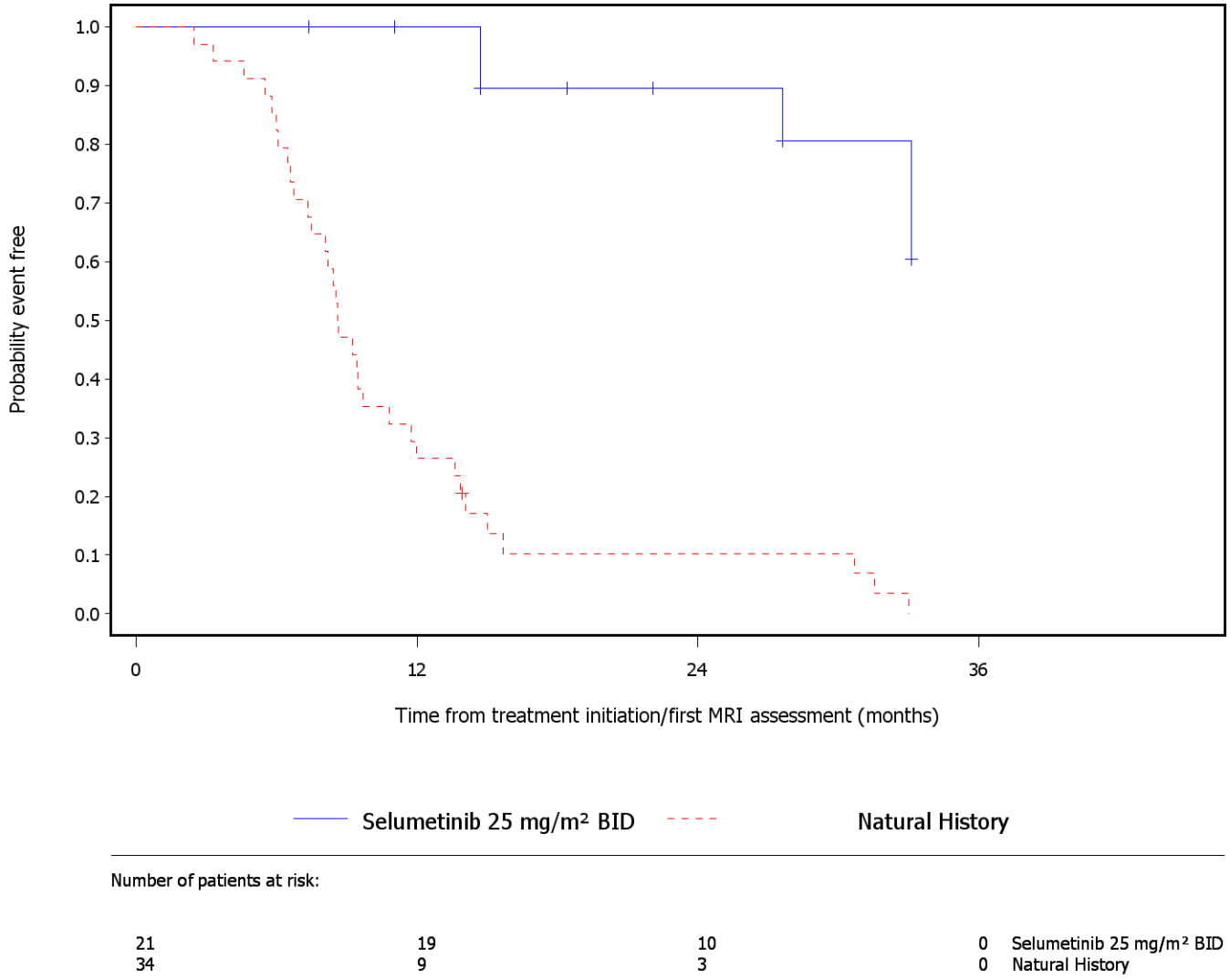


Number of patients at risk:

20	16	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Selumetinib 25 mg/m² BID
36	24	11	8	8	7	5	4	2	2	2	1	1	1	1	1	1	0 Natural History

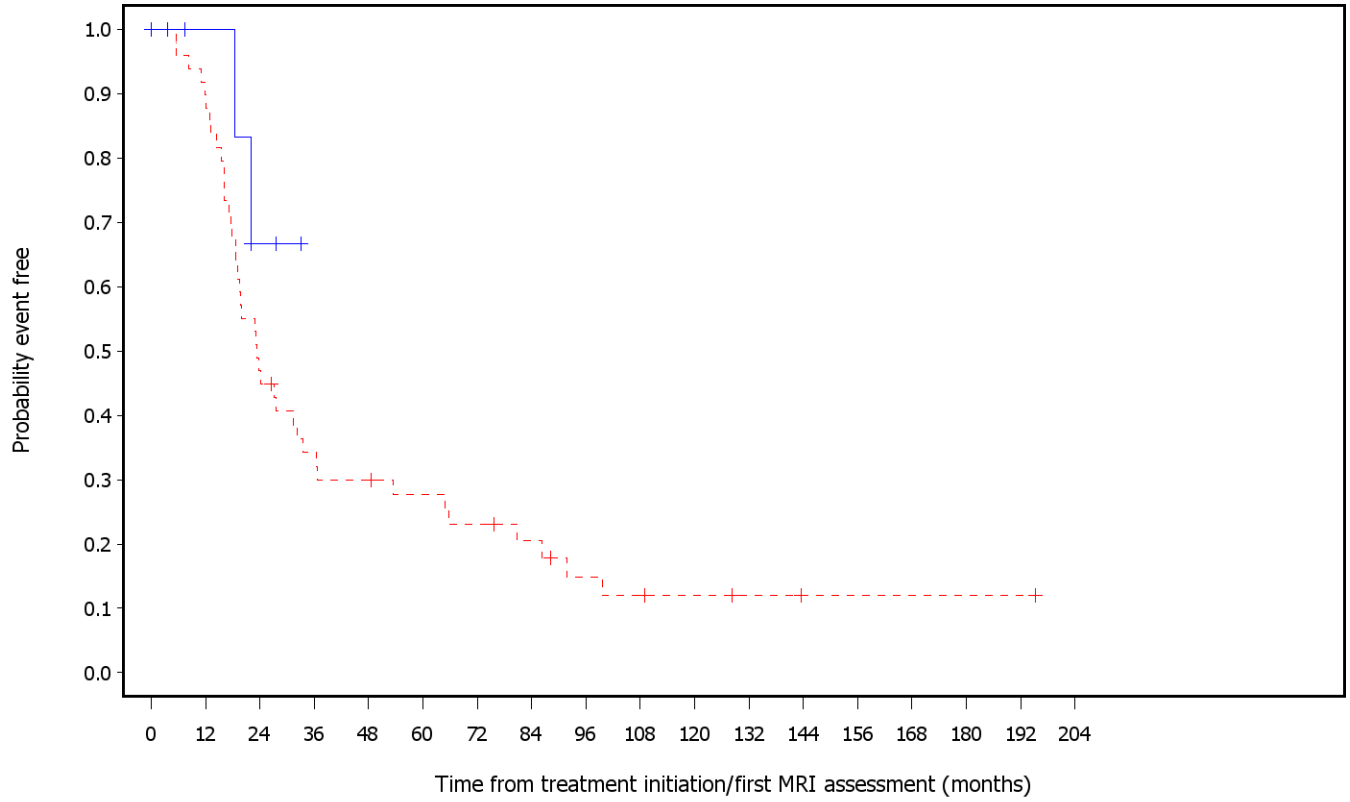
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Figure 1.1.6.3 Kaplan-Meier plot for PFS - ICR, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Progressive, Phase II Stratum 1, Data cut-off: 29th June 2018



Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Figure 1.1.6.4 Kaplan-Meier plot for PFS - ICR, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Not progressive, Phase II Stratum 1, Data cut-off: 29th June 2018

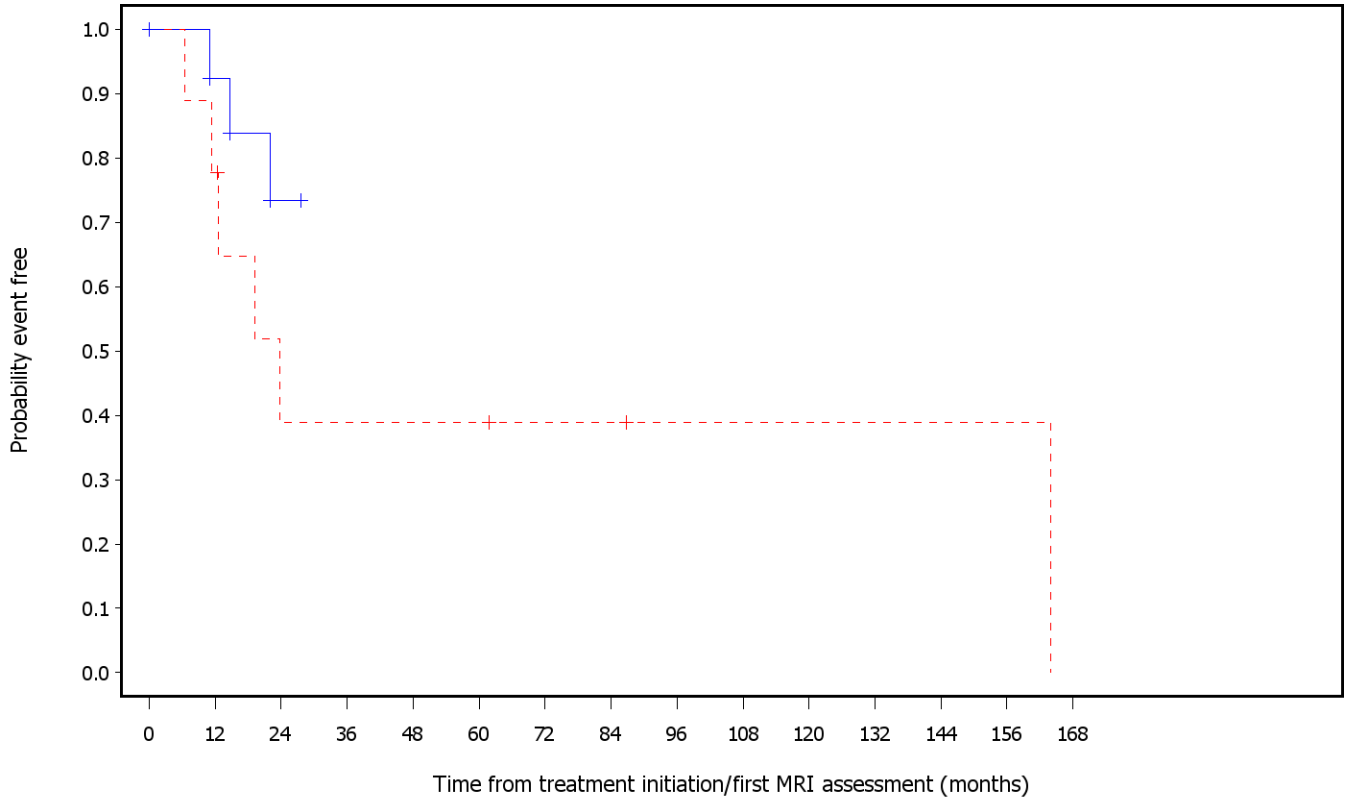


Number of patients at risk:

15	12	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Selumetinib 25 mg/m² BID
49	43	23	16	14	12	10	8	5	4	3	2	1	1	1	1	0	Natural History

Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Figure 1.1.6.5 Kaplan-Meier plot for PFS - ICR, Natural History Study (age-matched) vs. SPRINT Phase II Stratum I
PN status at enrollment = Unknown, Phase II Stratum 1, Data cut-off: 29th June 2018



Number of patients at risk:

14	11	2	0	0	0	0	0	0	0	0	0	0	0	0	Selumetinib 25 mg/m² BID
9	7	3	3	3	3	2	2	1	1	1	1	1	1	0	Natural History

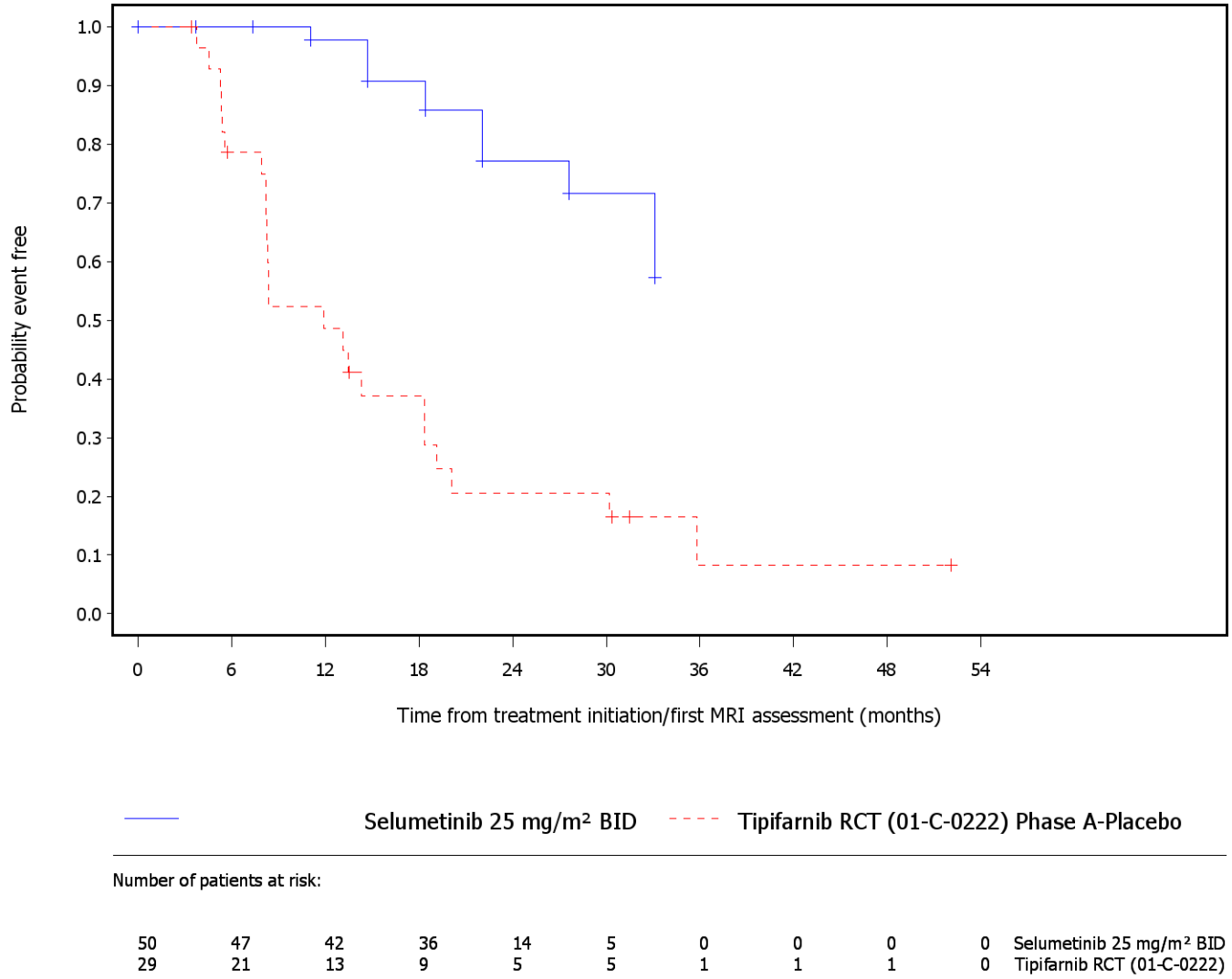
Natural History arm includes patients aged 3 to 18 years with at least one MRI within this age.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Table 1.1.7 Progression-free survival (PFS - ICR), Tipifarnib RCT (01-C-0222) Phase A-Placebo vs. SPRINT Phase II Stratum I Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=50)			Tipifarnib RCT (01-C-0222) Phase A-Placebo (N=29)					
	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	n	Number (%) of patients with events	Median time (95% CI) (years) [a]	Hazard ratio [b]	95% CI [b]	2-sided p-value [b]
Progression-free survival (PFS)	50	11 (22.0)	NE (NE, NE)	29	23 (79.3)	1.0 (0.7, 1.5)	0.10	0.05, 0.23	<0.0001

NC = Not calculated.
Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.
Hazard ratio <1 favours Selumetinib.
[a] Event includes deaths by any cause in the absence of progression.
[b] Calculated using the Kaplan-Meier technique.

Figure 1.1.8 Kaplan-Meier plot for PFS - ICR, Tipifarnib RCT (01-C-0222) Phase A-Placebo vs. SPRINT Phase II Stratum I Phase II Stratum 1, Data cut-off: 29th June 2018



Selumetinib 25 mg/m² BIDIncludes patients with a baseline MRI.

Table 1.2.1 Progression-free survival (PFS) - ICR assessment (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=50)
Total number of events (progression or death), n (%) [a]	11 (22.0)
Number of progressions, n (%)	11 (22.0)
Number of deaths, n (%)	0
Censored patients, n (%)	39 (78.0)
Median progression-free survival (cycles) [b]	NC
95% CI for median progression-free survival [b]	NC - NC
Progression-free at cycle 4 (%) [b]	100.0
95% CI for progression-free at cycle 4 (%) [b]	NE - NE
Progression-free at cycle 8 (%) [b]	100.0
95% CI for progression-free at cycle 8 (%) [b]	NE - NE
Progression-free at cycle 12 (%) [b]	97.8
95% CI for progression-free at cycle 12 (%) [b]	85.3 - 99.7
Progression-free at cycle 16 (%) [b]	90.8
95% CI for progression-free at cycle 16 (%) [b]	77.3 - 96.4
Progression-free at cycle 24 (%) [b]	77.2
95% CI for progression-free at cycle 24 (%) [b]	60.5 - 87.5
Progression-free at cycle 30 (%) [b]	71.7
95% CI for progression-free at cycle 30 (%) [b]	52.0 - 84.4
Progression-free at cycle 36 (%) [b]	57.3
95% CI for progression-free at cycle 36 (%) [b]	26.0 - 79.5
Median follow-up for Progression-free survival (cycles) [c]	20.0 (12.0 - 36.0)
Median follow-up for Progression-free survival (cycles) (censored patients only) [d]	24.0 (0.0 - 36.0)
Median follow-up (cycles) [e]	24.0 (0.0 - 36.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Progression includes deaths in the absence of progression. [b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression).
[d] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[e] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occured earlier). A cycle is defined as 28 days.
REiNS (ICR) assessment.
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Table 1.2.1.1 Progression-free survival (PFS) - Gender = Male (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=30)
Total number of events (progression or death), n (%) [a]	2 (6.7)
Number of progressions, n (%)	2 (6.7)
Number of deaths, n (%)	0
Censored patients, n (%)	28 (93.3)
Median progression-free survival (cycles) [b]	NC
95% CI for median progression-free survival [b]	NC - NC
Progression-free at cycle 4 (%) [b]	100.0
95% CI for progression-free at cycle 4 (%) [b]	NE - NE
Progression-free at cycle 8 (%) [b]	100.0
95% CI for progression-free at cycle 8 (%) [b]	NE - NE
Progression-free at cycle 12 (%) [b]	100.0
95% CI for progression-free at cycle 12 (%) [b]	NE - NE
Progression-free at cycle 16 (%) [b]	100.0
95% CI for progression-free at cycle 16 (%) [b]	NE - NE
Progression-free at cycle 24 (%) [b]	91.3
95% CI for progression-free at cycle 24 (%) [b]	69.5 - 97.8
Progression-free at cycle 30 (%) [b]	91.3
95% CI for progression-free at cycle 30 (%) [b]	69.5 - 97.8
Progression-free at cycle 36 (%) [b]	91.3
95% CI for progression-free at cycle 36 (%) [b]	69.5 - 97.8
Median follow-up for Progression-free survival (cycles) [c]	20.0 (20.0 - 20.0)
Median follow-up for Progression-free survival (cycles) (censored patients only) [d]	24.0 (0.0 - 36.0)
Median follow-up (cycles) [e]	24.0 (0.0 - 36.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Progression includes deaths in the absence of progression. [b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression).
[d] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[e] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occured earlier). A cycle is defined as 28 days.
REiNS assessment.
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Table 1.2.1.2 Progression-free survival (PFS) - Gender = Female (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=20)
Total number of events (progression or death), n (%) [a]	1 (5.0)
Number of progressions, n (%)	1 (5.0)
Number of deaths, n (%)	0
Censored patients, n (%)	19 (95.0)
Median progression-free survival (cycles) [b]	NC
95% CI for median progression-free survival [b]	NC - NC
Progression-free at cycle 4 (%) [b]	100.0
95% CI for progression-free at cycle 4 (%) [b]	NE - NE
Progression-free at cycle 8 (%) [b]	100.0
95% CI for progression-free at cycle 8 (%) [b]	NE - NE
Progression-free at cycle 12 (%) [b]	100.0
95% CI for progression-free at cycle 12 (%) [b]	NE - NE
Progression-free at cycle 16 (%) [b]	100.0
95% CI for progression-free at cycle 16 (%) [b]	NE - NE
Progression-free at cycle 24 (%) [b]	100.0
95% CI for progression-free at cycle 24 (%) [b]	NE - NE
Progression-free at cycle 30 (%) [b]	80.0
95% CI for progression-free at cycle 30 (%) [b]	20.4 - 96.9
Progression-free at cycle 36 (%) [b]	80.0
95% CI for progression-free at cycle 36 (%) [b]	20.4 - 96.9
Median follow-up for Progression-free survival (cycles) [c]	30.0 (30.0 - 30.0)
Median follow-up for Progression-free survival (cycles) (censored patients only) [d]	24.0 (0.0 - 36.0)
Median follow-up (cycles) [e]	24.0 (0.0 - 36.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Progression includes deaths in the absence of progression. [b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression).
[d] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[e] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occured earlier). A cycle is defined as 28 days.
REiNS assessment.
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Table 1.2.1.3 Progression-free survival (PFS) - PN status at enrollment (severity of disease) = Progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=21)
Total number of events (progression or death), n (%) [a]	3 (14.3)
Number of progressions, n (%)	3 (14.3)
Number of deaths, n (%)	0
Censored patients, n (%)	18 (85.7)
Median progression-free survival (cycles) [b]	NC
95% CI for median progression-free survival [b]	NC - NC
Progression-free at cycle 4 (%) [b]	100.0
95% CI for progression-free at cycle 4 (%) [b]	NE - NE
Progression-free at cycle 8 (%) [b]	100.0
95% CI for progression-free at cycle 8 (%) [b]	NE - NE
Progression-free at cycle 12 (%) [b]	100.0
95% CI for progression-free at cycle 12 (%) [b]	NE - NE
Progression-free at cycle 16 (%) [b]	100.0
95% CI for progression-free at cycle 16 (%) [b]	NE - NE
Progression-free at cycle 24 (%) [b]	88.9
95% CI for progression-free at cycle 24 (%) [b]	62.4 - 97.1
Progression-free at cycle 30 (%) [b]	80.8
95% CI for progression-free at cycle 30 (%) [b]	50.5 - 93.6
Progression-free at cycle 36 (%) [b]	80.8
95% CI for progression-free at cycle 36 (%) [b]	50.5 - 93.6
Median follow-up for Progression-free survival (cycles) [c]	20.0 (20.0 - 30.0)
Median follow-up for Progression-free survival (cycles) (censored patients only) [d]	30.0 (8.0 - 36.0)
Median follow-up (cycles) [e]	30.0 (8.0 - 36.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Progression includes deaths in the absence of progression. [b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression).
[d] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[e] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occured earlier). A cycle is defined as 28 days.
REiNS assessment.
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Table 1.2.1.4 Progression-free survival (PFS) - PN status at enrollment (severity of disease) = Non-progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=15)
Total number of events (progression or death), n (%) [a]	0
Number of progressions, n (%)	0
Number of deaths, n (%)	0
Censored patients, n (%)	15 (100.0)
Median progression-free survival (cycles) [b]	NC
95% CI for median progression-free survival [b]	NC - NC
Progression-free at cycle 4 (%) [b]	100.0
95% CI for progression-free at cycle 4 (%) [b]	NE - NE
Progression-free at cycle 8 (%) [b]	100.0
95% CI for progression-free at cycle 8 (%) [b]	NE - NE
Progression-free at cycle 12 (%) [b]	100.0
95% CI for progression-free at cycle 12 (%) [b]	NE - NE
Progression-free at cycle 16 (%) [b]	100.0
95% CI for progression-free at cycle 16 (%) [b]	NE - NE
Progression-free at cycle 24 (%) [b]	100.0
95% CI for progression-free at cycle 24 (%) [b]	NE - NE
Progression-free at cycle 30 (%) [b]	100.0
95% CI for progression-free at cycle 30 (%) [b]	NE - NE
Progression-free at cycle 36 (%) [b]	100.0
95% CI for progression-free at cycle 36 (%) [b]	NE - NE
Median follow-up for Progression-free survival (cycles) [c]	
Median follow-up for Progression-free survival (cycles) (censored patients only) [d]	24.0 (0.0 - 36.0)
Median follow-up (cycles) [e]	24.0 (0.0 - 36.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Progression includes deaths in the absence of progression. [b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression).
[d] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[e] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occured earlier). A cycle is defined as 28 days.
REiNS assessment.
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Table 1.2.1.5 Progression-free survival (PFS) - PN status at enrollment (severity of disease) = Unknown (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=14)
Total number of events (progression or death), n (%) [a]	0
Number of progressions, n (%)	0
Number of deaths, n (%)	0
Censored patients, n (%)	14 (100.0)
Median progression-free survival (cycles) [b]	NC
95% CI for median progression-free survival [b]	NC - NC
Progression-free at cycle 4 (%) [b]	100.0
95% CI for progression-free at cycle 4 (%) [b]	NE - NE
Progression-free at cycle 8 (%) [b]	100.0
95% CI for progression-free at cycle 8 (%) [b]	NE - NE
Progression-free at cycle 12 (%) [b]	100.0
95% CI for progression-free at cycle 12 (%) [b]	NE - NE
Progression-free at cycle 16 (%) [b]	100.0
95% CI for progression-free at cycle 16 (%) [b]	NE - NE
Progression-free at cycle 24 (%) [b]	100.0
95% CI for progression-free at cycle 24 (%) [b]	NE - NE
Progression-free at cycle 30 (%) [b]	100.0
95% CI for progression-free at cycle 30 (%) [b]	NE - NE
Progression-free at cycle 36 (%) [b]	100.0
95% CI for progression-free at cycle 36 (%) [b]	NE - NE
Median follow-up for Progression-free survival (cycles) [c]	
Median follow-up for Progression-free survival (cycles) (censored patients only) [d]	24.0 (0.0 - 30.0)
Median follow-up (cycles) [e]	24.0 (0.0 - 30.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Progression includes deaths in the absence of progression. [b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression).
[d] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[e] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occured earlier). A cycle is defined as 28 days.
REiNS assessment.
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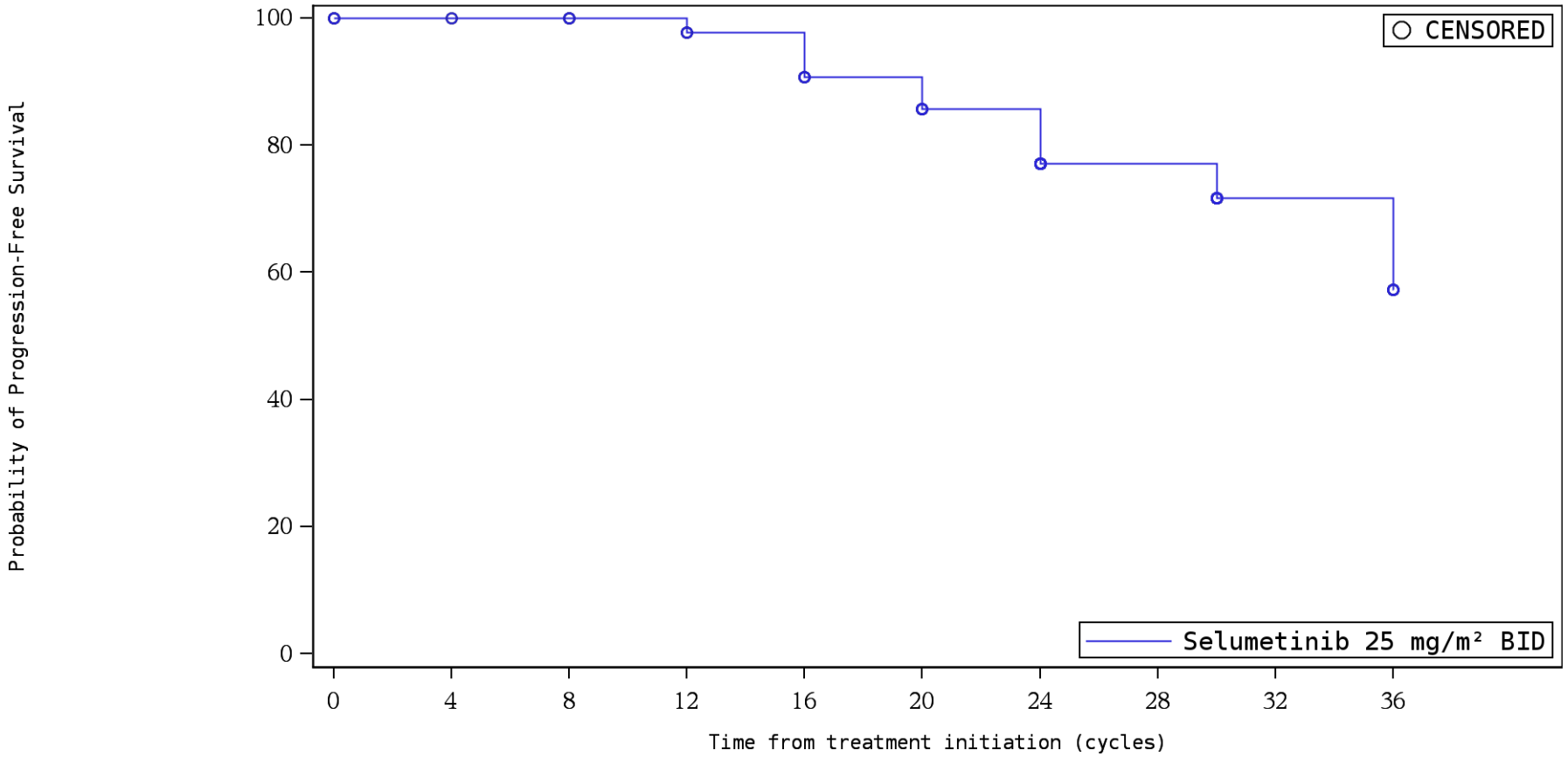
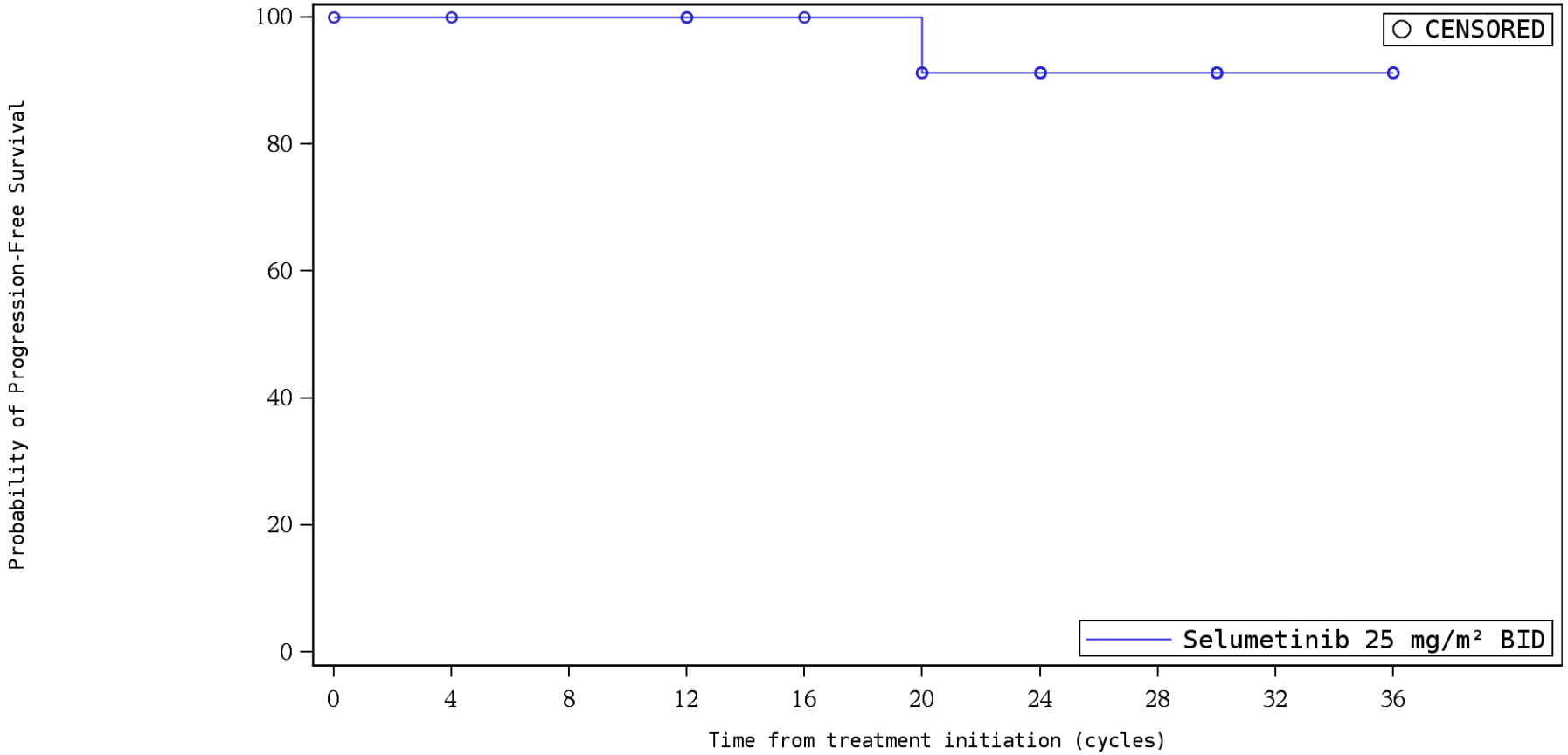
Figure 1.2.2 Kaplan-meier plot of progression-free survival (PFS) - ICR assessment (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	50	48	47	45	42	36	30	14	5	5

Progression-free survival (PFS) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression). Patients not known to have progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS (ICR) assessment.

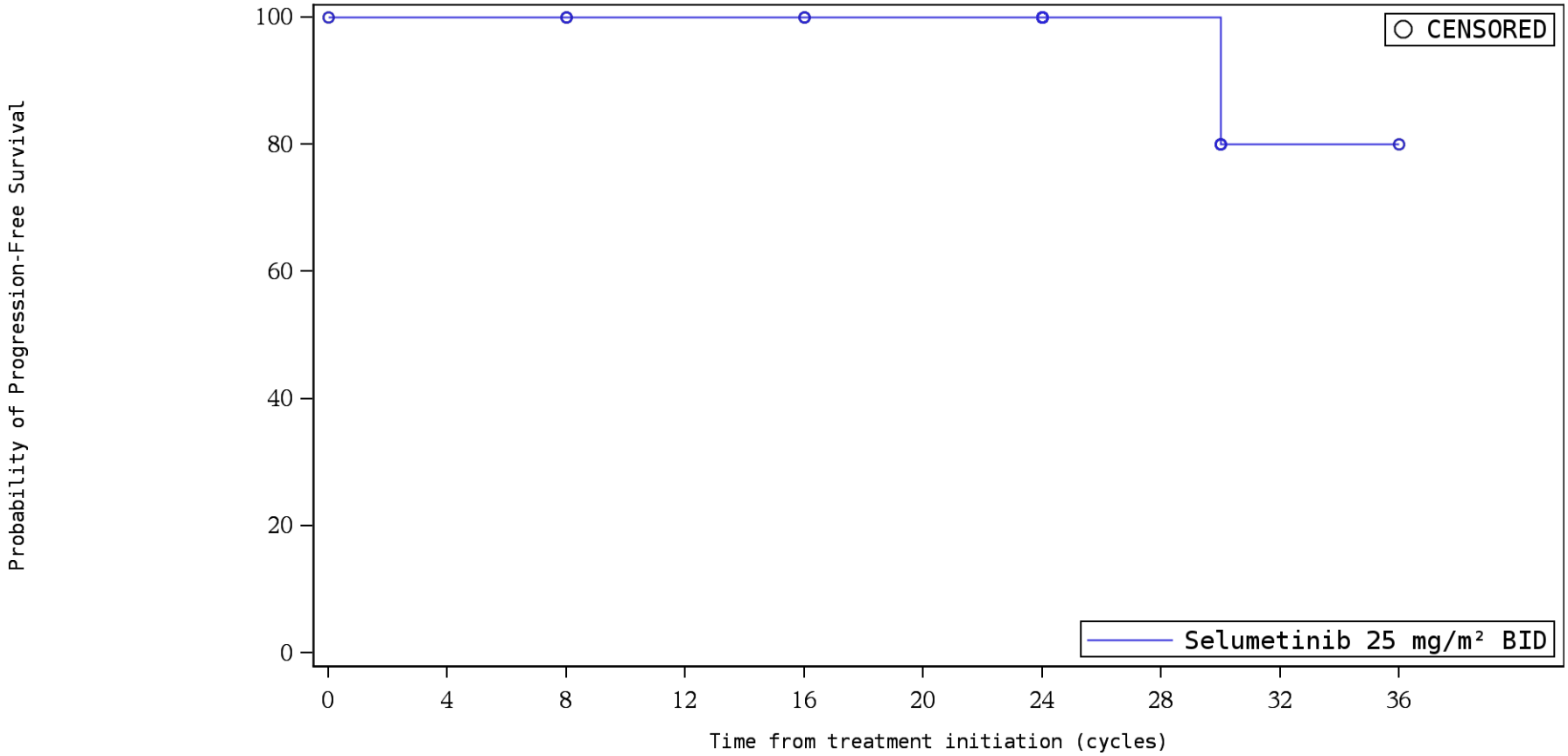
Figure 1.2.2.1 Kaplan-meier plot of progression-free survival (PFS)
Gender = Male (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



Number of patients:										
Selumetinib 25 mg/m² BID	30	29	28	28	24	23	18	11	4	4

Progression-free survival (PFS) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression). Patients not known to have progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

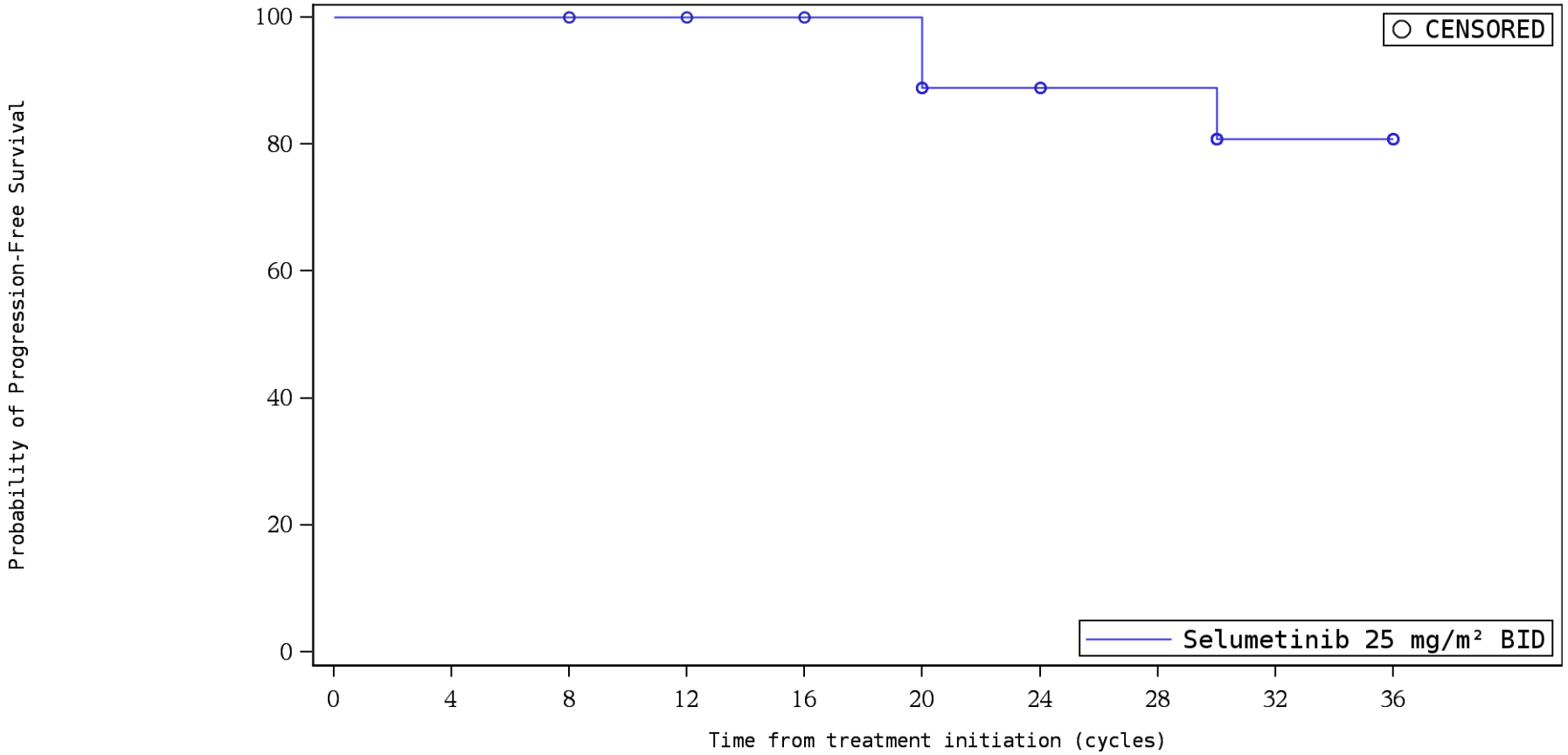
Figure 1.2.2.2 Kaplan-meier plot of progression-free survival (PFS)
Gender = Female (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	20	19	19	17	17	15	15	5	1	1

Progression-free survival (PFS) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression). Patients not known to have progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

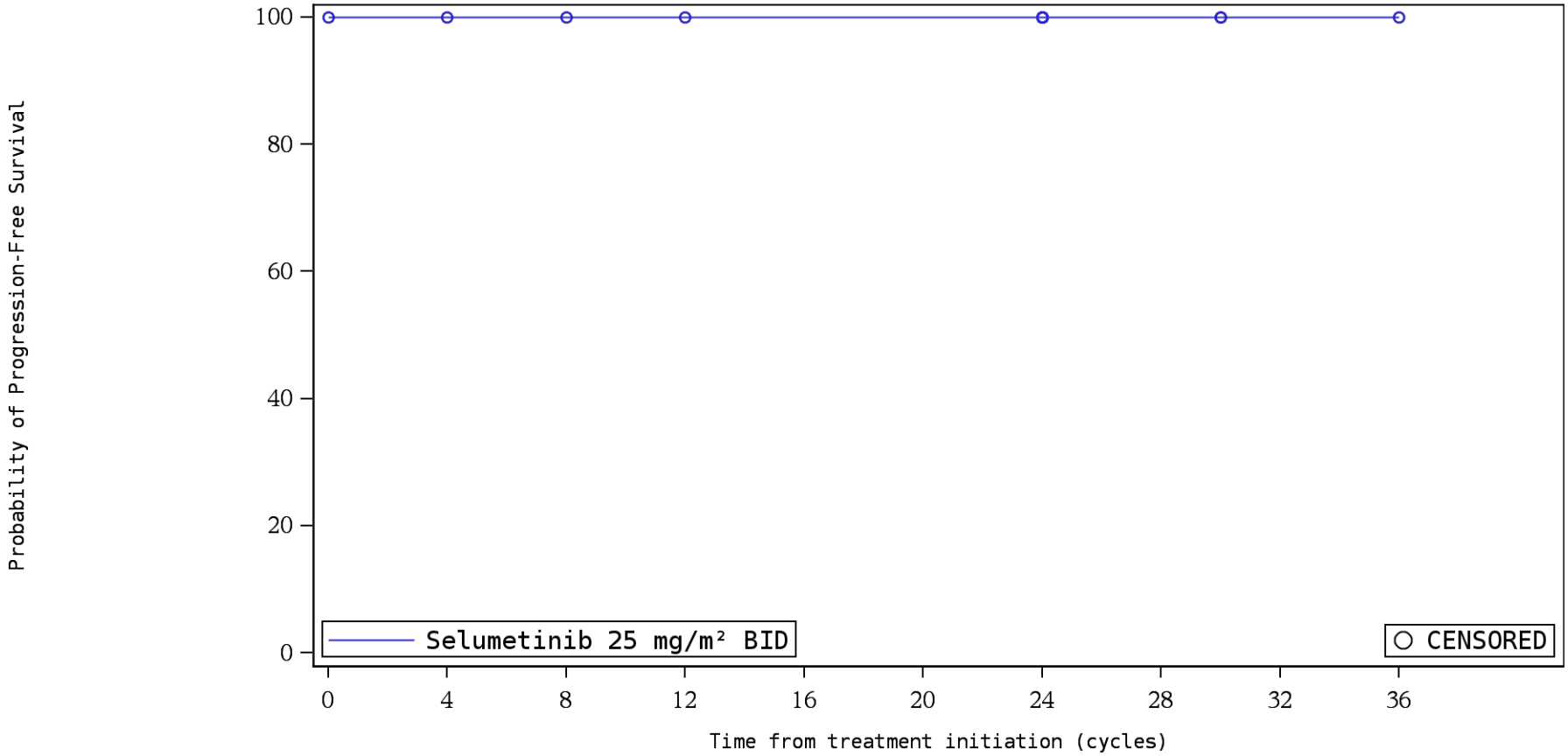
Figure 1.2.2.3 Kaplan-meier plot of progression-free survival (PFS)
PN status at enrollment (severity of disease) = Progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	21	21	21	20	19	18	13	11	4	4

Progression-free survival (PFS) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression). Patients not known to have progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

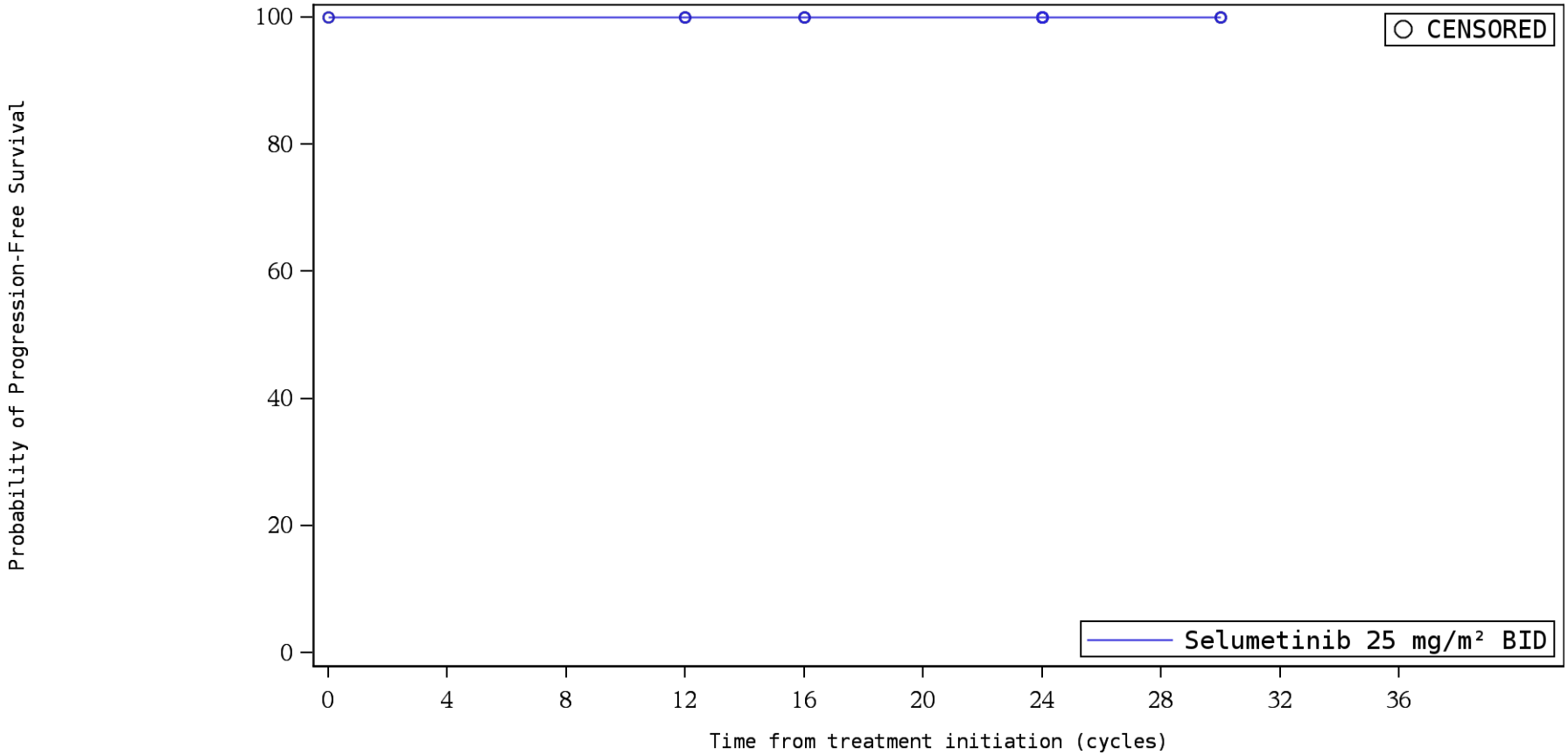
Figure 1.2.2.4 Kaplan-meier plot of progression-free survival (PFS)
PN status at enrollment (severity of disease) = Non-progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	15	14	13	12	11	11	11	3	1	1

Progression-free survival (PFS) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression). Patients not known to have progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

Figure 1.2.2.5 Kaplan-meier plot of progression-free survival (PFS)
PN status at enrollment (severity of disease) = Unknown (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	14	13	13	13	11	9	9	2	0	0

Progression-free survival (PFS) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression or death (by any cause in the absence of progression). Patients not known to have progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

Table 1.3.1 Time to progression (TTP) - ICR assessment (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=50)
Total events, n (%)	11 (22.0)
Number of progressions n (%)	11 (22.0)
Censored patients, n (%)	39 (78.0)
Median time to progression (cycles) [a]	NC
95% CI for median time to progression [a]	NC - NC
Median follow-up for Time to progression (cycles) [b]	20.0 (12.0 - 36.0)
Median follow-up for Time to progression (cycles) (censored patients only) [c]	24.0 (0.0 - 36.0)
Median follow-up (cycles) [d]	24.0 (0.0 - 36.0)

CI = Confidence interval. NC = Not calculated.
[a] Calculated using the Kaplan-Meier technique.
[b] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression.
[c] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[d] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occurred earlier).
A cycle is defined as 28 days.
REiNS (ICR) assessment.
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Table 1.3.1.1 Time to progression (TTP) - Gender = Male (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=30)
Total events, n (%)	2 (6.7)
Number of progressions n (%)	2 (6.7)
Censored patients, n (%)	28 (93.3)
Median time to progression (cycles) [a]	NC
95% CI for median time to progression [a]	NC - NC
Median follow-up for Time to progression (cycles) [b]	20.0 (20.0 - 20.0)
Median follow-up for Time to progression (cycles) (censored patients only) [c]	24.0 (0.0 - 36.0)
Median follow-up (cycles) [d]	24.0 (0.0 - 36.0)

CI = Confidence interval. NC = Not calculated.
[a] Calculated using the Kaplan-Meier technique.
[b] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression.
[c] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[d] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occurred earlier).
A cycle is defined as 28 days.
REiNS assessment.
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Table 1.3.1.2 Time to progression (TTP) - Gender = Female (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=20)
Total events, n (%)	1 (5.0)
Number of progressions n (%)	1 (5.0)
Censored patients, n (%)	19 (95.0)
Median time to progression (cycles) [a]	NC
95% CI for median time to progression [a]	NC - NC
Median follow-up for Time to progression (cycles) [b]	30.0 (30.0 - 30.0)
Median follow-up for Time to progression (cycles) (censored patients only) [c]	24.0 (0.0 - 36.0)
Median follow-up (cycles) [d]	24.0 (0.0 - 36.0)

CI = Confidence interval. NC = Not calculated.
[a] Calculated using the Kaplan-Meier technique.
[b] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression.
[c] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[d] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occurred earlier).
A cycle is defined as 28 days.
REiNS assessment.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/ttpsub.sas ttpsubb.rtf 21APR2021:10:45 icesas167PD

Table 1.3.1.3 Time to progression (TTP) - PN status at enrollment (severity of disease) = Progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=21)
Total events, n (%)	3 (14.3)
Number of progressions n (%)	3 (14.3)
Censored patients, n (%)	18 (85.7)
Median time to progression (cycles) [a]	NC
95% CI for median time to progression [a]	NC - NC
Median follow-up for Time to progression (cycles) [b]	20.0 (20.0 - 30.0)
Median follow-up for Time to progression (cycles) (censored patients only) [c]	30.0 (8.0 - 36.0)
Median follow-up (cycles) [d]	30.0 (8.0 - 36.0)

CI = Confidence interval. NC = Not calculated.
[a] Calculated using the Kaplan-Meier technique.
[b] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression.
[c] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[d] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occurred earlier).
A cycle is defined as 28 days.
REiNS assessment.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/ttpsub.sas ttpsubc.rtf 21APR2021:10:45 icesas167PD

Table 1.3.1.4 Time to progression (TTP) - PN status at enrollment (severity of disease) = Non-progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=15)
Total events, n (%)	0
Number of progressions n (%)	0
Censored patients, n (%)	15 (100.0)
Median time to progression (cycles) [a]	NC
95% CI for median time to progression [a]	NC - NC
Median follow-up for Time to progression (cycles) [b]	
Median follow-up for Time to progression (cycles) (censored patients only) [c]	24.0 (0.0 - 36.0)
Median follow-up (cycles) [d]	24.0 (0.0 - 36.0)

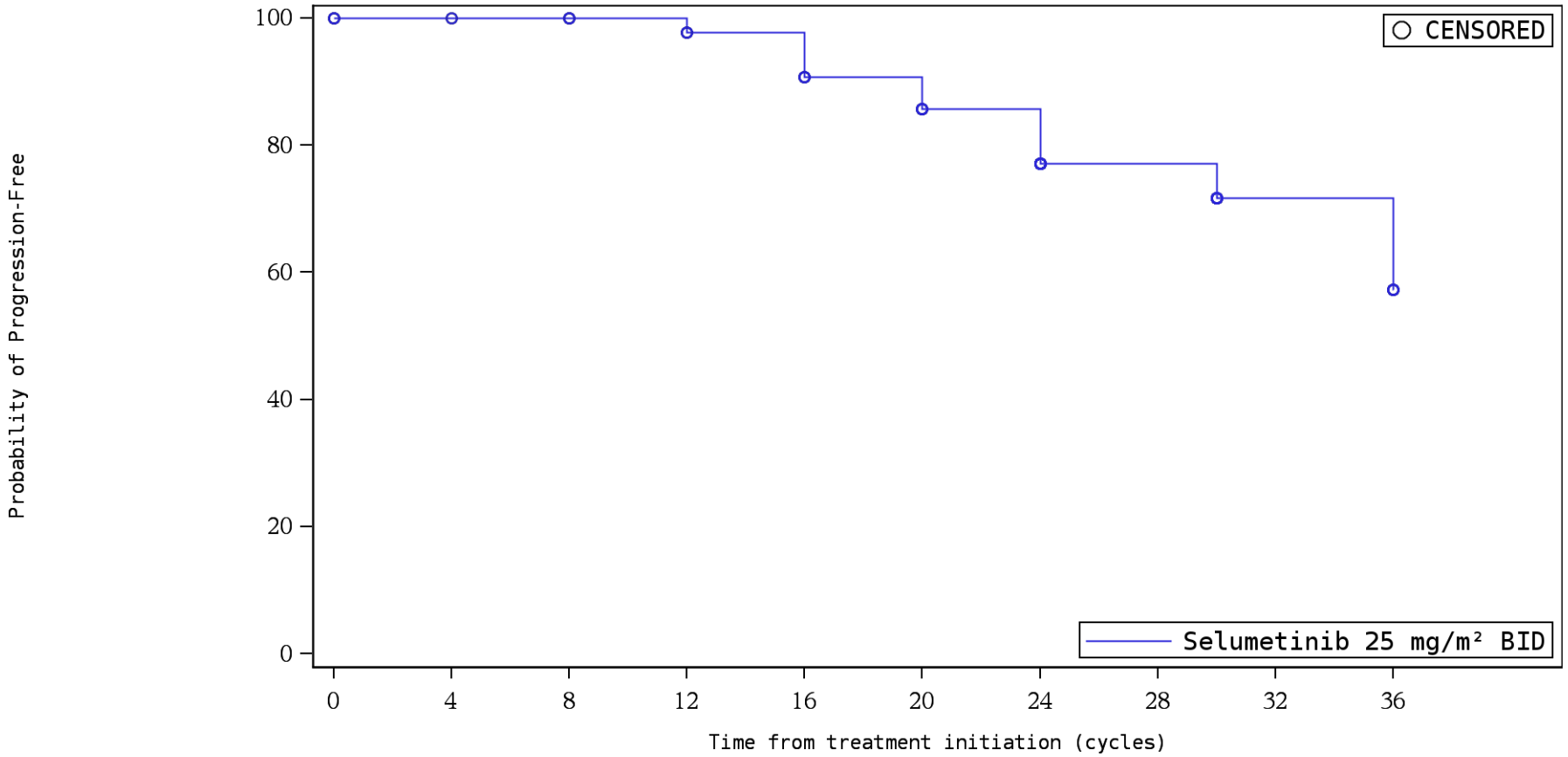
CI = Confidence interval. NC = Not calculated.
[a] Calculated using the Kaplan-Meier technique.
[b] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression.
[c] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[d] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occurred earlier).
A cycle is defined as 28 days.
REiNS assessment.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/ttpsub.sas ttpsubd.rtf 21APR2021:10:45 icesas167PD

Table 1.3.1.5 Time to progression (TTP) - PN status at enrollment (severity of disease) = Unknown (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=14)
Total events, n (%)	0
Number of progressions n (%)	0
Censored patients, n (%)	14 (100.0)
Median time to progression (cycles) [a]	NC
95% CI for median time to progression [a]	NC - NC
Median follow-up for Time to progression (cycles) [b]	
Median follow-up for Time to progression (cycles) (censored patients only) [c]	24.0 (0.0 - 30.0)
Median follow-up (cycles) [d]	24.0 (0.0 - 30.0)

CI = Confidence interval. NC = Not calculated.
[a] Calculated using the Kaplan-Meier technique.
[b] Calculated as the median time from study treatment initiation until the pre-cycle of objective disease progression.
[c] Calculated as the median time from study treatment initiation to pre-cycle of censoring (last evaluable pre-cycle volumetric MRI assessment known to be non-progression) in censored (not progressed) patients only.
[d] Calculated as the median time from study treatment initiation to data cut-off or study discontinuation (whichever occurred earlier).
A cycle is defined as 28 days.
REiNS assessment.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/ttpsub.sas ttpsube.rtf 21APR2021:10:45 icesas167PD

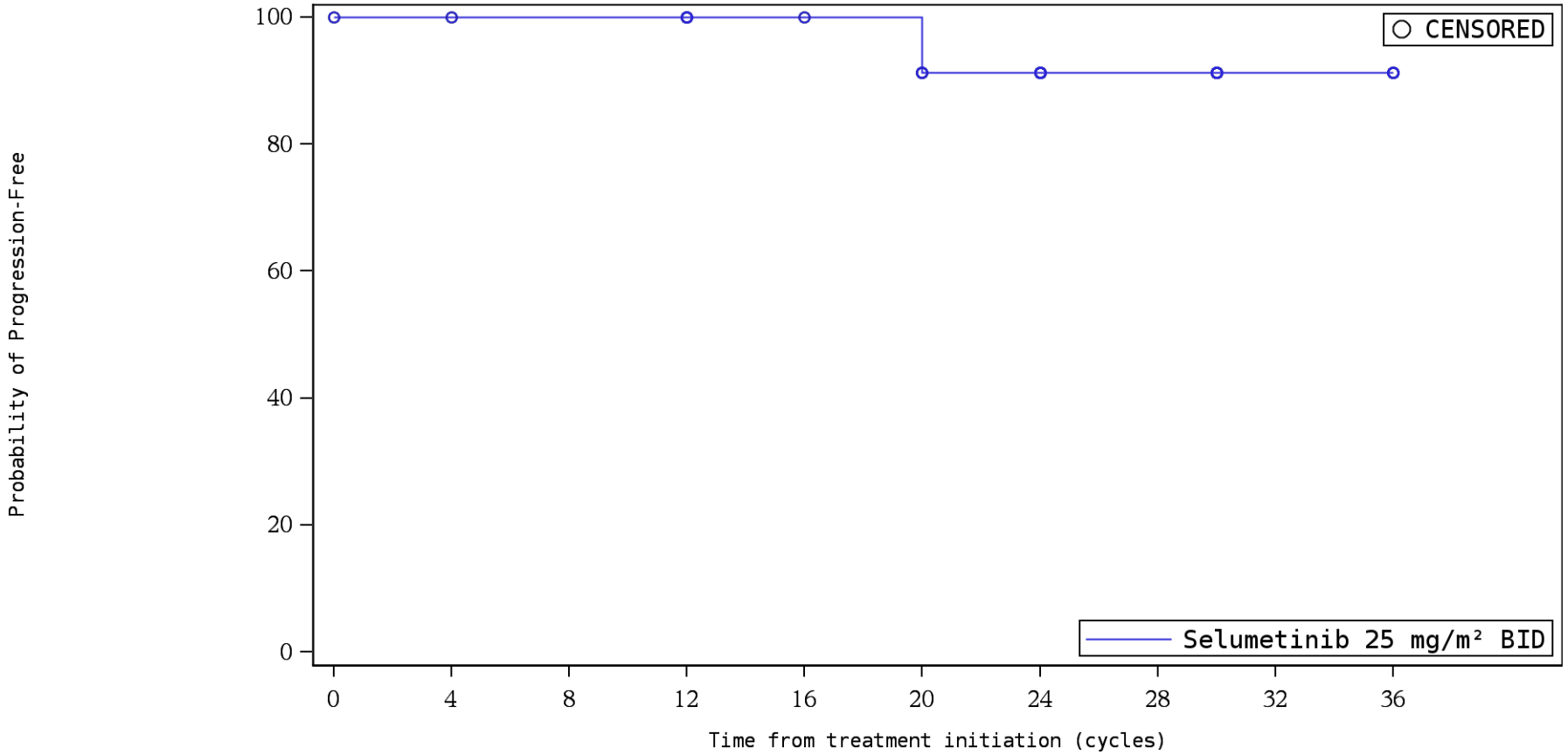
Figure 1.3.2 Kaplan-meier plot of time to progression (TTP) - ICR assessment (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



Number of patients:										
Selumetinib 25 mg/m² BID	50	48	47	45	42	36	30	14	5	5

Time to progression (TTP) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression. Patients who have not progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS (ICR) assessment.

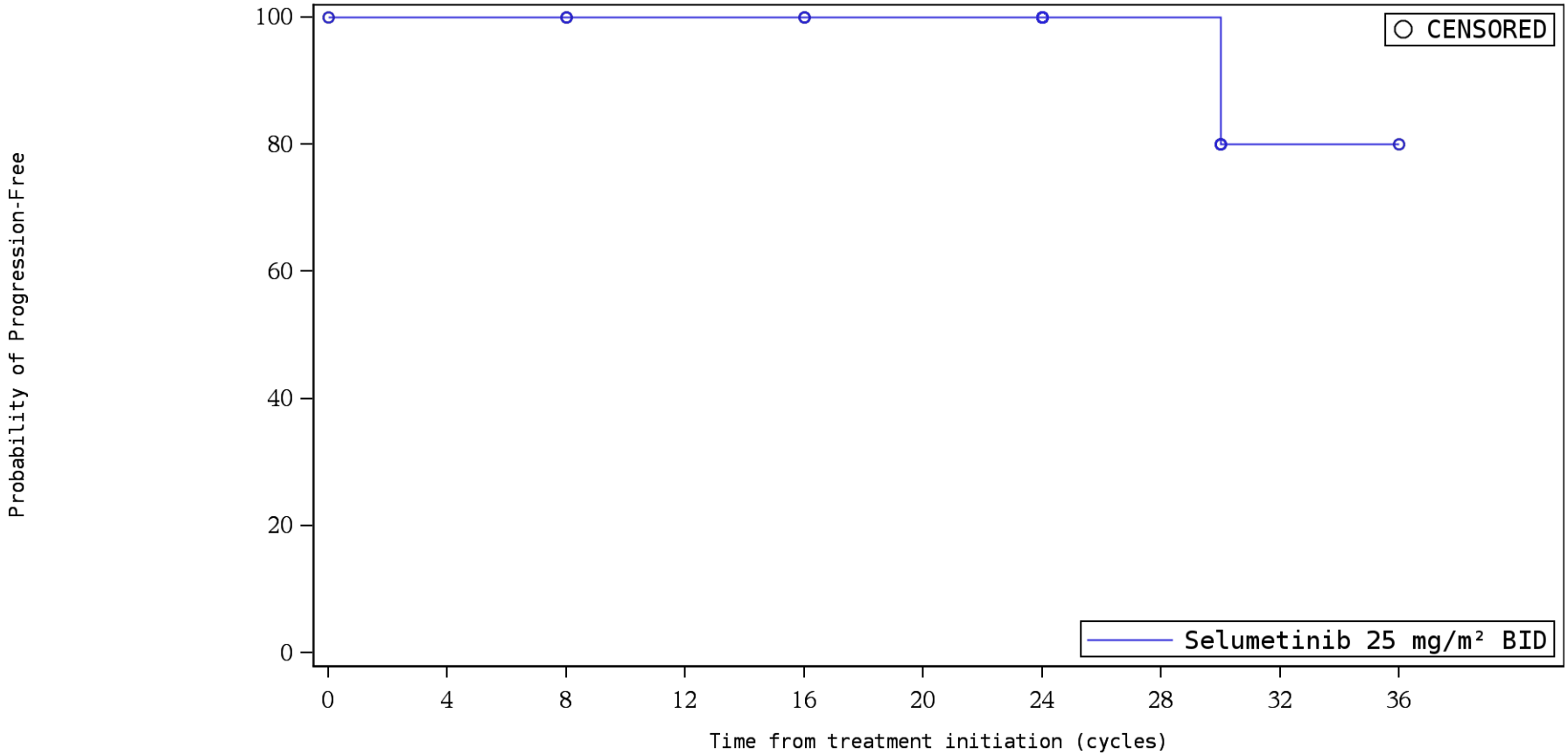
Figure 1.3.2.1 Kaplan-meier plot of time to progression (TTP)
Gender = Male (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	30	29	28	28	24	23	18	11	4	4

Time to progression (TTP) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression. Patients who have not progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

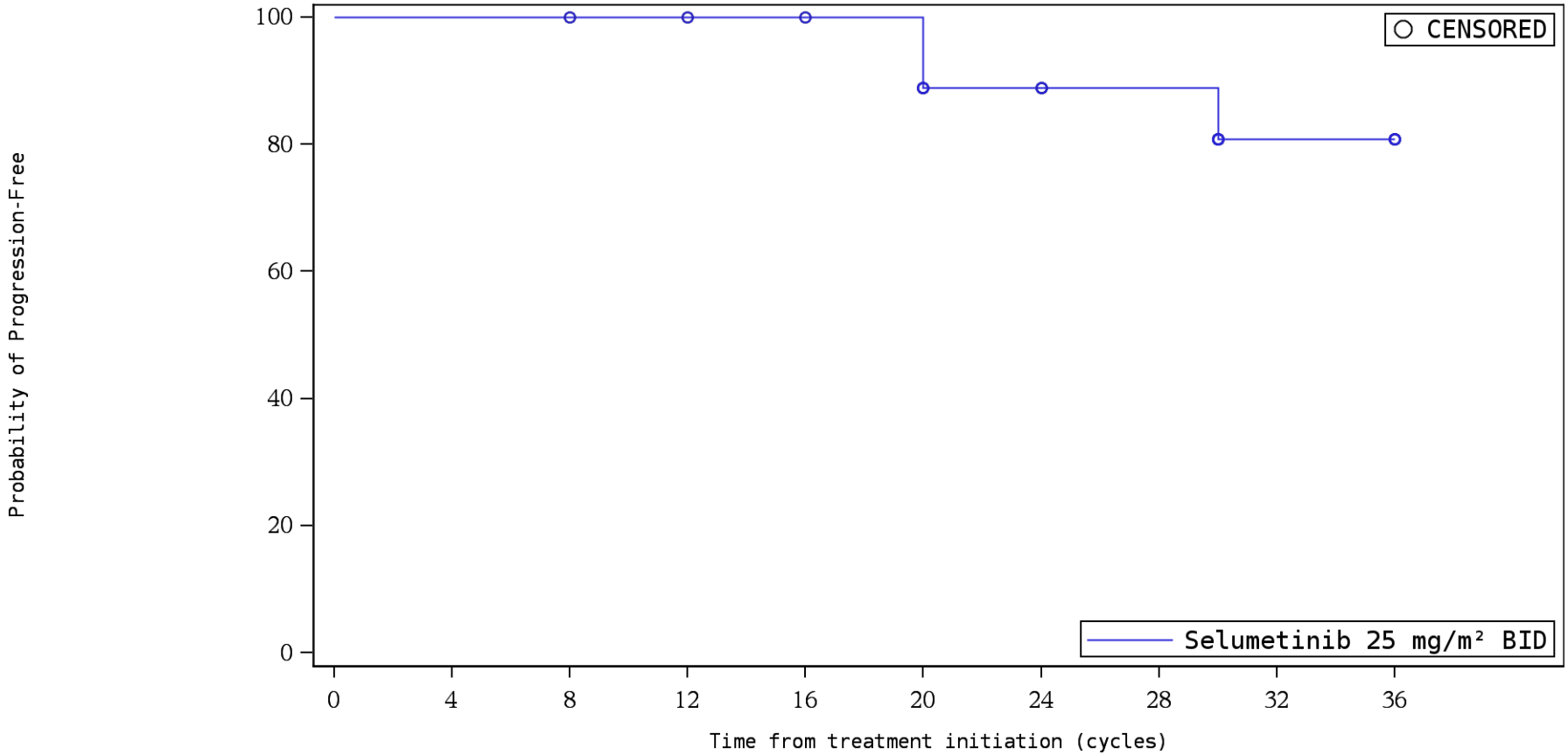
Figure 1.3.2.2 Kaplan-meier plot of time to progression (TTP)
Gender = Female (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	20	19	19	17	17	15	15	5	1	1

Time to progression (TTP) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression. Patients who have not progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

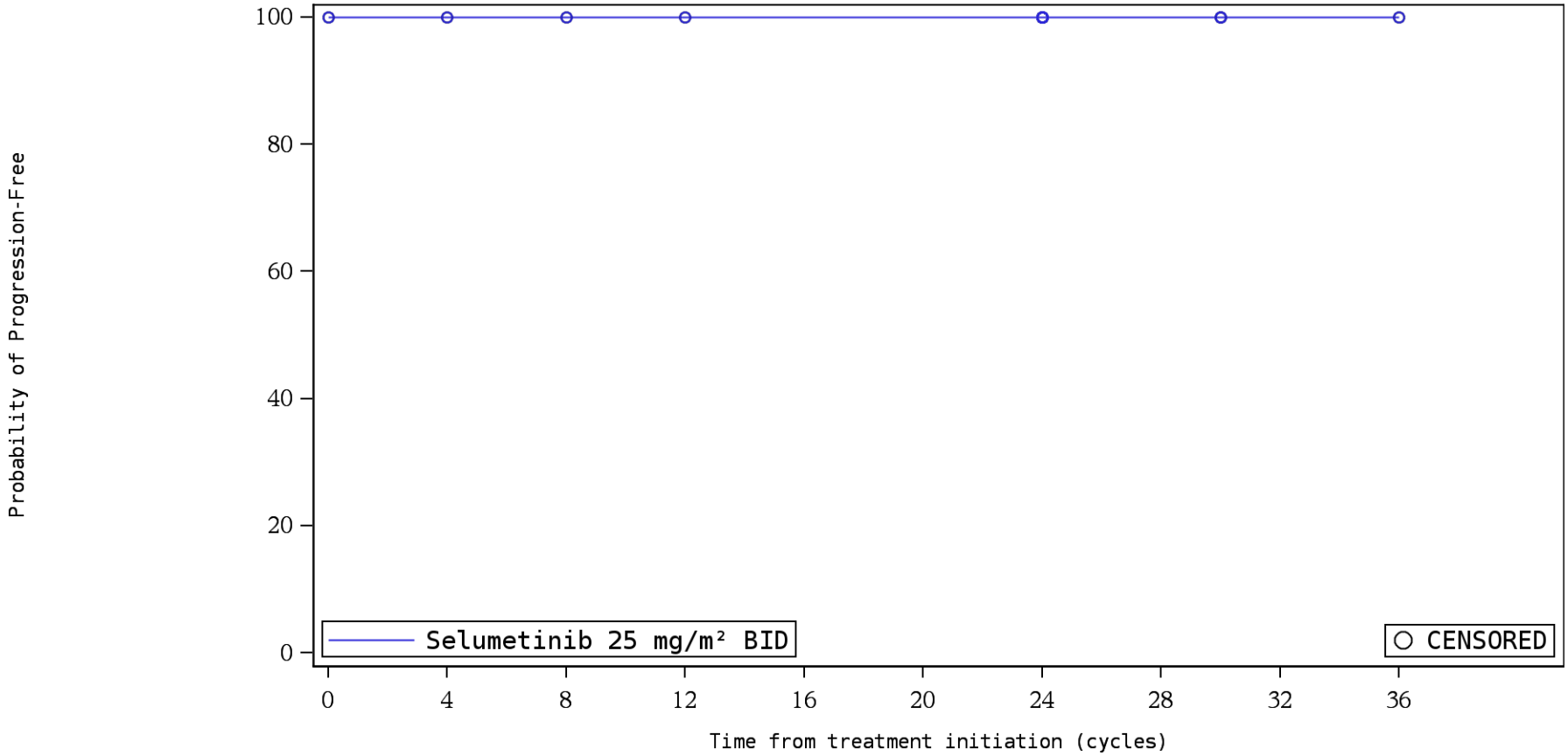
Figure 1.3.2.3 Kaplan-meier plot of time to progression (TTP)
PN status at enrollment (severity of disease) = Progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



Number of patients:									
Selumetinib 25 mg/m² BID	21	21	21	20	19	18	13	11	4	4

Time to progression (TTP) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression. Patients who have not progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

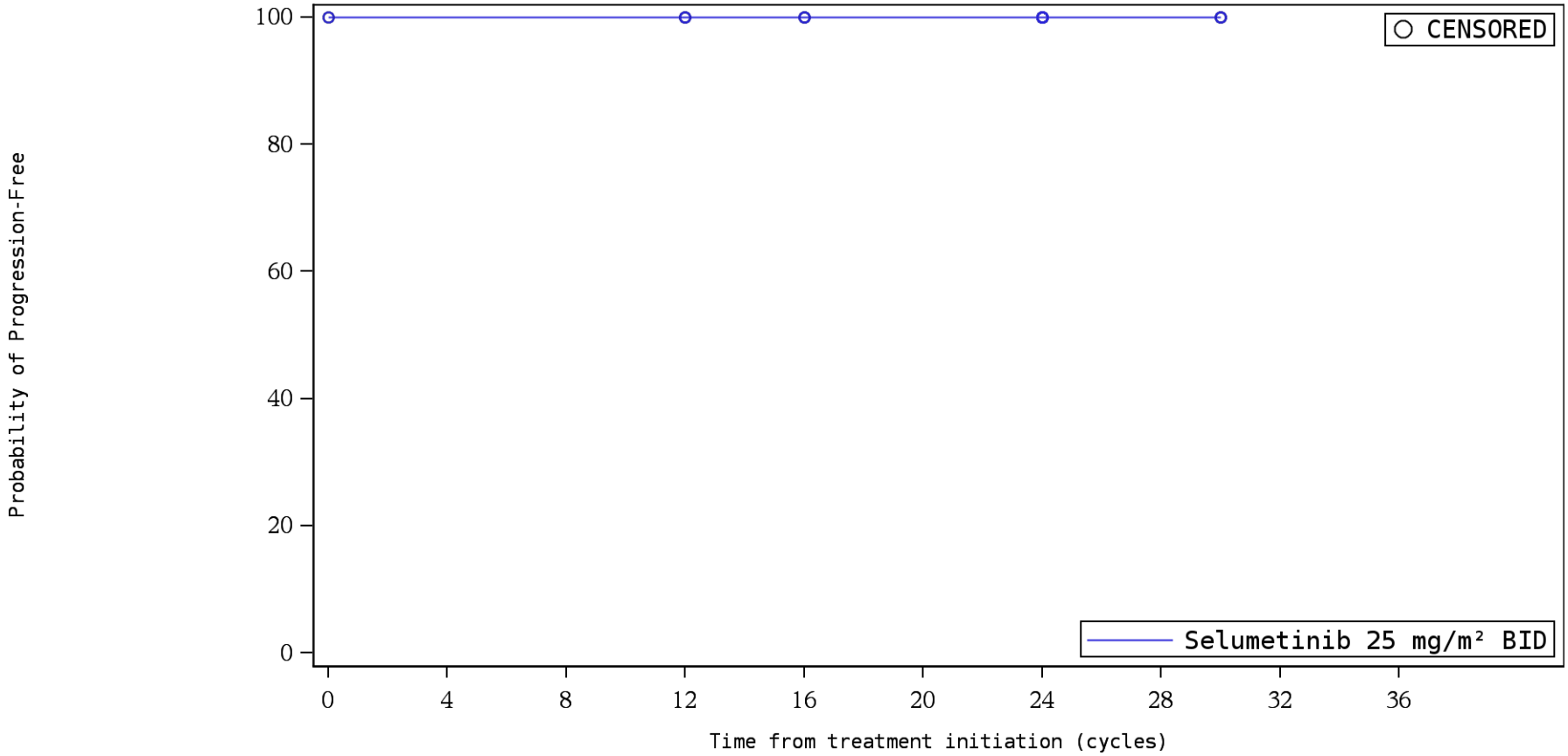
Figure 1.3.2.4 Kaplan-meier plot of time to progression (TTP)
PN status at enrollment (severity of disease) = Non-progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	15	14	13	12	11	11	11	3	1	1

Time to progression (TTP) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression. Patients who have not progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

Figure 1.3.2.5 Kaplan-meier plot of time to progression (TTP)
PN status at enrollment (severity of disease) = Unknown (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	14	13	13	13	11	9	9	2	0	0

Time to progression (TTP) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression. Patients who have not progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

Table 1.4.1 Confirmed Objective Response Rate - NCI assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup	N	Number (%) of patients with response [a]	95% CI [b]
Gender: Female	20	15 (75.0)	50.9, 91.3
Gender: Male	30	18 (60.0)	40.6, 77.3
PN status at enrollment: Not progressive	15	10 (66.7)	38.4, 88.2
PN status at enrollment: Progressive	21	13 (61.9)	38.4, 81.9
PN status at enrollment: Unknown	14	10 (71.4)	41.9, 91.6

CI = Confidence interval.
Objective response rate is defined as the number (%) of patients with PN-related morbidity who received at least one dose of selumetinib and have at least one complete response (CR) or confirmed partial response (PR) occuring prior to study treatment discontinuation.
[a] The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] The CIs are calculated using Clopper-Pearson exact method for binomial proportions.
REiNS assessment.

Table 1.4.2 Confirmed Objective Response Rate - ICR assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup	N	Number (%) of patients with response [a]	95% CI [b]
Gender: Female	20	9 (45.0)	23.1, 68.5
Gender: Male	30	13 (43.3)	25.5, 62.6
PN status at enrollment: Not progressive	15	6 (40.0)	16.3, 67.7
PN status at enrollment: Progressive	21	12 (57.1)	34.0, 78.2
PN status at enrollment: Unknown	14	4 (28.6)	8.4, 58.1

CI = Confidence interval. ICR = Independent Central Review.
Objective response rate is defined as the number (%) of patients with PN-related morbidity who received at least one dose of selumetinib and have at least one complete response (CR) or confirmed partial response (PR) occuring prior to study treatment discontinuation.
[a] The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] The CIs are calculated using Clopper-Pearson exact method for binomial proportions.
Modified REiNS assessment performed by Independent Central Review.

Table 1.5.1.1 Time to response (TTR) - NCI assessment - Gender = Male
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=30)
Total events [a], n (%)	18 (60.0)
Median time to response (cycles) [b]	6.0
95% CI for Median time to response [b]	4.0 - 8.0
Not in response at cycle 5 (%) [b]	50.0
95% CI for not in response at cycle 5 [b]	25.9 - 70.1
Not in response at cycle 9 (%) [b]	11.1
95% CI for not in response at cycle 9 [b]	1.9 - 29.8
Not in response at cycle 13 (%) [b]	0.0
95% CI for not in response at cycle 13 [b]	NE - NE
Not in response at cycle 17 (%) [b]	0.0
95% CI for not in response at cycle 17 [b]	NE - NE
Not in response at cycle 21 (%) [b]	0.0
95% CI for not in response at cycle 21 [b]	NE - NE
Median follow-up for Time to response (cycles) [c]	6.0 (4.0 - 12.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Patients with a confirmed Partial Response or Complete Response.
[b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of first documentation of complete response or a subsequently confirmed partial response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.5.1.2 Time to response (TTR) - NCI assessment - Gender = Female
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=20)
Total events [a], n (%)	15 (75.0)
Median time to response (cycles) [b]	8.0
95% CI for Median time to response [b]	4.0 - 12.0
Not in response at cycle 5 (%) [b]	66.7
95% CI for not in response at cycle 5 [b]	37.5 - 84.6
Not in response at cycle 9 (%) [b]	46.7
95% CI for not in response at cycle 9 [b]	21.2 - 68.7
Not in response at cycle 13 (%) [b]	6.7
95% CI for not in response at cycle 13 [b]	0.4 - 26.0
Not in response at cycle 17 (%) [b]	6.7
95% CI for not in response at cycle 17 [b]	0.4 - 26.0
Not in response at cycle 21 (%) [b]	0.0
95% CI for not in response at cycle 21 [b]	NE - NE
Median follow-up for Time to response (cycles) [c]	8.0 (4.0 - 20.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Patients with a confirmed Partial Response or Complete Response.
[b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of first documentation of complete response or a subsequently confirmed partial response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.5.1.3 Time to response (TTR) - NCI assessment - PN status at enrollment (severity of disease) = Progressive
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=21)
Total events [a], n (%)	13 (61.9)
Median time to response (cycles) [b]	8.0
95% CI for Median time to response [b]	4.0 - 8.0
Not in response at cycle 5 (%) [b]	53.8
95% CI for not in response at cycle 5 [b]	24.8 - 76.0
Not in response at cycle 9 (%) [b]	23.1
95% CI for not in response at cycle 9 [b]	5.6 - 47.5
Not in response at cycle 13 (%) [b]	0.0
95% CI for not in response at cycle 13 [b]	NE - NE
Not in response at cycle 17 (%) [b]	0.0
95% CI for not in response at cycle 17 [b]	NE - NE
Not in response at cycle 21 (%) [b]	0.0
95% CI for not in response at cycle 21 [b]	NE - NE
Median follow-up for Time to response (cycles) [c]	8.0 (4.0 - 12.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Patients with a confirmed Partial Response or Complete Response.
[b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of first documentation of complete response or a subsequently confirmed partial response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.5.1.4 Time to response (TTR) - NCI assessment - PN status at enrollment (severity of disease) = Non-progressive
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=15)
Total events [a], n (%)	10 (66.7)
Median time to response (cycles) [b]	8.0
95% CI for Median time to response [b]	4.0 - 12.0
Not in response at cycle 5 (%) [b]	60.0
95% CI for not in response at cycle 5 [b]	25.3 - 82.7
Not in response at cycle 9 (%) [b]	40.0
95% CI for not in response at cycle 9 [b]	12.3 - 67.0
Not in response at cycle 13 (%) [b]	0.0
95% CI for not in response at cycle 13 [b]	NE - NE
Not in response at cycle 17 (%) [b]	0.0
95% CI for not in response at cycle 17 [b]	NE - NE
Not in response at cycle 21 (%) [b]	0.0
95% CI for not in response at cycle 21 [b]	NE - NE
Median follow-up for Time to response (cycles) [c]	8.0 (4.0 - 12.0)

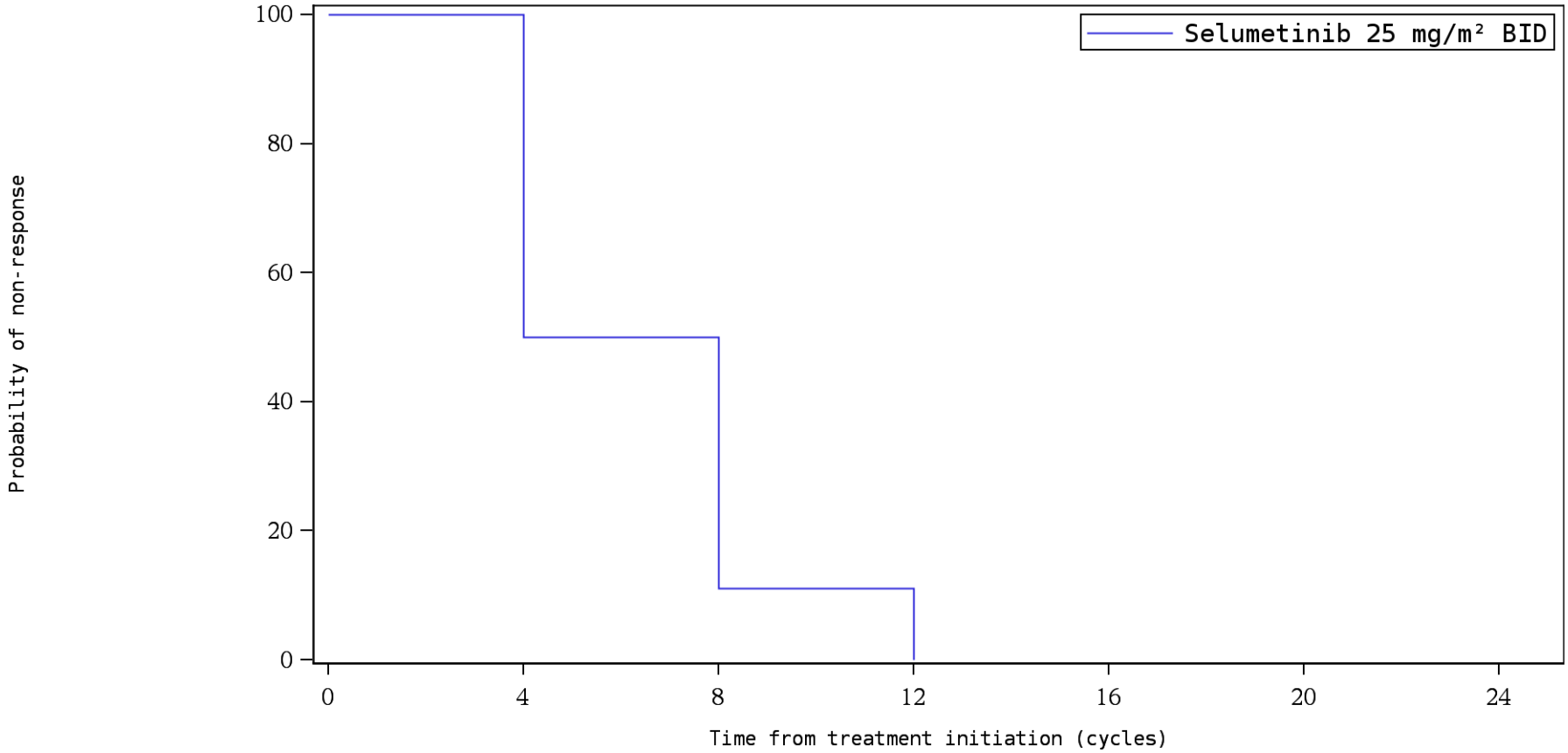
CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Patients with a confirmed Partial Response or Complete Response.
[b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of first documentation of complete response or a subsequently confirmed partial response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.5.1.5 Time to response (TTR) - NCI assessment - PN status at enrollment (severity of disease) = Unknown
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=14)
Total events [a], n (%)	10 (71.4)
Median time to response (cycles) [b]	8.0
95% CI for Median time to response [b]	4.0 - 8.0
Not in response at cycle 5 (%) [b]	60.0
95% CI for not in response at cycle 5 [b]	25.3 - 82.7
Not in response at cycle 9 (%) [b]	20.0
95% CI for not in response at cycle 9 [b]	3.1 - 47.5
Not in response at cycle 13 (%) [b]	10.0
95% CI for not in response at cycle 13 [b]	0.6 - 35.8
Not in response at cycle 17 (%) [b]	10.0
95% CI for not in response at cycle 17 [b]	0.6 - 35.8
Not in response at cycle 21 (%) [b]	0.0
95% CI for not in response at cycle 21 [b]	NE - NE
Median follow-up for Time to response (cycles) [c]	8.0 (4.0 - 20.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Patients with a confirmed Partial Response or Complete Response.
[b] Calculated using the Kaplan-Meier technique.
[c] Calculated as the median time from study treatment initiation until the pre-cycle of first documentation of complete response or a subsequently confirmed partial response.
A cycle is defined as 28 days.
REiNS assessment.

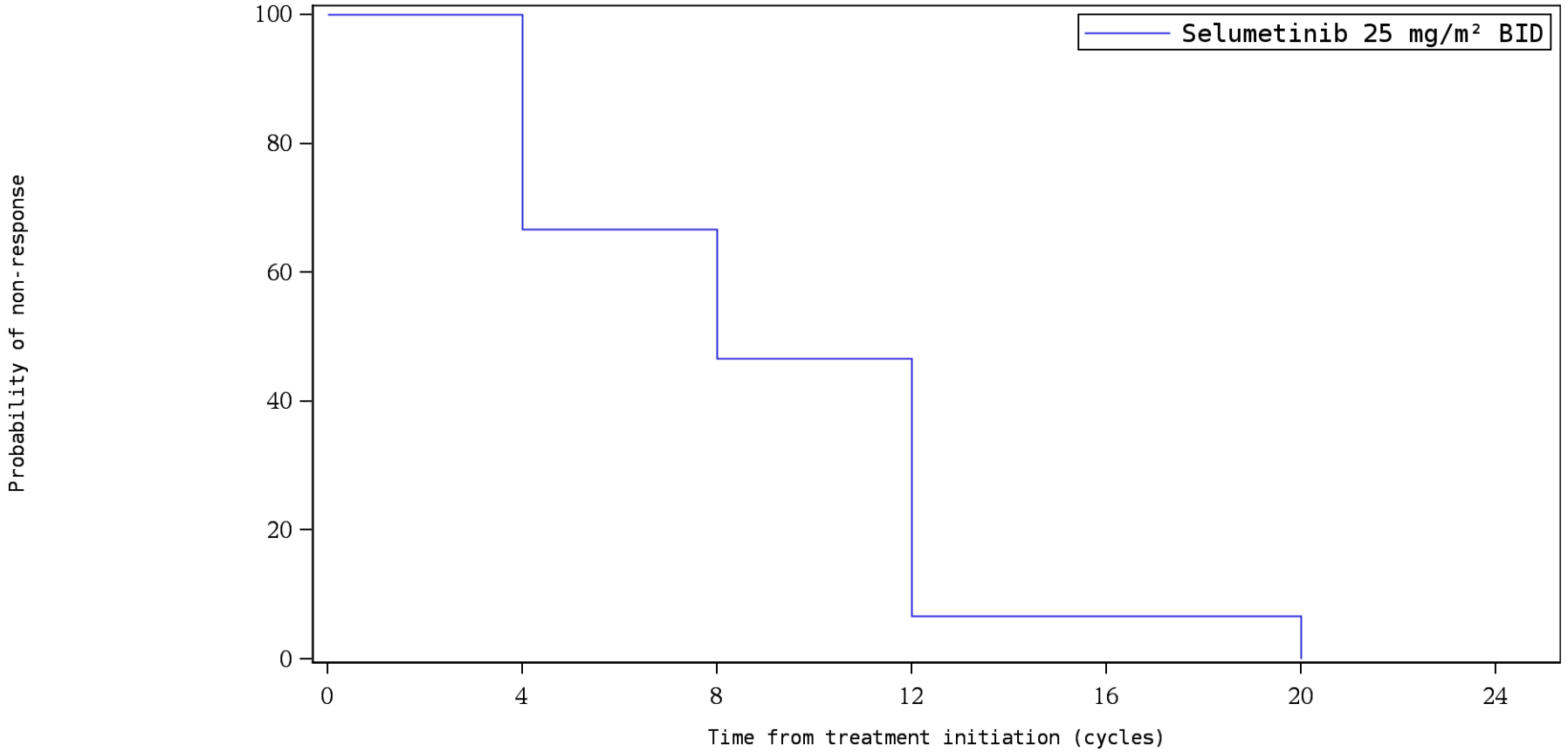
Figure 1.5.2.1 Kaplan-meier plot of time to response (TTR) - NCI assessment
Gender = Male (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:						
Selumetinib 25 mg/m² BID	18	18	9	2	0	0	0

Time to response (TTR) is defined as the time from study treatment initiation until the pre-cycle of the first documentation of complete response or a subsequently confirmed partial response.
Only patients who have achieved a confirmed partial response will be evaluated for TTR.
The values at the base of the figure indicate number of patients at risk.
A cycle is defined as 28 days.
REiNS assessment.

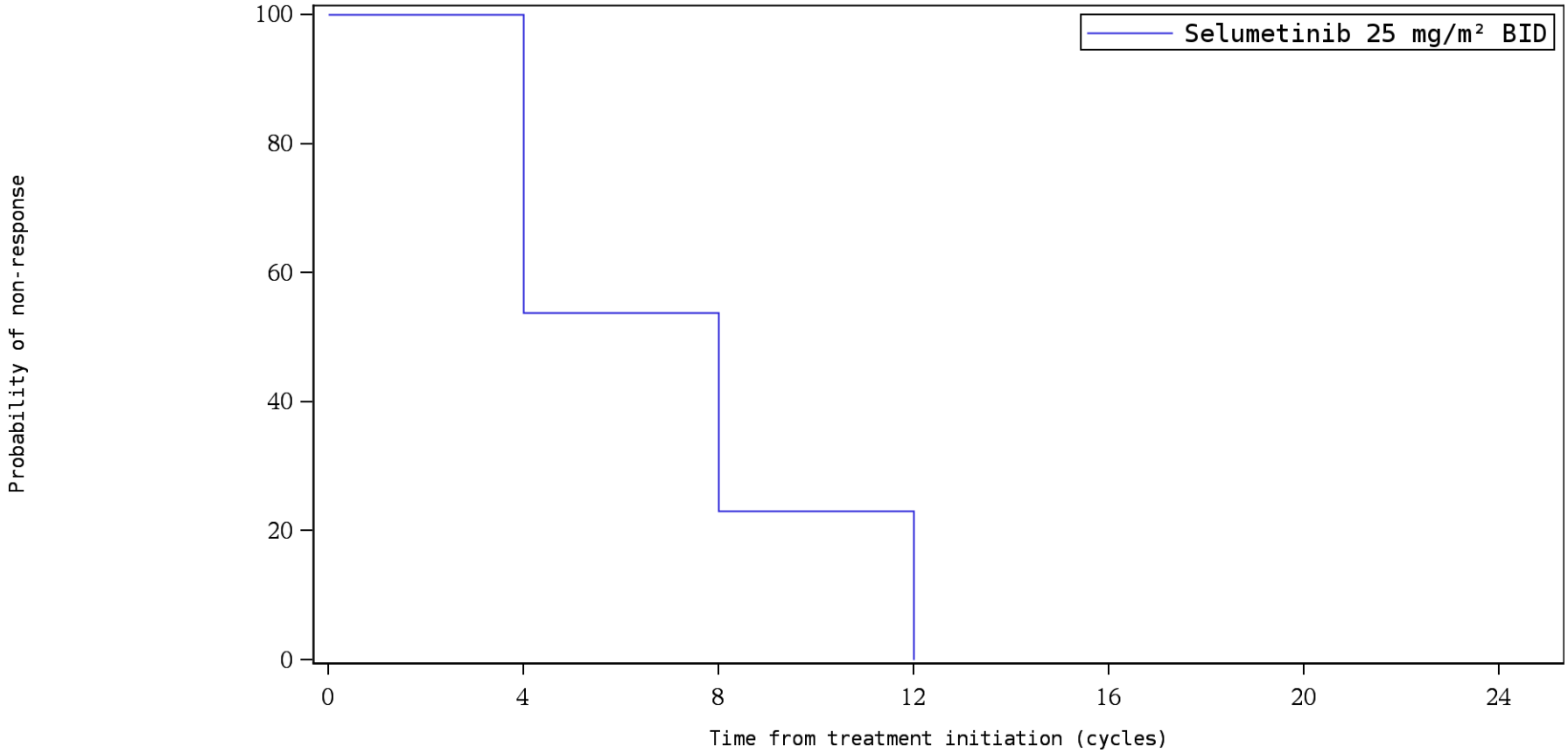
Figure 1.5.2.2 Kaplan-meier plot of time to response (TTR) - NCI assessment
Gender = Female (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:						
Selumetinib 25 mg/m² BID	15	15	10	7	1	1	0

Time to progression (TTP) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression. Patients who have not progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

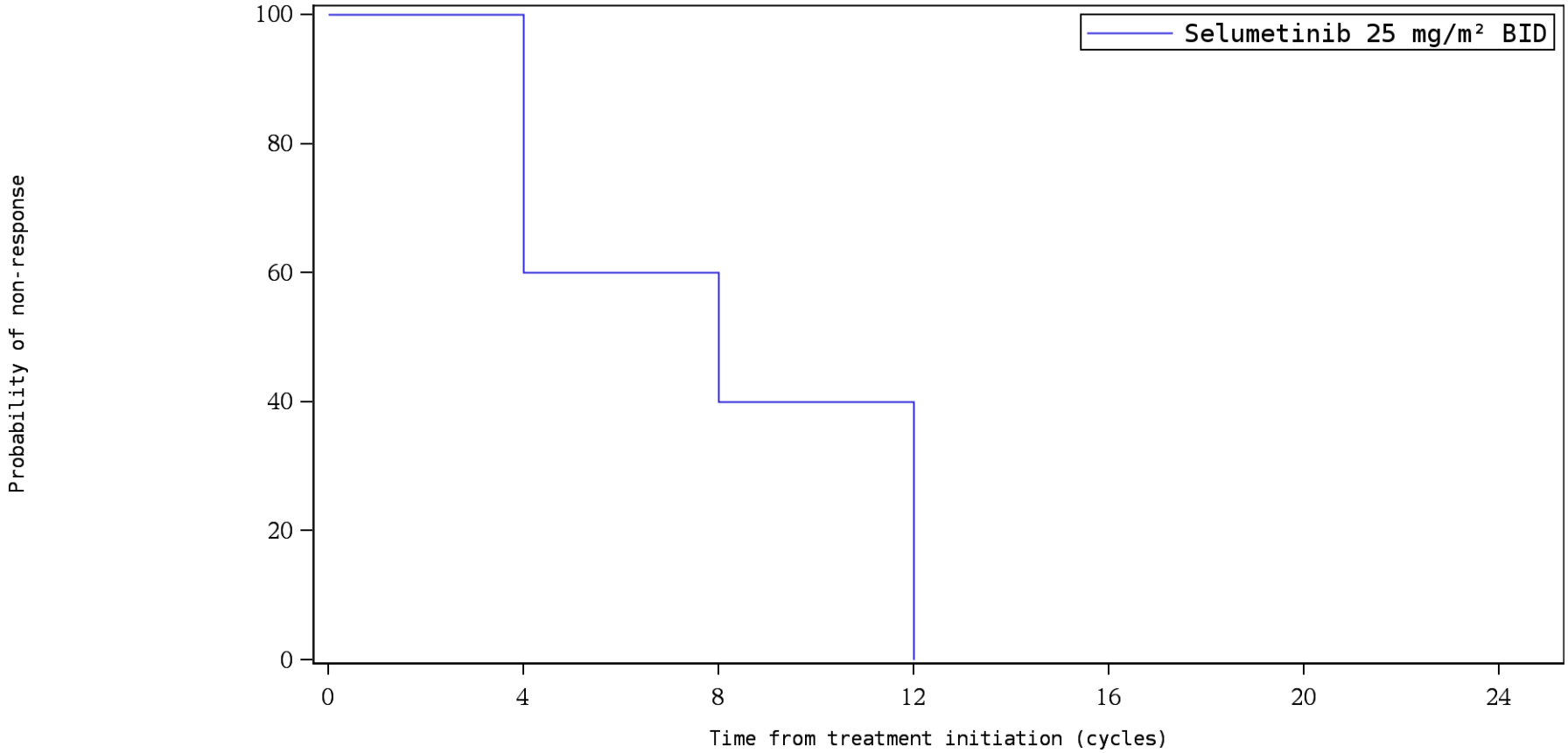
Figure 1.5.2.3 Kaplan-meier plot of time to response (TTR) - NCI assessment
PN status at enrollment (severity of disease) = Progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:						
Selumetinib 25 mg/m² BID	13	13	7	3	0	0	0

Time to progression (TTP) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression. Patients who have not progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

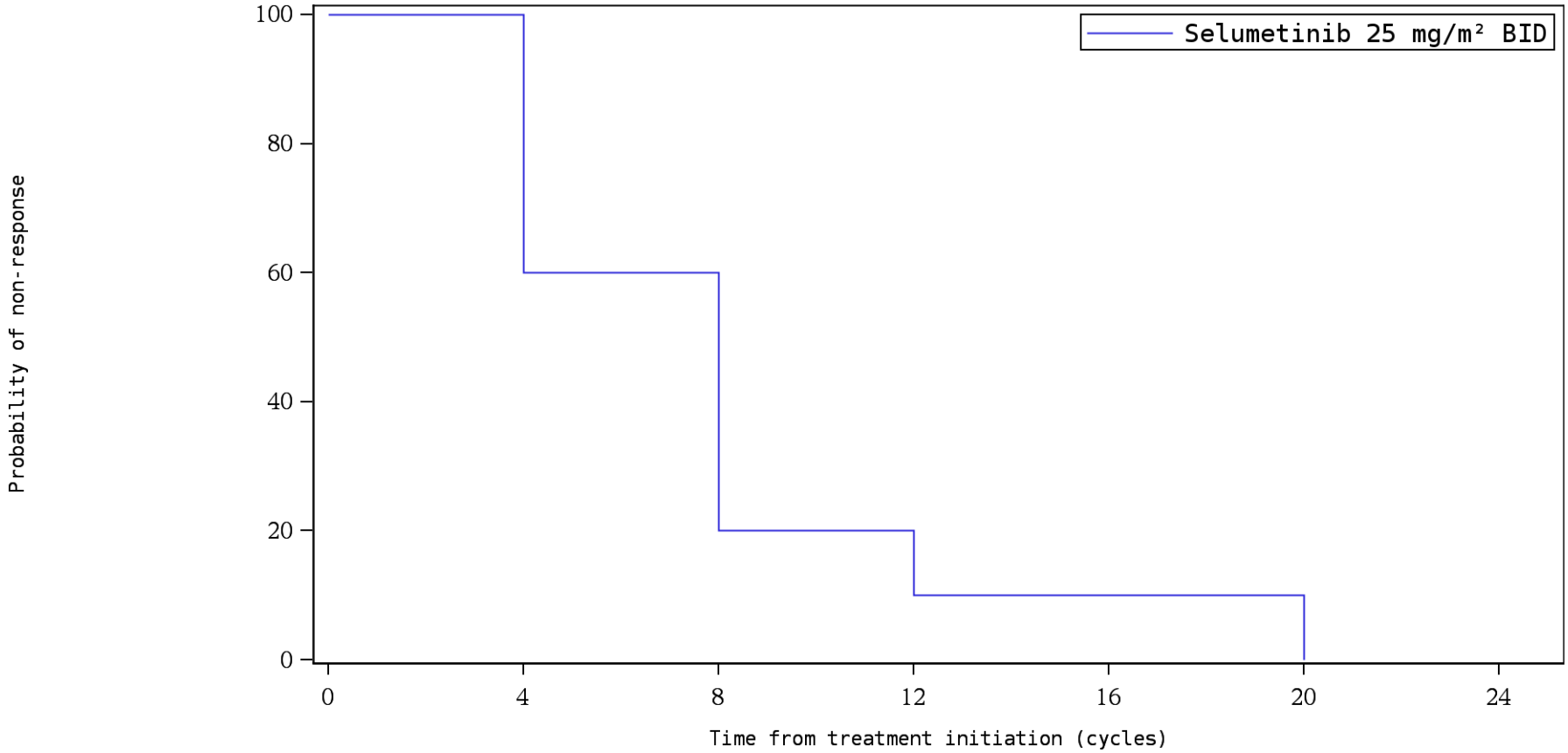
Figure 1.5.2.4 Kaplan-meier plot of time to response (TTR) - NCI assessment
PN status at enrollment (severity of disease) = Non-progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:						
Selumetinib 25 mg/m² BID	10	10	6	4	0	0	0

Time to progression (TTP) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression. Patients who have not progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

Figure 1.5.2.5 Kaplan-meier plot of time to response (TTR) - NCI assessment
PN status at enrollment (severity of disease) = Unknown (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:						
Selumetinib 25 mg/m² BID	10	10	6	2	1	1	0

Time to progression (TTP) is defined as the time from study treatment initiation until the pre-cycle of objective disease progression. Patients who have not progressed at the time of analysis are censored at the last evaluable on-treatment pre-cycle volumetric MRI assessment.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations. A cycle is defined as 28 days.
REiNS assessment.

Table 1.6.1 Best objective response - NCI assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup	Best objective response	Number (%) of patients Selumetinib 25 mg/m² BID (N=50) [e]
Gender: Male (n=30)	Complete response	0
	Confirmed partial response [a]	18 (60.0)
	Unconfirmed partial response [b]	3 (10.0)
	Stable disease [c]	8 (26.7)
	Progression [d]	0
	REiNS progression	0
	Death	0
	Not evaluable	1 (3.3)
Gender: Female (n=20)	Complete response	0
	Confirmed partial response [a]	15 (75.0)
	Unconfirmed partial response [b]	1 (5.0)
	Stable disease [c]	3 (15.0)
	Progression [d]	0
	REiNS progression	0
	Death	0
	Not evaluable	1 (5.0)

[a] The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
Partial Response = A decrease in the volume of the target PN by 20% or more compared to the baseline.
[b] PR achieved but either no confirmation assessment performed or a confirmation assessment performed but response not confirmed.
[c] Insufficient volume change from baseline to qualify for either Partial Response (PR) or Progressive Disease (PD).
[d] Increase in the volume of the target plexiform neurofibroma by 20% or more compared to baseline or the time of best response (maximal tumour shrinkage) after documenting a PR.
[e] Percentages are based on the number of patients within each subgroup.
REiNS assessment.
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Table 1.6.1 Best objective response - NCI assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup	Best objective response	Number (%) of patients Selumetinib 25 mg/m² BID (N=50) [e]
PN status at enrollment: Progressive (n=21)	Complete response	0
	Confirmed partial response [a]	13 (61.9)
	Unconfirmed partial response [b]	1 (4.8)
	Stable disease [c]	7 (33.3)
	Progression [d]	0
	REiNS progression	0
	Death	0
	Not evaluable	0
PN status at enrollment: Not progressive (n=15)	Complete response	0
	Confirmed partial response [a]	10 (66.7)
	Unconfirmed partial response [b]	1 (6.7)
	Stable disease [c]	3 (20.0)
	Progression [d]	0
	REiNS progression	0
	Death	0
	Not evaluable	1 (6.7)
PN status at enrollment: Unknown (n=14)	Complete response	0
	Confirmed partial response [a]	10 (71.4)
	Unconfirmed partial response [b]	2 (14.3)
	Stable disease [c]	1 (7.1)
	Progression [d]	0
	REiNS progression	0
	Death	0
	Not evaluable	1 (7.1)

[a] The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
Partial Response = A decrease in the volume of the target PN by 20% or more compared to the baseline.
[b] PR achieved but either no confirmation assessment performed or a confirmation assessment performed but response not confirmed.
[c] Insufficient volume change from baseline to qualify for either Partial Response (PR) or Progressive Disease (PD).
[d] Increase in the volume of the target plexiform neurofibroma by 20% or more compared to baseline or the time of best response (maximal tumour shrinkage) after documenting a PR.
[e] Percentages are based on the number of patients within each subgroup.
REiNS assessment.
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Table 1.6.2 Best objective response - ICR assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup	Best objective response	Number (%) of patients Selumetinib 25 mg/m² BID (N=50) [c]
Gender: Male (n=30)	Complete response	0
	Confirmed partial response [a]	13 (43.3)
	Unconfirmed partial response [b]	2 (6.7)
	Stable disease	14 (46.7)
	Progression	0
	REiNS progression	0
	Death	0
	Not evaluable	1 (3.3)
Gender: Female (n=20)	Complete response	0
	Confirmed partial response [a]	9 (45.0)
	Unconfirmed partial response [b]	3 (15.0)
	Stable disease	7 (35.0)
	Progression	0
	REiNS progression	0
	Death	0
	Not evaluable	1 (5.0)

[a] The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
[b] PR achieved but either no confirmation assessment performed or a confirmation assessment performed but response not confirmed.
Modified REiNS assessment performed by Independent Central Review.
[c] Percentages are based on the number of patients within each subgroup.

Table 1.6.2 Best objective response - ICR assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup	Best objective response	Number (%) of patients Selumetinib 25 mg/m² BID (N=50) [c]
PN status at enrollment: Progressive (n=21)	Complete response	0
	Confirmed partial response [a]	12 (57.1)
	Unconfirmed partial response [b]	3 (14.3)
	Stable disease	6 (28.6)
	Progression	0
	REiNS progression	0
	Death	0
	Not evaluable	0
PN status at enrollment: Not progressive (n=15)	Complete response	0
	Confirmed partial response [a]	6 (40.0)
	Unconfirmed partial response [b]	1 (6.7)
	Stable disease	7 (46.7)
	Progression	0
	REiNS progression	0
	Death	0
	Not evaluable	1 (6.7)
PN status at enrollment: Unknown (n=14)	Complete response	0
	Confirmed partial response [a]	4 (28.6)
	Unconfirmed partial response [b]	1 (7.1)
	Stable disease	8 (57.1)
	Progression	0
	REiNS progression	0
	Death	0
	Not evaluable	1 (7.1)

[a] The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
[b] PR achieved but either no confirmation assessment performed or a confirmation assessment performed but response not confirmed.
Modified REiNS assessment performed by Independent Central Review.
[c] Percentages are based on the number of patients within each subgroup.

Table 1.7.1.1 Duration and onset of confirmed objective response in patients with objective response - NCI assessment
Gender = Male (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=30)
Number of patients with an objective response	18
Number of patients with an objective response who subsequently progressed or died	1
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	NC
- Median	NC
- 95% CI for median	NC
- 75th percentile	NC
Estimated percentage remaining in response [b]	
- >= 4 cycles (95% CI)	100 (NE, NE)
- >= 8 cycles (95% CI)	100 (NE, NE)
- >= 12 cycles (95% CI)	100 (NE, NE)
- >= 16 cycles (95% CI)	93.3 (61.3, 99.0)
- >= 20 cycles (95% CI)	93.3 (61.3, 99.0)
- >= 24 cycles (95% CI)	93.3 (61.3, 99.0)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.7.1.1 Duration and onset of confirmed objective response in patients with objective response - NCI assessment
Gender = Male (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=30)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	18 (100)
- >= 8 cycles	18 (100)
- >= 12 cycles	15 (83.3)
- >= 16 cycles	15 (83.3)
- >= 20 cycles	12 (66.7)
- >= 24 cycles	7 (38.9)
Minimum duration of response (cycles)	8.0
Maximum duration of response (cycles)	32.0
Time to onset of response from first dose (cycles) [b]	
- 25th percentile	4.0
- Median	6.0
- 95% CI for median	4.0, 8.0
- 75th percentile	8.0
Time to onset of response from first dose - n(%) [b]	
- <= 4 cycles	9 (50.0)
- <= 8 cycles	16 (88.9)
- <= 12 cycles	18 (100)
- <= 16 cycles	18 (100)
- <= 20 cycles	18 (100)
- <= 24 cycles	18 (100)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.7.1.2 Duration and onset of confirmed objective response in patients with objective response - NCI assessment
Gender = Female (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=20)
Number of patients with an objective response	15
Number of patients with an objective response who subsequently progressed or died	1
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	NC
- Median	NC
- 95% CI for median	NC
- 75th percentile	NC
Estimated percentage remaining in response [b]	
- >= 4 cycles (95% CI)	100 (NE, NE)
- >= 8 cycles (95% CI)	100 (NE, NE)
- >= 12 cycles (95% CI)	100 (NE, NE)
- >= 16 cycles (95% CI)	100 (NE, NE)
- >= 20 cycles (95% CI)	87.5 (38.7, 98.1)
- >= 24 cycles (95% CI)	87.5 (38.7, 98.1)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.7.1.2 Duration and onset of confirmed objective response in patients with objective response - NCI assessment
Gender = Female (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=20)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	15 (100)
- >= 8 cycles	14 (93.3)
- >= 12 cycles	14 (93.3)
- >= 16 cycles	11 (73.3)
- >= 20 cycles	5 (33.3)
- >= 24 cycles	2 (13.3)
Minimum duration of response (cycles)	4.0
Maximum duration of response (cycles)	32.0
Time to onset of response from first dose (cycles) [b]	
- 25th percentile	4.0
- Median	8.0
- 95% CI for median	4.0, 12.0
- 75th percentile	12.0
Time to onset of response from first dose - n(%) [b]	
- <= 4 cycles	5 (33.3)
- <= 8 cycles	8 (53.3)
- <= 12 cycles	14 (93.3)
- <= 16 cycles	14 (93.3)
- <= 20 cycles	15 (100)
- <= 24 cycles	15 (100)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.7.1.3 Duration and onset of confirmed objective response in patients with objective response - NCI assessment
PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=21)
Number of patients with an objective response	13
Number of patients with an objective response who subsequently progressed or died	2
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	NC
- Median	NC
- 95% CI for median	NC
- 75th percentile	NC
Estimated percentage remaining in response [b]	
- >= 4 cycles (95% CI)	100 (NE, NE)
- >= 8 cycles (95% CI)	100 (NE, NE)
- >= 12 cycles (95% CI)	100 (NE, NE)
- >= 16 cycles (95% CI)	91.7 (53.9, 98.8)
- >= 20 cycles (95% CI)	83.3 (48.2, 95.6)
- >= 24 cycles (95% CI)	83.3 (48.2, 95.6)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.7.1.3 Duration and onset of confirmed objective response in patients with objective response - NCI assessment
PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=21)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	13 (100)
- >= 8 cycles	13 (100)
- >= 12 cycles	13 (100)
- >= 16 cycles	12 (92.3)
- >= 20 cycles	9 (69.2)
- >= 24 cycles	7 (53.8)
Minimum duration of response (cycles)	12.0
Maximum duration of response (cycles)	32.0
Time to onset of response from first dose (cycles) [b]	
- 25th percentile	4.0
- Median	8.0
- 95% CI for median	4.0, 8.0
- 75th percentile	8.0
Time to onset of response from first dose - n(%) [b]	
- <= 4 cycles	6 (46.2)
- <= 8 cycles	10 (76.9)
- <= 12 cycles	13 (100)
- <= 16 cycles	13 (100)
- <= 20 cycles	13 (100)
- <= 24 cycles	13 (100)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.7.1.4 Duration and onset of confirmed objective response in patients with objective response - NCI assessment
PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=15)
Number of patients with an objective response	10
Number of patients with an objective response who subsequently progressed or died	0
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	NC
- Median	NC
- 95% CI for median	NC
- 75th percentile	NC
Estimated percentage remaining in response [b]	
- >= 4 cycles (95% CI)	100 (NE, NE)
- >= 8 cycles (95% CI)	100 (NE, NE)
- >= 12 cycles (95% CI)	100 (NE, NE)
- >= 16 cycles (95% CI)	100 (NE, NE)
- >= 20 cycles (95% CI)	100 (NE, NE)
- >= 24 cycles (95% CI)	100 (NE, NE)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.7.1.4 Duration and onset of confirmed objective response in patients with objective response - NCI assessment
PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=15)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	10 (100)
- >= 8 cycles	10 (100)
- >= 12 cycles	9 (90.0)
- >= 16 cycles	8 (80.0)
- >= 20 cycles	4 (40.0)
- >= 24 cycles	1 (10.0)
Minimum duration of response (cycles)	8.0
Maximum duration of response (cycles)	24.0
Time to onset of response from first dose (cycles) [b]	
- 25th percentile	4.0
- Median	8.0
- 95% CI for median	4.0, 12.0
- 75th percentile	12.0
Time to onset of response from first dose - n(%) [b]	
- <= 4 cycles	4 (40.0)
- <= 8 cycles	6 (60.0)
- <= 12 cycles	10 (100)
- <= 16 cycles	10 (100)
- <= 20 cycles	10 (100)
- <= 24 cycles	10 (100)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.7.1.5 Duration and onset of confirmed objective response in patients with objective response - NCI assessment
PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=14)
Number of patients with an objective response	10
Number of patients with an objective response who subsequently progressed or died	0
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	NC
- Median	NC
- 95% CI for median	NC
- 75th percentile	NC
Estimated percentage remaining in response [b]	
- >= 4 cycles (95% CI)	100 (NE, NE)
- >= 8 cycles (95% CI)	100 (NE, NE)
- >= 12 cycles (95% CI)	100 (NE, NE)
- >= 16 cycles (95% CI)	100 (NE, NE)
- >= 20 cycles (95% CI)	100 (NE, NE)
- >= 24 cycles (95% CI)	100 (NE, NE)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.7.1.5 Duration and onset of confirmed objective response in patients with objective response - NCI assessment
PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=14)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	10 (100)
- >= 8 cycles	9 (90.0)
- >= 12 cycles	7 (70.0)
- >= 16 cycles	6 (60.0)
- >= 20 cycles	4 (40.0)
- >= 24 cycles	1 (10.0)
Minimum duration of response (cycles)	4.0
Maximum duration of response (cycles)	26.0
Time to onset of response from first dose (cycles) [b]	
- 25th percentile	4.0
- Median	8.0
- 95% CI for median	4.0, 8.0
- 75th percentile	8.0
Time to onset of response from first dose - n(%) [b]	
- <= 4 cycles	4 (40.0)
- <= 8 cycles	8 (80.0)
- <= 12 cycles	9 (90.0)
- <= 16 cycles	9 (90.0)
- <= 20 cycles	10 (100)
- <= 24 cycles	10 (100)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
REiNS assessment.

Table 1.7.2.1 Duration and onset of confirmed objective response in patients with objective response - ICR assessment
Gender = Male (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=30)
Number of patients with an objective response	13
Number of patients with an objective response who subsequently progressed or died	4
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	20.0
- Median	32.0
- 95% CI for median	18.0, 32.0
- 75th percentile	32.0
Estimated percentage remaining in response [b]	
- >= 4 cycles (95% CI)	100 (NE, NE)
- >= 8 cycles (95% CI)	100 (NE, NE)
- >= 12 cycles (95% CI)	91.7 (53.9, 98.8)
- >= 16 cycles (95% CI)	91.7 (53.9, 98.8)
- >= 20 cycles (95% CI)	64.2 (22.5, 87.6)
- >= 24 cycles (95% CI)	64.2 (22.5, 87.6)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.7.2.1 Duration and onset of confirmed objective response in patients with objective response - ICR assessment
Gender = Male (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=30)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	13 (100)
- >= 8 cycles	12 (92.3)
- >= 12 cycles	12 (92.3)
- >= 16 cycles	9 (69.2)
- >= 20 cycles	5 (38.5)
- >= 24 cycles	4 (30.8)
Minimum duration of response (cycles)	6.0
Maximum duration of response (cycles)	32.0

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.7.2.2 Duration and onset of confirmed objective response in patients with objective response - ICR assessment
Gender = Female (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=20)
Number of patients with an objective response	9
Number of patients with an objective response who subsequently progressed or died	3
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	8.0
- Median	NC
- 95% CI for median	NC
- 75th percentile	NC
Estimated percentage remaining in response [b]	
- >= 4 cycles (95% CI)	100 (NE, NE)
- >= 8 cycles (95% CI)	62.5 (22.9, 86.1)
- >= 12 cycles (95% CI)	62.5 (22.9, 86.1)
- >= 16 cycles (95% CI)	62.5 (22.9, 86.1)
- >= 20 cycles (95% CI)	NE
- >= 24 cycles (95% CI)	NE

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.7.2.2 Duration and onset of confirmed objective response in patients with objective response - ICR assessment
Gender = Female (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=20)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	9 (100)
- >= 8 cycles	8 (88.9)
- >= 12 cycles	4 (44.4)
- >= 16 cycles	1 (11.1)
- >= 20 cycles	0
- >= 24 cycles	0
Minimum duration of response (cycles)	6.0
Maximum duration of response (cycles)	16.0

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.7.2.3 Duration and onset of confirmed objective response in patients with objective response - ICR assessment
PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=21)
Number of patients with an objective response	12
Number of patients with an objective response who subsequently progressed or died	3
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	32.0
- Median	32.0
- 95% CI for median	12.0, 32.0
- 75th percentile	32.0
Estimated percentage remaining in response [b]	
- >= 4 cycles (95% CI)	100 (NE, NE)
- >= 8 cycles (95% CI)	100 (NE, NE)
- >= 12 cycles (95% CI)	90.0 (47.3, 98.5)
- >= 16 cycles (95% CI)	90.0 (47.3, 98.5)
- >= 20 cycles (95% CI)	77.1 (34.5, 93.9)
- >= 24 cycles (95% CI)	77.1 (34.5, 93.9)

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.7.2.3 Duration and onset of confirmed objective response in patients with objective response - ICR assessment
PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=21)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	12 (100)
- >= 8 cycles	10 (83.3)
- >= 12 cycles	10 (83.3)
- >= 16 cycles	7 (58.3)
- >= 20 cycles	4 (33.3)
- >= 24 cycles	4 (33.3)
Minimum duration of response (cycles)	6.0
Maximum duration of response (cycles)	32.0

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.7.2.4 Duration and onset of confirmed objective response in patients with objective response - ICR assessment
PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=15)
Number of patients with an objective response	6
Number of patients with an objective response who subsequently progressed or died	3
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	8.0
- Median	20.0
- 95% CI for median	8.0, 20.0
- 75th percentile	20.0
Estimated percentage remaining in response [b]	
- >= 4 cycles (95% CI)	100 (NE, NE)
- >= 8 cycles (95% CI)	66.7 (19.5, 90.4)
- >= 12 cycles (95% CI)	66.7 (19.5, 90.4)
- >= 16 cycles (95% CI)	66.7 (19.5, 90.4)
- >= 20 cycles (95% CI)	0
- >= 24 cycles (95% CI)	0

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.7.2.4 Duration and onset of confirmed objective response in patients with objective response - ICR assessment
PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=15)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	6 (100)
- >= 8 cycles	6 (100)
- >= 12 cycles	4 (66.7)
- >= 16 cycles	2 (33.3)
- >= 20 cycles	1 (16.7)
- >= 24 cycles	0
Minimum duration of response (cycles)	8.0
Maximum duration of response (cycles)	20.0

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.7.2.5 Duration and onset of confirmed objective response in patients with objective response - ICR assessment
PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=14)
Number of patients with an objective response	4
Number of patients with an objective response who subsequently progressed or died	1
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	NC
- Median	NC
- 95% CI for median	NC
- 75th percentile	NC
Estimated percentage remaining in response [b]	
- >= 4 cycles (95% CI)	100 (NE, NE)
- >= 8 cycles (95% CI)	75.0 (12.8, 96.1)
- >= 12 cycles (95% CI)	75.0 (12.8, 96.1)
- >= 16 cycles (95% CI)	75.0 (12.8, 96.1)
- >= 20 cycles (95% CI)	NE
- >= 24 cycles (95% CI)	NE

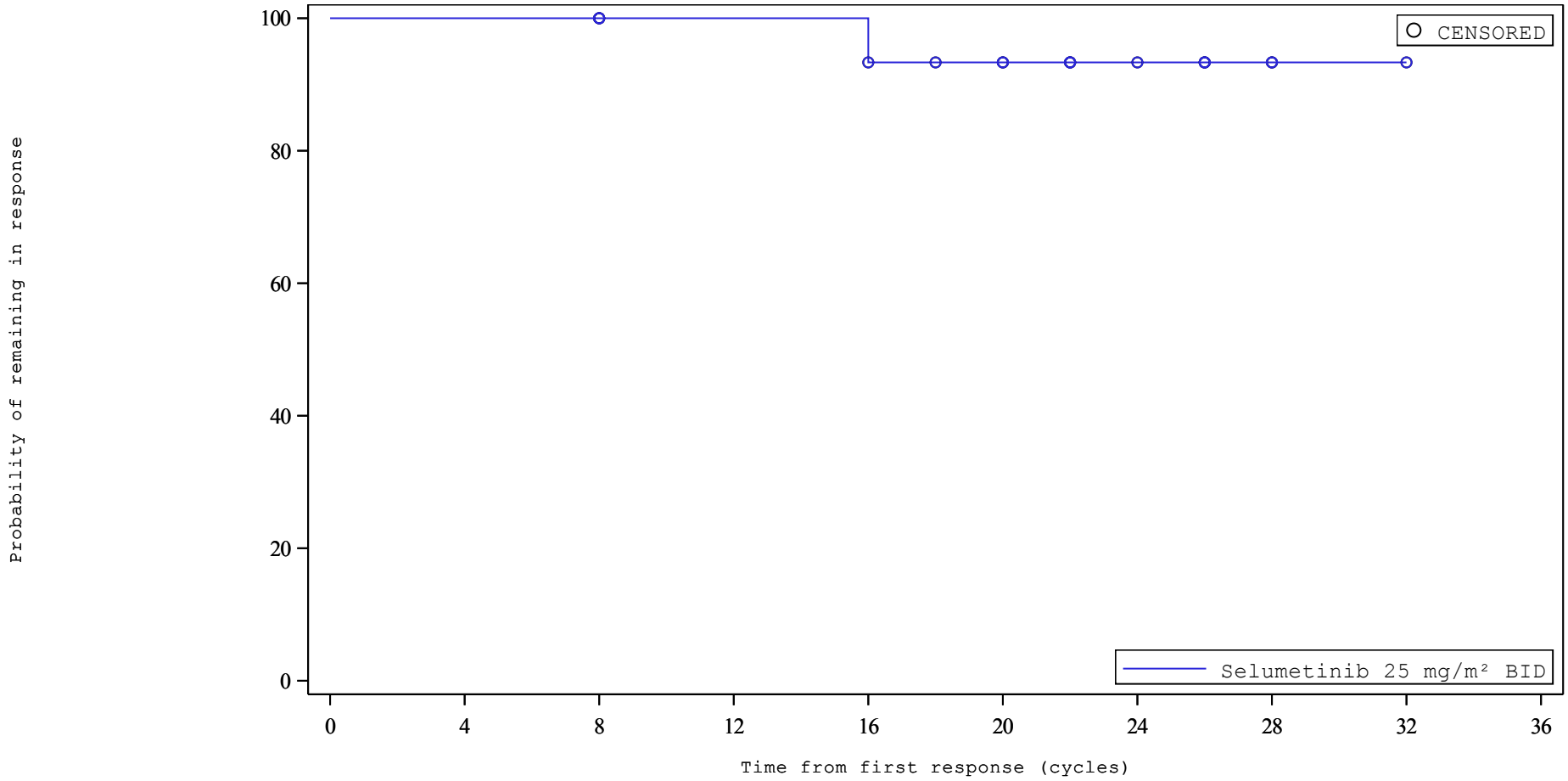
CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.7.2.5 Duration and onset of confirmed objective response in patients with objective response - ICR assessment
PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

	Selumetinib 25 mg/m² BID (N=14)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	4 (100)
- >= 8 cycles	4 (100)
- >= 12 cycles	2 (50.0)
- >= 16 cycles	1 (25.0)
- >= 20 cycles	0
- >= 24 cycles	0
Minimum duration of response (cycles)	8.0
Maximum duration of response (cycles)	16.0

CI = Confidence interval. NC = Not calculated. NE = Not evaluable.
[a] Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again at 3-6 months.
[b] Calculated using Kaplan-Meier technique. The denominator is the number of patients with objective response.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

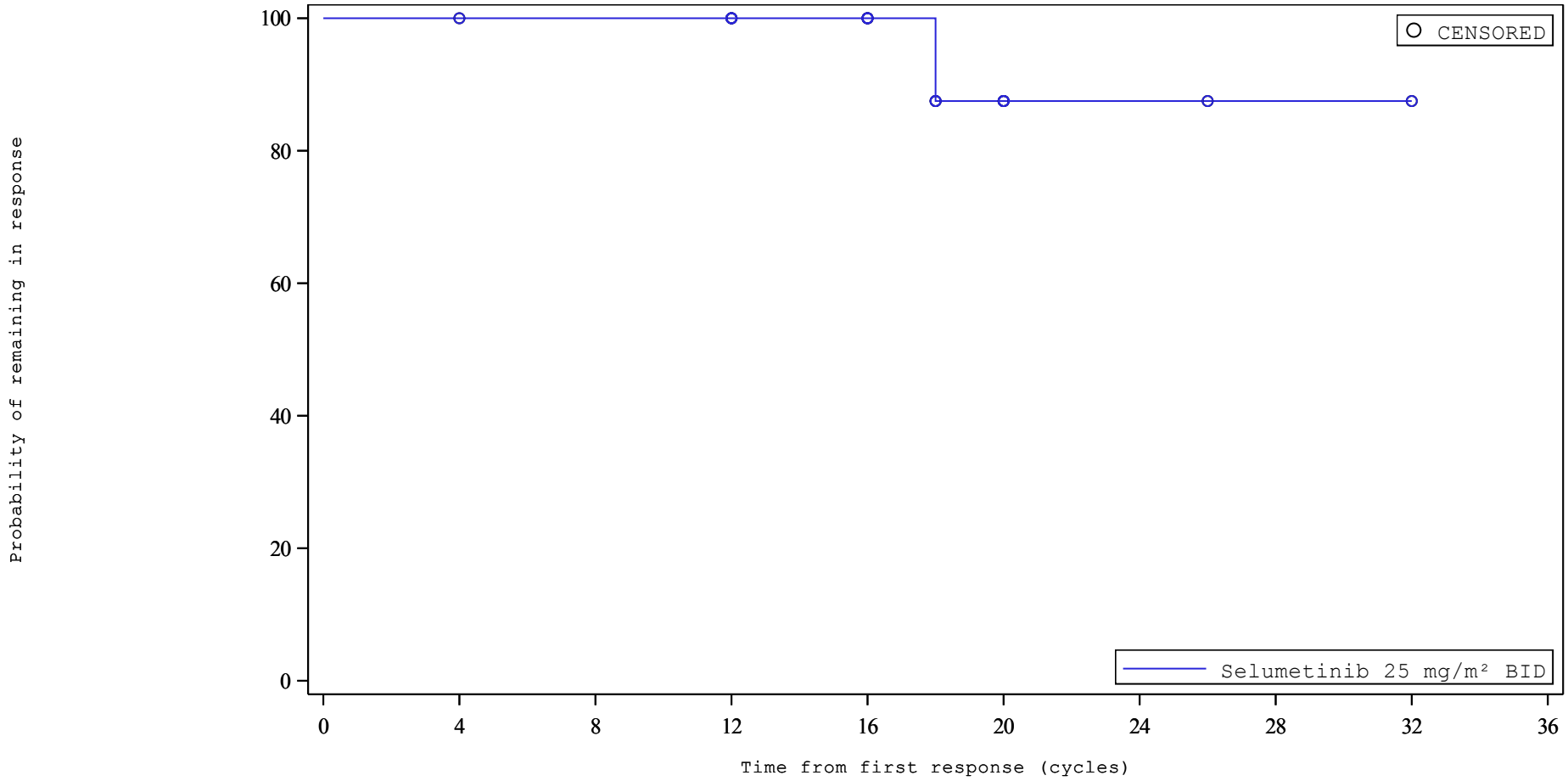
Table 1.7.3.1 Kaplan-meier plot of duration of response (DoR) - NCI assessment, Gender = Male (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	18	18	18	15	15	12	7	3	1	0

Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations.
A cycle is defined as 28 days.
REiNS assessment

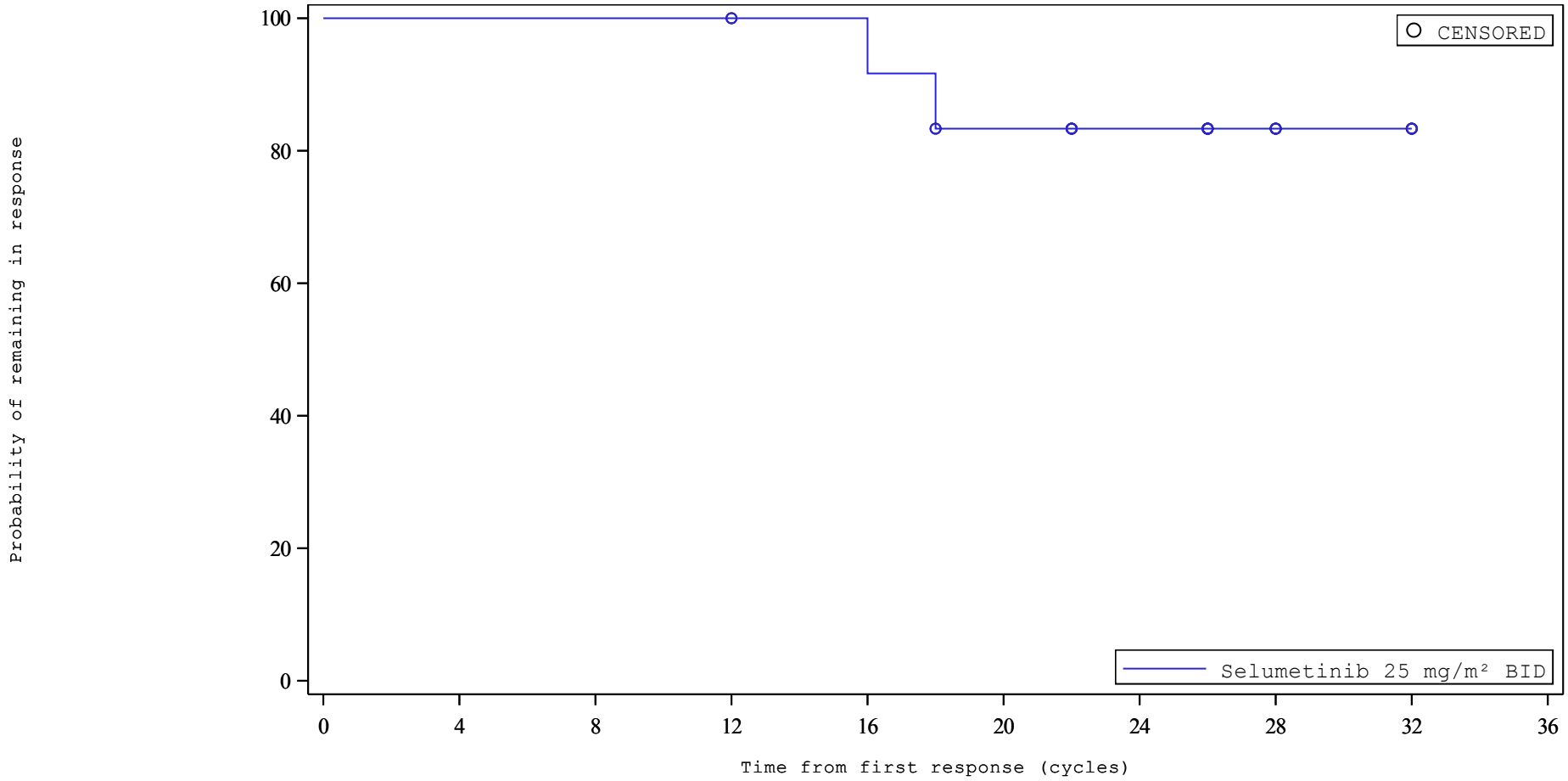
Table 1.7.3.2 Kaplan-meier plot of duration of response (DoR) - NCI assessment, Gender = Female (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	15	15	14	14	11	5	2	1	1	0

Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations.
A cycle is defined as 28 days.
REiNS assessment

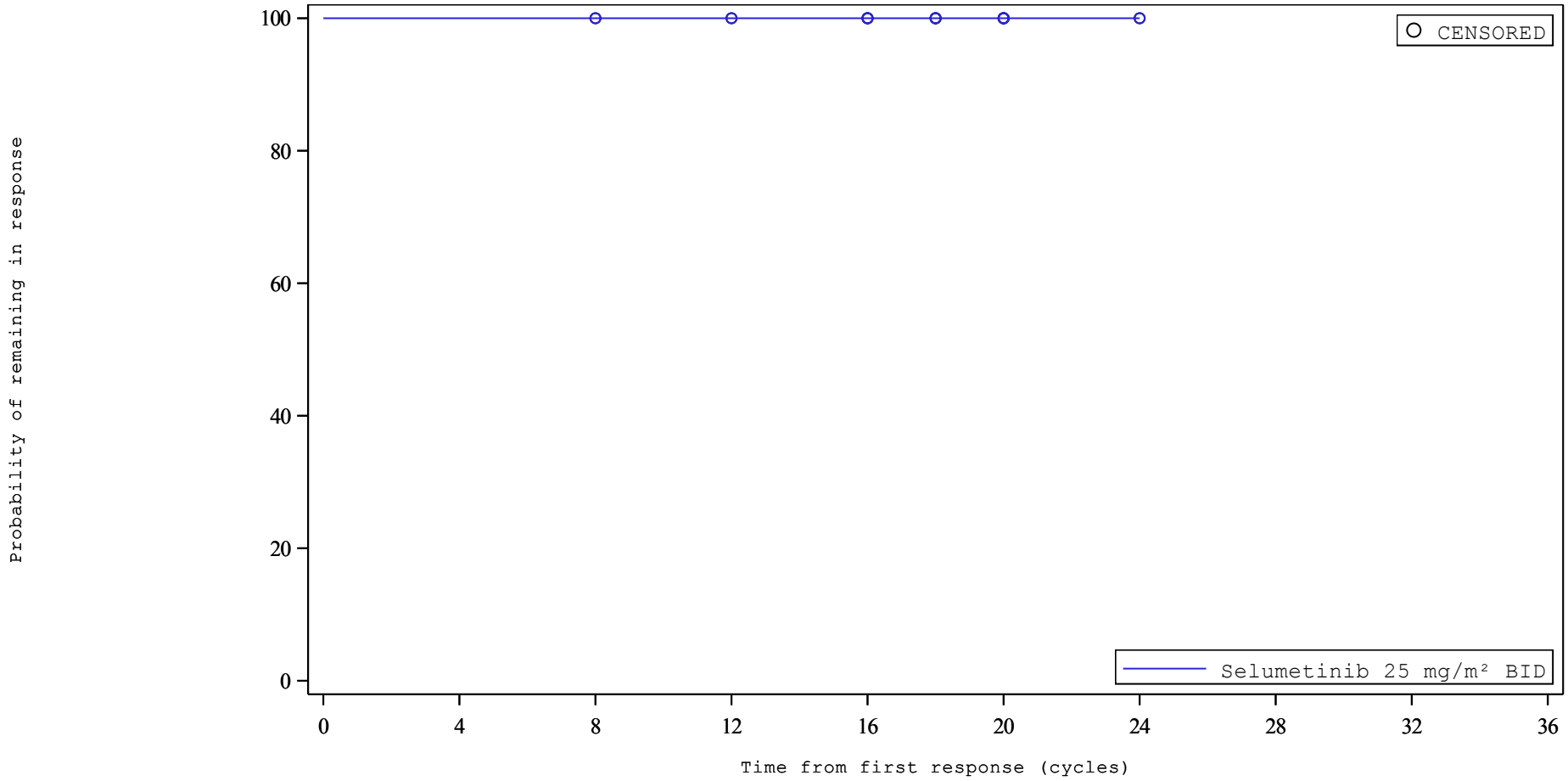
Table 1.7.3.3 Kaplan-meier plot of duration of response (DoR) - NCI assessment, PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	13	13	13	13	12	9	7	4	2	0

Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations.
A cycle is defined as 28 days.
REiNS assessment

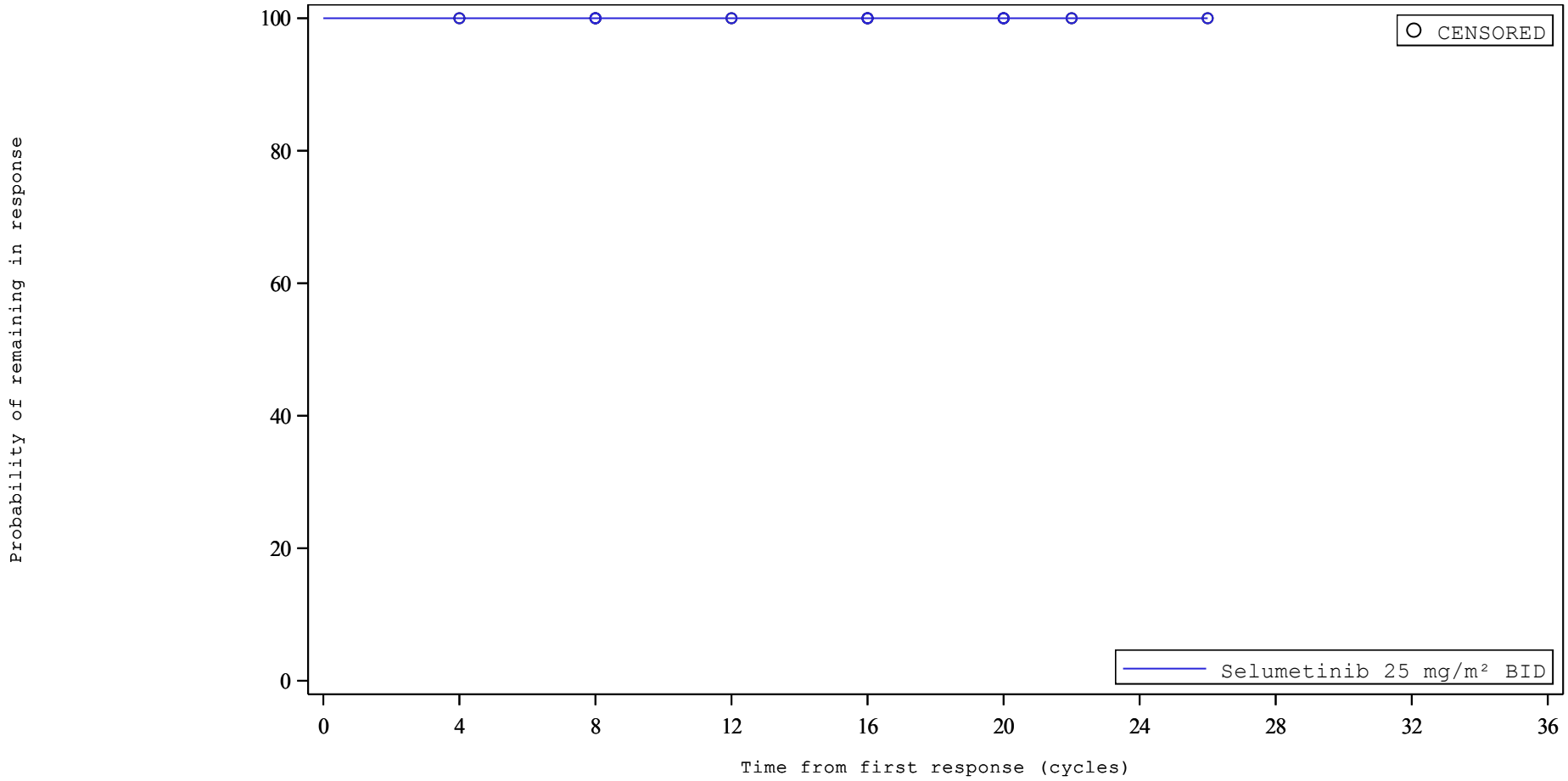
Table 1.7.3.4 Kaplan-meier plot of duration of response (DoR) - NCI assessment, PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	10	10	10	9	8	4	1	0	0	0

Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations.
A cycle is defined as 28 days.
REiNS assessment

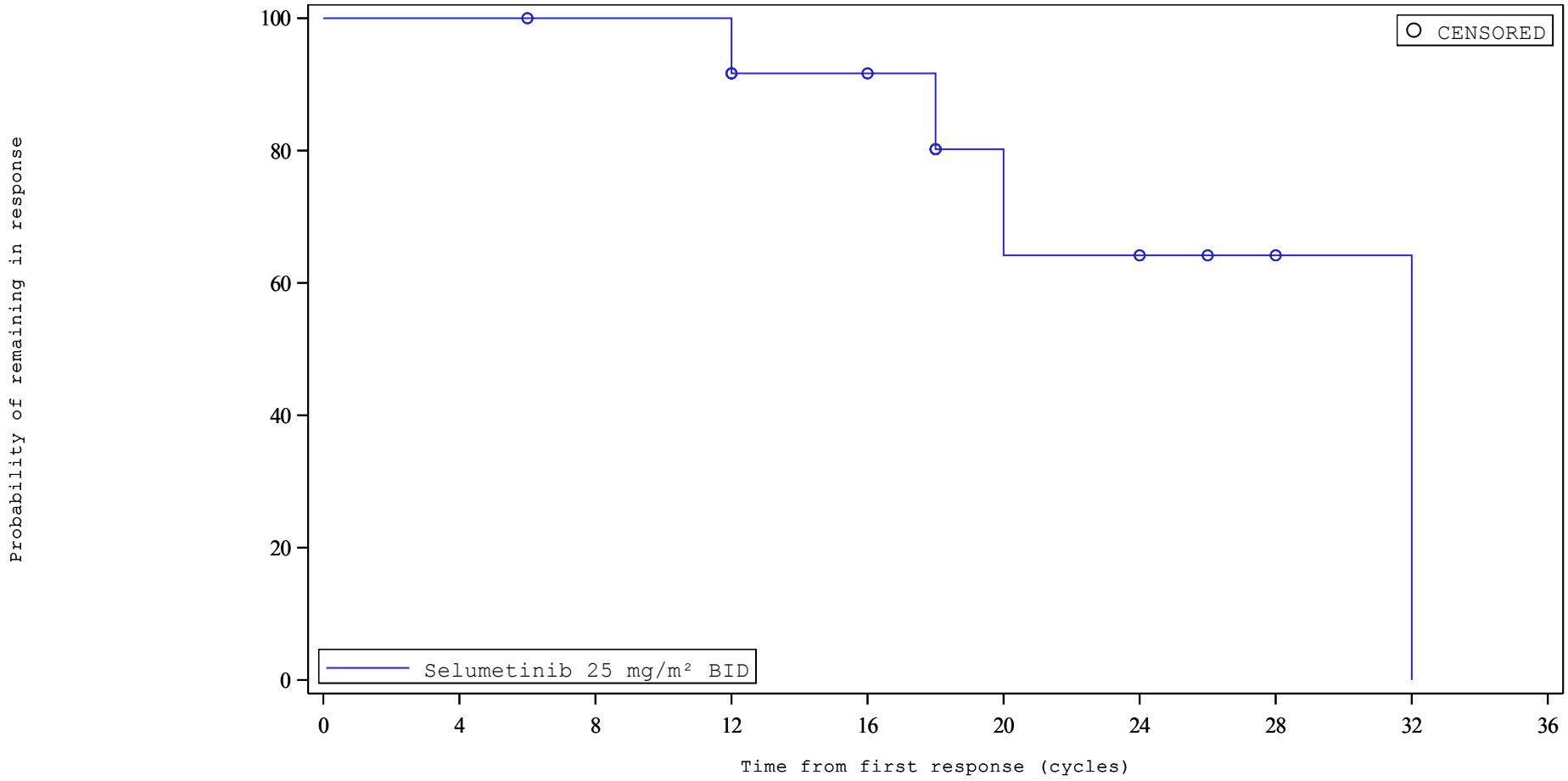
Table 1.7.3.5 Kaplan-meier plot of duration of response (DoR) - NCI assessment, PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	10	10	9	7	6	4	1	0	0	0

Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations.
A cycle is defined as 28 days.
REiNS assessment

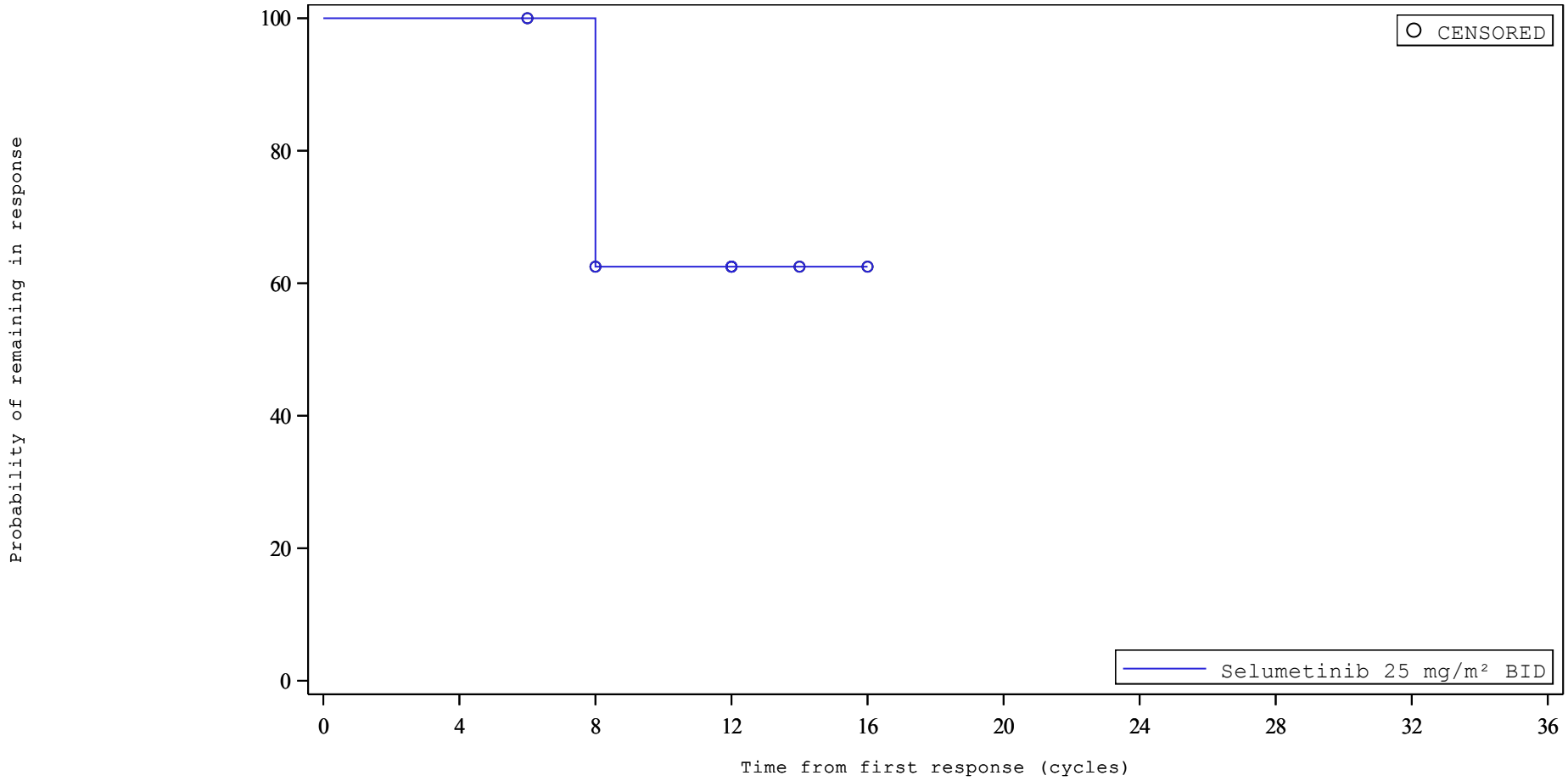
Table 1.7.4.1 Kaplan-meier plot of duration of response (DoR) - ICR assessment, Gender = Male (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	13	13	12	12	9	5	4	2	1	0

Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

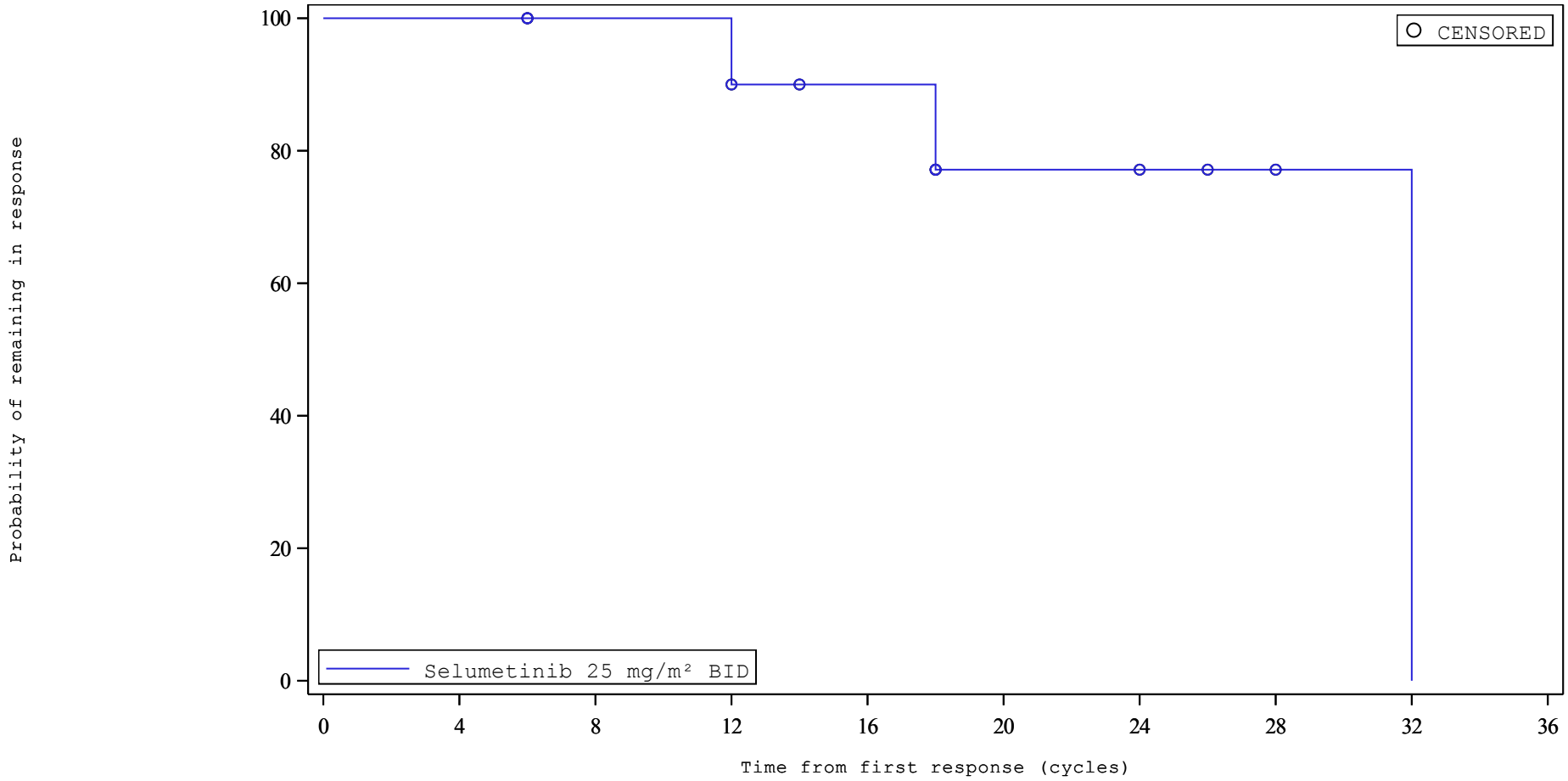
Table 1.7.4.2 Kaplan-meier plot of duration of response (DoR) - ICR assessment, Gender = Female (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	9	9	8	4	1	0	0	0	0	0

Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

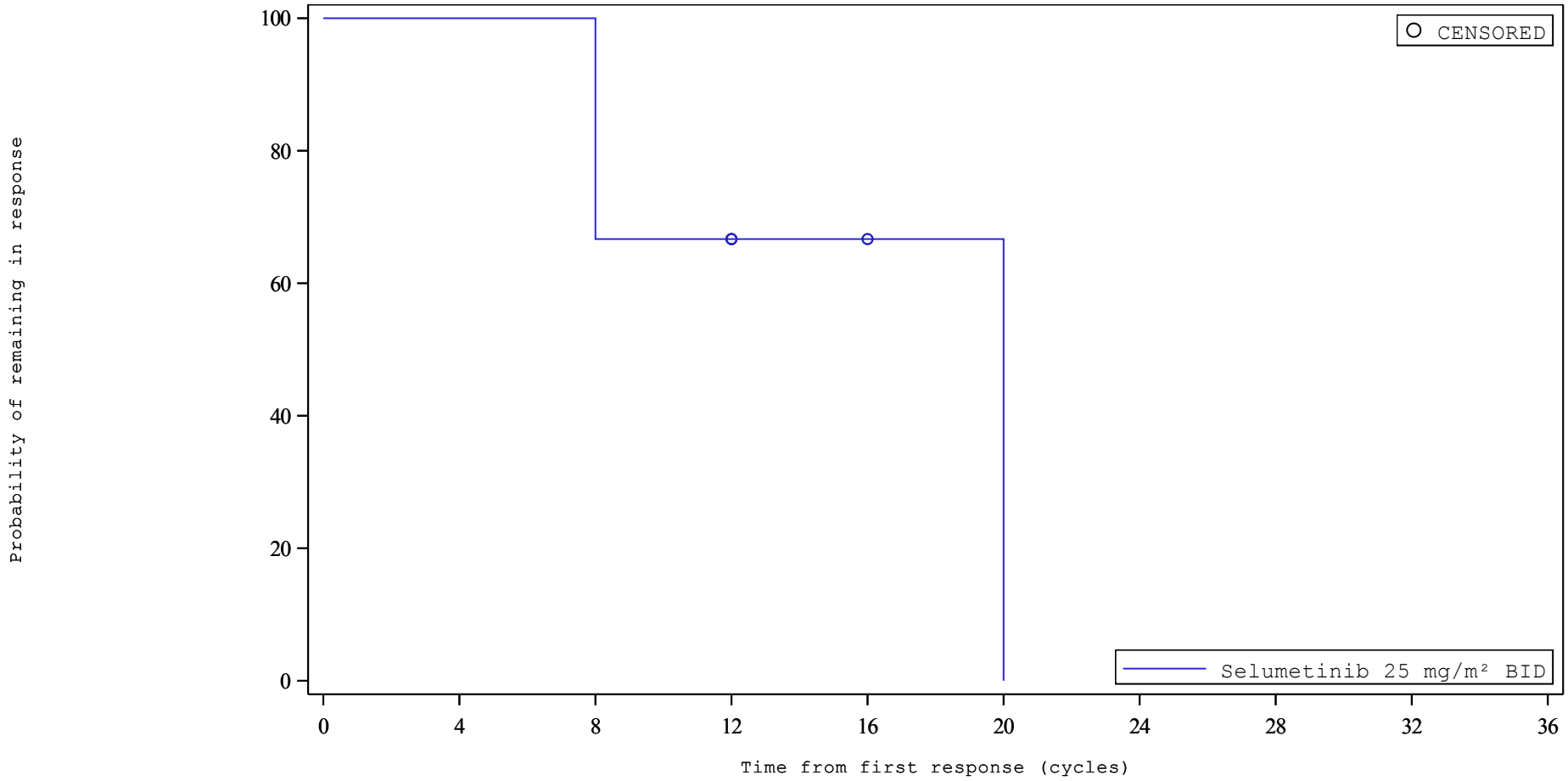
Table 1.7.4.3 Kaplan-meier plot of duration of response (DoR) - ICR assessment, PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	12	12	10	10	7	4	4	2	1	0

Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

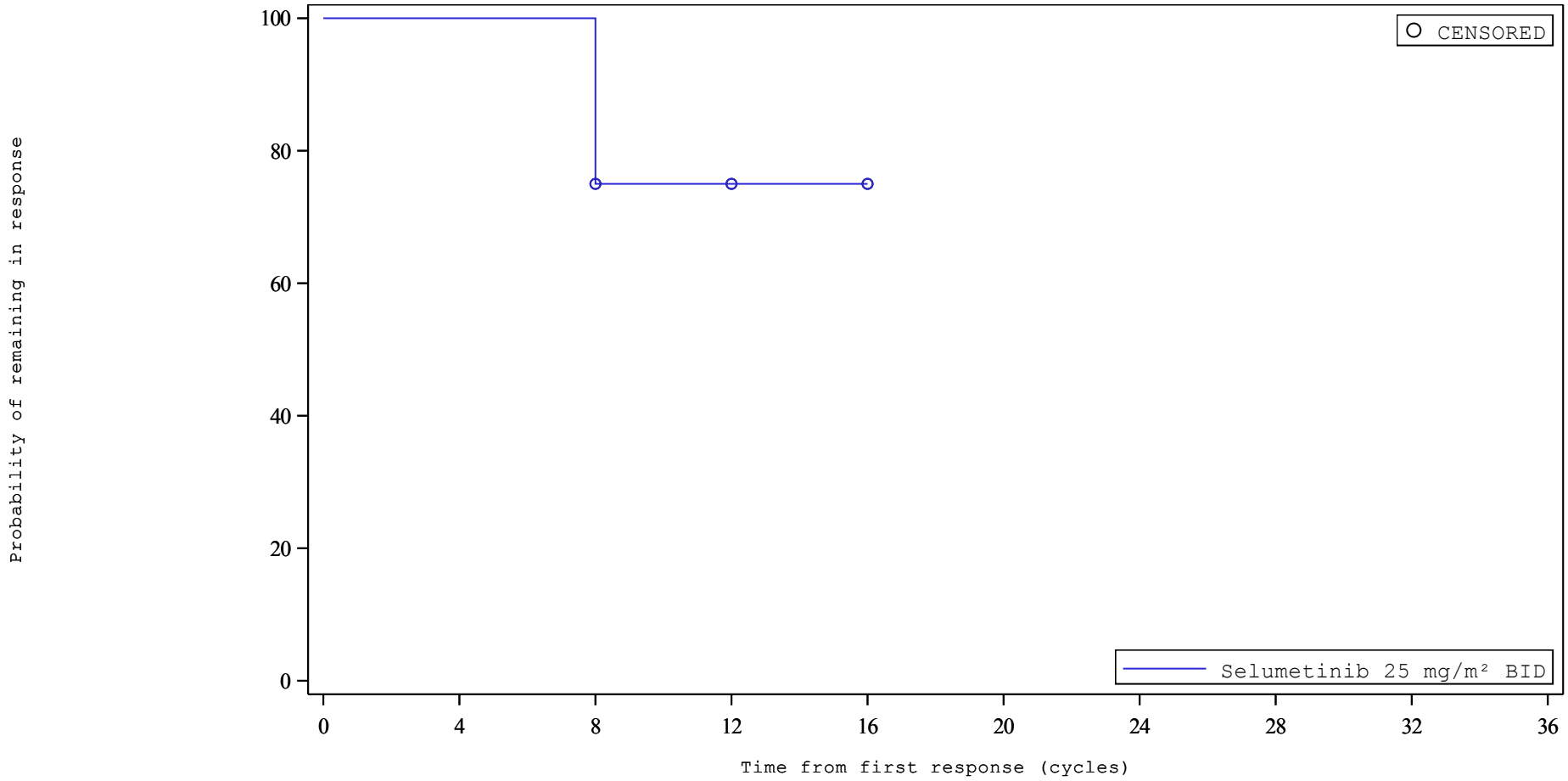
Table 1.7.4.4 Kaplan-meier plot of duration of response (DoR) - ICR assessment, PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	6	6	6	4	2	1	0	0	0	0

Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.7.4.5 Kaplan-meier plot of duration of response (DoR) - ICR assessment, PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018



	Number of patients:									
Selumetinib 25 mg/m² BID	4	4	4	2	1	0	0	0	0	0

Duration of response (DoR) is defined as the time from the pre-cycle of the first documented (which is subsequently confirmed) response until the pre-cycle of documented progression or death in the absence of disease progression (i.e. pre-cycle of progression event or censoring - pre-cycle of first response where each cycle is 28 days).
The PR is considered unconfirmed at the first detection, confirmed when observed again within 3-6 months.
The values at the base of the figure indicate number of patients at risk.
Dots represent censored observations.
A cycle is defined as 28 days.
Modified REiNS assessment performed by Independent Central Review.

Table 1.8.1 Percent change in target PN volume Mean-Difference - Intervention vs. Control
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural Histry Study NF1 age-matched and Tipifarnib

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	48	1.8 (1.7, 2.0)	-9.4 (-12.2, -6.5)	-16.9	-20.2, -13.5
Natural History (age-matched) [e]	92	7.2 (6.3, 8.0)	22.9 (17.6, 28.3)	20.5	16.5, 24.5
Tipifarnib [f]	29	1.2 (0.8, 1.6)	27.4 (19.9, 35.0)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first). TIPI: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up. [b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years. [c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH and TIPI mixed models also contain a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment. [e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI. [f] Includes patients with at least one MRI and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. TIPI = Tipifarnib. FU = Follow-up
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Table 1.8.2 Absolute change in target PN volume Mean-Difference - Intervention vs. Control
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural Histry Study NF1 age-matched and Tipifarnib

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	48	1.8 (1.7, 2.0)	-116 (-178.5, -52.4)	-89.5	-112.4, -66.6
Natural History (age-matched) [e]	92	7.2 (6.3, 8.0)	97.9 (62.0, 133.8)	NC	NC
Tipifarnib [f]	29	1.2 (0.8, 1.6)	115.9 (39.4, 192.4)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first). TIPI: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up. [b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years. [c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH and TIPI mixed models also contain a quadratic term for time. [d] Includes patients with baseline and at least one subsequent MRI assessment. [e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI. [f] Includes patients with at least one MRI and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. TIPI = Tipifarnib. FU = Follow-up
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smptefpn.sas smptefpnb.rtf 22MAR2021:17:13 icesas236PD

Table 1.8.3 Percent change in target PN volume Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

Gender = Male

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	29	1.8 (1.6, 2.1)	-9.4 (-13.3, -5.5)	-16.3	-21.2, -11.4
Natural History (age-matched) [e]	56	7.3 (6.1, 8.4)	24.1 (16.8, 31.4)	22.2	17.2, 27.2

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.8.3 Percent change in target PN volume Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

Gender = Female

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	19	1.8 (1.6, 2.1)	-9.4 (-13.9, -4.8)	-18.1	-22.9, -13.3
Natural History (age-matched) [e]	36	7.0 (5.6, 8.4)	21.1 (13.0, 29.2)	16.6	6.1, 27.1

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.8.3 Percent change in target PN volume Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Progressive

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	21	2.0 (1.7, 2.3)	-4.4 (-9.3, 0.4)	-15.1	-21.7, -8.5
Natural History (age-matched) [e]	34	6.7 (5.4, 8.1)	40.5 (29.0, 51.9)	31.2	22.8, 39.6

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.8.3 Percent change in target PN volume Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Not progressive

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	14	1.7 (1.4, 2.1)	-11.5 (-15.7, -7.3)	-19.2	-24.4, -13.9
Natural History (age-matched) [e]	49	8.1 (6.9, 9.2)	12.2 (8.9, 15.6)	13.1	9.6, 16.6

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.8.3 Percent change in target PN volume Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Unknown

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	13	1.7 (1.4, 2.0)	-15.1 (-19.6, -10.6)	-19.3	-24.0, -14.6
Natural History (age-matched) [e]	9	3.8 (0.9, 6.7)	14.7 (1.8, 27.6)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.8.4 Absolute change in target PN volume Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

Gender = Male

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	29	1.8 (1.6, 2.1)	-155 (-256.1, -53.8)	-91.3	-114.7, -67.9
Natural History (age-matched) [e]	56	7.3 (6.1, 8.4)	111.9 (59.7, 164.1)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.8.4 Absolute change in target PN volume Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

Gender = Female

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	Estimated annual PN growth rate Mixed Model [c] 95% CI
SPRINT Phase II Stratum I [d]	19	1.8 (1.6, 2.1)	-55.2 (-94.5, -15.9)	-98.8	-140.7, -56.9
Natural History (age-matched) [e]	36	7.0 (5.6, 8.4)	76.2 (31.3, 121.2)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.8.4 Absolute change in target PN volume Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Progressive

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	Estimated annual PN growth rate Mixed Model [c] 95% CI
SPRINT Phase II Stratum I [d]	21	2.0 (1.7, 2.3)	-35.4 (-70.2, -0.6)	-78.5	-110.5, -46.5
Natural History (age-matched) [e]	34	6.7 (5.4, 8.1)	148.0 (85.5, 210.5)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.8.4 Absolute change in target PN volume Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Not progressive

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	14	1.7 (1.4, 2.1)	-121 (-246.7, 4.0)	-90.6	-158.5, -22.8
Natural History (age-matched) [e]	49	8.1 (6.9, 9.2)	65.0 (17.4, 112.6)	54.3	28.1, 80.6

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.8.4 Absolute change in target PN volume Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Unknown

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	13	1.7 (1.4, 2.0)	-238 (-425.7, -51.1)	-113.5	-161.0, -66.1
Natural History (age-matched) [e]	9	3.8 (0.9, 6.7)	88.1 (-40.3, 216.4)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.9.1 Percent change in sum of all PN volumes Mean-Difference - Intervention vs. Control
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural Histry Study NF1 age-matched and Tipifarnib

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	48	1.8 (1.7, 2.0)	-10.1 (-12.8, -7.4)	-17.5	-20.7, -14.3
Natural History (age-matched) [e]	92	7.2 (6.3, 8.0)	22.9 (17.6, 28.3)	20.5	16.5, 24.5
Tipifarnib [f]	29	1.2 (0.8, 1.6)	32.7 (19.8, 45.6)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first). TIPI: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up. [b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years. [c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH and TIPI mixed models also contain a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment. [e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI. [f] Includes patients with at least one MRI and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. TIPI = Tipifarnib. FU = Follow-up
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Table 1.9.2 Absolute change in sum of all PN volumes Mean-Difference - Intervention vs. Control
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural Histry Study NF1 age-matched and Tipifarnib

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	48	1.8 (1.7, 2.0)	-128 (-195.1, -61.7)	-99.5	-130.3, -68.8
Natural History (age-matched) [e]	92	7.2 (6.3, 8.0)	97.9 (62.0, 133.8)	NC	NC
Tipifarnib [f]	29	1.2 (0.8, 1.6)	142.5 (65.7, 219.4)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first). TIPI: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up. [b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years. [c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH and TIPI mixed models also contain a quadratic term for time. [d] Includes patients with baseline and at least one subsequent MRI assessment. [e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI. [f] Includes patients with at least one MRI and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. TIPI = Tipifarnib. FU = Follow-up
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Table 1.9.3 Percent change in sum of all PN volumes Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

Gender = Male

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	29	1.8 (1.6, 2.1)	-10.5 (-14.1, -6.9)	-17.2	-21.9, -12.5
Natural History (age-matched) [e]	56	7.3 (6.1, 8.4)	24.1 (16.8, 31.4)	22.3	17.3, 27.3

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.

Table 1.9.3 Percent change in sum of all PN volumes Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

Gender = Female

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	19	1.8 (1.6, 2.1)	-9.4 (-14.1, -4.8)	-18.2	-23.1, -13.3
Natural History (age-matched) [e]	36	7.0 (5.6, 8.4)	21.1 (13.0, 29.2)	16.6	6.2, 27.1

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.9.3 Percent change in sum of all PN volumes Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Progressive

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	21	2.0 (1.7, 2.3)	-4.9 (-9.5, -0.4)	-15.9	-22.3, -9.4
Natural History (age-matched) [e]	34	6.7 (5.4, 8.1)	40.5 (29.0, 51.9)	31.2	22.8, 39.6

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.9.3 Percent change in sum of all PN volumes Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Not progressive

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	14	1.7 (1.4, 2.1)	-12.5 (-16.3, -8.6)	-19.9	-25.0, -14.8
Natural History (age-matched) [e]	49	8.1 (6.9, 9.2)	12.2 (8.9, 15.6)	13.2	9.7, 16.7

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.9.3 Percent change in sum of all PN volumes Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Unknown

Group	n	Time period, years [a] Mean (95% CI)	PN volume % change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	Estimated annual PN growth rate Mixed Model [c] 95% CI
SPRINT Phase II Stratum I [d]	13	1.7 (1.4, 2.0)	-15.9 (-19.9, -11.9)	-19.9	-24.1, -15.6
Natural History (age-matched) [e]	9	3.8 (0.9, 6.7)	14.7 (1.8, 27.6)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] % PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume % change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.9.4 Absolute change in sum of all PN volumes Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

Gender = Male

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	29	1.8 (1.6, 2.1)	-173 (-279.8, -65.7)	-109.0	-150.9, -67.1
Natural History (age-matched) [e]	56	7.3 (6.1, 8.4)	111.9 (59.7, 164.1)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.9.4 Absolute change in sum of all PN volumes Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

Gender = Female

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	19	1.8 (1.6, 2.1)	-60.7 (-100.1, -21.2)	-103.1	-145.3, -61.0
Natural History (age-matched) [e]	36	7.0 (5.6, 8.4)	76.2 (31.3, 121.2)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.9.4 Absolute change in sum of all PN volumes Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Progressive

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	Estimated annual PN growth rate Mixed Model [c] 95% CI
SPRINT Phase II Stratum I [d]	21	2.0 (1.7, 2.3)	-32.9 (-74.1, 8.3)	-79.3	-122.8, -35.9
Natural History (age-matched) [e]	34	6.7 (5.4, 8.1)	148.0 (85.5, 210.5)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.9.4 Absolute change in sum of all PN volumes Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Not progressive

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	95% CI
SPRINT Phase II Stratum I [d]	14	1.7 (1.4, 2.1)	-153 (-290.5, -15.1)	-118.6	-191.5, -45.8
Natural History (age-matched) [e]	49	8.1 (6.9, 9.2)	65.0 (17.4, 112.6)	73.4	47.4, 99.5

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.9.4 Absolute change in sum of all PN volumes Mean-Difference - Intervention vs. Control by subgroups
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018 and Natural Histry Study NF1 age-matched

PN status at enrollment = Unknown

Group	n	Time period, years [a] Mean (95% CI)	PN volume change / year [b], Mean (95% CI)	Estimated annual PN growth rate Mixed Model [c] Adjusted Mean	Estimated annual PN growth rate Mixed Model [c] 95% CI
SPRINT Phase II Stratum I [d]	13	1.7 (1.4, 2.0)	-256 (-444.8, -68.0)	-175.0	-224.6, -125.3
Natural History (age-matched) [e]	9	3.8 (0.9, 6.7)	88.1 (-40.3, 216.4)	NC	NC

[a] NH: Time period is defined from the first to the last available MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib. SPRINT: Time period is defined from the baseline MRI assessment date to the last evaluable assessment date up to data cut-off or treatment discontinuation (whichever occurred first).
[b] PN volume change from the first MRI (baseline MRI for SPRINT) to the last MRI assessment over time period in years.
[c] Mixed models include PN volume change as response, time (years), baseline age and baseline PN volume as covariates. NH mixed model also contains a quadratic term for time.
[d] Includes patients with baseline and at least one subsequent MRI assessment.
[e] Includes patients aged 3 to 18 years with at least one MRI within this age and one subsequent MRI.
NC = Not Calculable. CI = Confidence interval. PN = Plexiform neurofibromas. NH = Natural History. FU = Follow-up.
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Table 1.10.1 Best percentage change from baseline in target PN volume - NCI assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup		Selumetinib 25 mg/m² BID (N=50)
Gender: Male (n=30)	n	29
	Mean	-24.58
	SD	12.481
	Min	-54.5
	Median	-25.24
	Max	-1.0
	Proportion with any reduction	100
	Proportion with reduction >= 20%	72.4
	Proportion with reduction >= 40%	6.9
	Proportion with reduction >= 60%	0
	Proportion with reduction >= 80%	0
Gender: Female (n=20)	n	19
	Mean	-26.34
	SD	12.357
	Min	-43.1
	Median	-28.78
	Max	2.2
	Proportion with any reduction	89.5
	Proportion with reduction >= 20%	84.2
	Proportion with reduction >= 40%	5.3
	Proportion with reduction >= 60%	0
	Proportion with reduction >= 80%	0

Best change in PN volume is the maximum reduction from baseline, or the minimum increase from baseline in the absence of a reduction.
n is the number of patients with at least one post-baseline PN volume measurement.
A negative value denotes a reduction in PN volume.
Proportion is based on number of non-missing results within each subgroup.
SD = Standard deviation
Includes patient 2019002 who only has partial volumes throughout the study.
REiNS assessment.

Table 1.10.1 Best percentage change from baseline in target PN volume - NCI assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup		Selumetinib 25 mg/m² BID (N=50)
PN status at enrollment: Progressive (n=21)	n	21
	Mean	-24.08
	SD	15.483
	Min	-54.5
	Median	-28.49
	Max	2.2
	Proportion with any reduction	90.5
	Proportion with reduction >= 20%	66.7
	Proportion with reduction >= 40%	9.5
	Proportion with reduction >= 60%	0
	Proportion with reduction >= 80%	0
PN status at enrollment: Non-progressive (n=15)	n	14
	Mean	-24.74
	SD	11.098
	Min	-43.1
	Median	-26.43
	Max	-1.0
	Proportion with any reduction	100
	Proportion with reduction >= 20%	78.6
	Proportion with reduction >= 40%	7.1
	Proportion with reduction >= 60%	0
	Proportion with reduction >= 80%	0

Best change in PN volume is the maximum reduction from baseline, or the minimum increase from baseline in the absence of a reduction.
n is the number of patients with at least one post-baseline PN volume measurement.
A negative value denotes a reduction in PN volume.
Proportion is based on number of non-missing results within each subgroup.
SD = Standard deviation
Includes patient 2019002 who only has partial volumes throughout the study.
REiNS assessment.

Table 1.10.1 Best percentage change from baseline in target PN volume - NCI assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup		Selumetinib 25 mg/m² BID (N=50)
PN status at enrollment: Unknown (n=14)	n	13
	Mean	-27.80
	SD	7.266
	Min	-38.9
	Median	-25.24
	Max	-16.4
	Proportion with any reduction	100
	Proportion with reduction >= 20%	92.3
	Proportion with reduction >= 40%	0
	Proportion with reduction >= 60%	0
	Proportion with reduction >= 80%	0

Best change in PN volume is the maximum reduction from baseline, or the minimum increase from baseline in the absence of a reduction.
n is the number of patients with at least one post-baseline PN volume measurement.
A negative value denotes a reduction in PN volume.
Proportion is based on number of non-missing results within each subgroup.
SD = Standard deviation
Includes patient 2019002 who only has partial volumes throughout the study.
REiNS assessment.

Table 1.10.2 Best percentage change from baseline in target PN volume - ICR assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup		Selumetinib 25 mg/m² BID (N=50)
Gender: Male (n=30)	n	29
	Mean	-23.32
	SD	11.594
	Min	-53.7
	Median	-20.50
	Max	-5.2
	Proportion with any reduction	100
	Proportion with reduction >= 20%	51.7
	Proportion with reduction >= 40%	13.8
	Proportion with reduction >= 60%	0
	Proportion with reduction >= 80%	0
Gender: Female (n=20)	n	19
	Mean	-23.56
	SD	16.003
	Min	-45.6
	Median	-23.60
	Max	9.5
	Proportion with any reduction	89.5
	Proportion with reduction >= 20%	63.2
	Proportion with reduction >= 40%	26.3
	Proportion with reduction >= 60%	0
	Proportion with reduction >= 80%	0

Best change in PN volume is the maximum reduction from baseline, or the minimum increase from baseline in the absence of a reduction.
n is the number of patients with at least one post-baseline PN volume measurement.
A negative value denotes a reduction in PN volume.
Proportion is based on number of non-missing results within each subgroup.
SD = Standard deviation
Modified REiNS (ICR) assessment.

Table 1.10.2 Best percentage change from baseline in target PN volume - ICR assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup		Selumetinib 25 mg/m² BID (N=50)
PN status at enrollment: Progressive (n=21)	n	21
	Mean	-24.35
	SD	13.753
	Min	-53.7
	Median	-25.50
	Max	2.6
	Proportion with any reduction	95.2
	Proportion with reduction >= 20%	71.4
	Proportion with reduction >= 40%	19.0
	Proportion with reduction >= 60%	0
	Proportion with reduction >= 80%	0
PN status at enrollment: Non-progressive (n=15)	n	14
	Mean	-24.24
	SD	12.655
	Min	-43.8
	Median	-20.85
	Max	-6.9
	Proportion with any reduction	100
	Proportion with reduction >= 20%	50.0
	Proportion with reduction >= 40%	21.4
	Proportion with reduction >= 60%	0
	Proportion with reduction >= 80%	0

Best change in PN volume is the maximum reduction from baseline, or the minimum increase from baseline in the absence of a reduction.
n is the number of patients with at least one post-baseline PN volume measurement.
A negative value denotes a reduction in PN volume.
Proportion is based on number of non-missing results within each subgroup.
SD = Standard deviation
Modified REiNS (ICR) assessment.

Table 1.10.2 Best percentage change from baseline in target PN volume - ICR assessment by subgroups (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Subgroup		Selumetinib 25 mg/m² BID (N=50)
PN status at enrollment: Unknown (n=14)	n	13
	Mean	-21.01
	SD	14.158
	Min	-45.6
	Median	-19.80
	Max	9.5
	Proportion with any reduction	92.3
	Proportion with reduction >= 20%	38.5
	Proportion with reduction >= 40%	15.4
	Proportion with reduction >= 60%	0
	Proportion with reduction >= 80%	0

Best change in PN volume is the maximum reduction from baseline, or the minimum increase from baseline in the absence of a reduction.
n is the number of patients with at least one post-baseline PN volume measurement.
A negative value denotes a reduction in PN volume.
Proportion is based on number of non-missing results within each subgroup.
SD = Standard deviation
Modified REiNS (ICR) assessment.

Table 1.11.1 Progression-free Survival (Unadjusted Cox model) - Gender = Male
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019

Analysis	Hazard Ratio	95% CI	P-value
Cox model: Naïve analysis	0.09	0.02, 0.39	<0.001
Cox model: Weighted by stabilized IPTW	0.09	0.02, 0.39	<0.001
Cox model: Weighted by IPTW (robust variance estimator)	0.09	0.02, 0.37	<0.001
Cox model: Matched patients 1:1 (robust variance estimator) [a][c]	0.12	0.03, 0.51	0.004
Cox model: Matched patients 1:2 (robust variance estimator) [b][c]	0.11	0.03, 0.41	0.001

HR is obtained using Cox regression including study as the only covariate.
[a] Greedy Matching algorithm is used without replacement.
[b] Each treated patient is matched up to 2 controls. Matching is performed with replacement.
[c] The difference in the logit of the propensity score for a match must be less than or equal to 0.2 times the pooled estimate of the common standard deviation of the logits of the propensity scores.
NC = Not calculated.

Table 1.11.2 Progression-free Survival (Unadjusted Cox model) - Gender = Female
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019

Analysis	Hazard Ratio	95% CI	P-value
Cox model: Naïve analysis	0.10	0.01, 0.74	0.002
Cox model: Weighted by stabilized IPTW	0.05	0.00, 0.65	<0.001
Cox model: Weighted by IPTW (robust variance estimator)	0.05	0.01, 0.45	0.007
Cox model: Matched patients 1:1 (robust variance estimator) [a][c]	0.12	0.02, 0.87	0.037
Cox model: Matched patients 1:2 (robust variance estimator) [b][c]	0.11	0.02, 0.78	0.027

HR is obtained using Cox regression including study as the only covariate.
[a] Greedy Matching algorithm is used without replacement.
[b] Each treated patient is matched up to 2 controls. Matching is performed with replacement.
[c] The difference in the logit of the propensity score for a match must be less than or equal to 0.2 times the pooled estimate of the common standard deviation of the logits of the propensity scores.
NC = Not calculated.

Table 1.11.3 Progression-free Survival (Unadjusted Cox model) - PN status at enrollment = Progressive
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019

Analysis	Hazard Ratio	95% CI	P-value
Cox model: Naïve analysis	0.10	0.03, 0.35	<0.001
Cox model: Weighted by stabilized IPTW	0.11	0.03, 0.41	<0.001
Cox model: Weighted by IPTW (robust variance estimator)	0.11	0.04, 0.35	<0.001
Cox model: Matched patients 1:1 (robust variance estimator) [a][c]	0.17	0.05, 0.66	0.010
Cox model: Matched patients 1:2 (robust variance estimator) [b][c]	0.19	0.07, 0.57	0.003

HR is obtained using Cox regression including study as the only covariate.
[a] Greedy Matching algorithm is used without replacement.
[b] Each treated patient is matched up to 2 controls. Matching is performed with replacement.
[c] The difference in the logit of the propensity score for a match must be less than or equal to 0.2 times the pooled estimate of the common standard deviation of the logits of the propensity scores.
NC = Not calculated.

Table 1.11.4 Progression-free Survival (Unadjusted Cox model) - PN status at enrollment = Non-progressive
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019

Analysis	Hazard Ratio	95% CI	P-value
Cox model: Naïve analysis	<0.001	0.00, NC	0.001
Cox model: Weighted by stabilized IPTW	<0.001	0.00, NC	<0.001
Cox model: Weighted by IPTW (robust variance estimator)	<0.001	<0.001, <0.001	<0.001
Cox model: Matched patients 1:1 (robust variance estimator) [a][c]	<0.001	<0.001, <0.001	<0.001
Cox model: Matched patients 1:2 (robust variance estimator) [b][c]	<0.001	<0.001, <0.001	<0.001

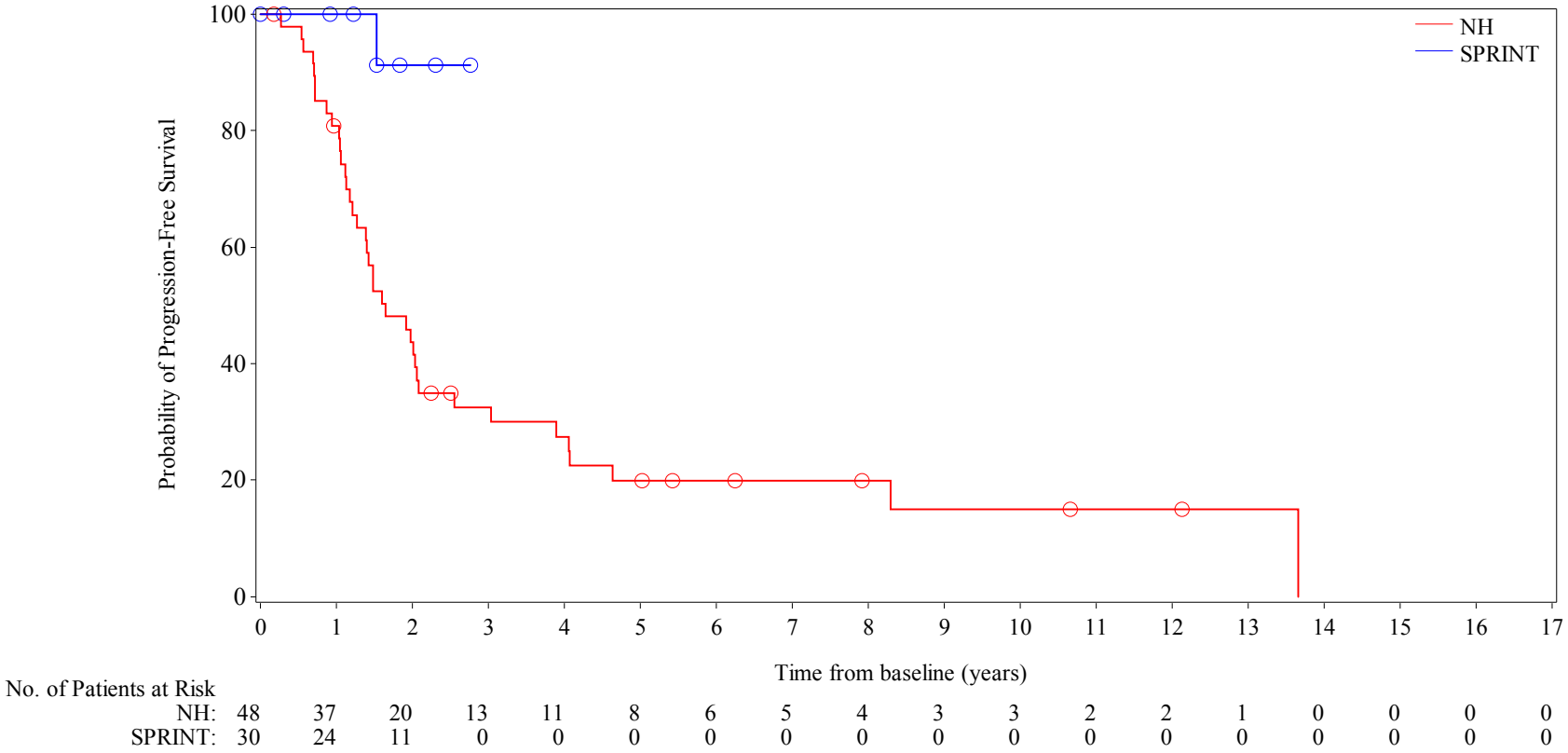
HR is obtained using Cox regression including study as the only covariate.
[a] Greedy Matching algorithm is used without replacement.
[b] Each treated patient is matched up to 2 controls. Matching is performed with replacement.
[c] The difference in the logit of the propensity score for a match must be less than or equal to 0.2 times the pooled estimate of the common standard deviation of the logits of the propensity scores.
NC = Not calculated.

Table 1.11.5 Progression-free Survival (Unadjusted Cox model) - PN status at enrollment = Unknown
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019

Analysis	Hazard Ratio	95% CI	P-value
Cox model: Naïve analysis	<0.001	0.00, NC	0.002
Cox model: Weighted by stabilized IPTW	<0.001	0.00, NC	0.006
Cox model: Weighted by IPTW (robust variance estimator)	<0.001	<0.001, <0.001	<0.001
Cox model: Matched patients 1:1 (robust variance estimator) [a][c]	<0.001	<0.001, <0.001	<0.001
Cox model: Matched patients 1:2 (robust variance estimator) [b][c]	<0.001	<0.001, <0.001	<0.001

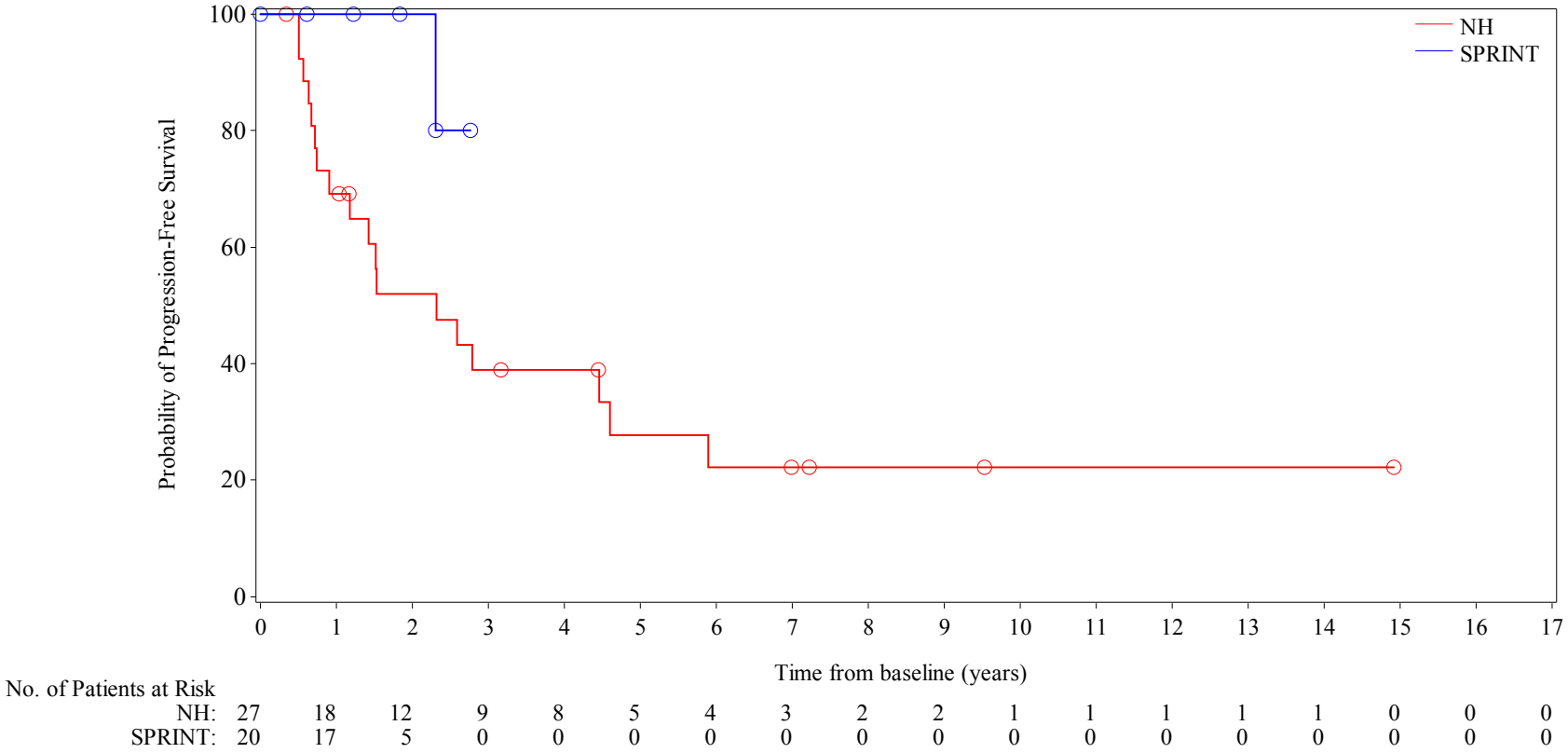
HR is obtained using Cox regression including study as the only covariate.
[a] Greedy Matching algorithm is used without replacement.
[b] Each treated patient is matched up to 2 controls. Matching is performed with replacement.
[c] The difference in the logit of the propensity score for a match must be less than or equal to 0.2 times the pooled estimate of the common standard deviation of the logits of the propensity scores.
NC = Not calculated.

Figure 1.12.1.1 Progression-free Survival (PFS) Kaplan-Meier plot - Gender = Male
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



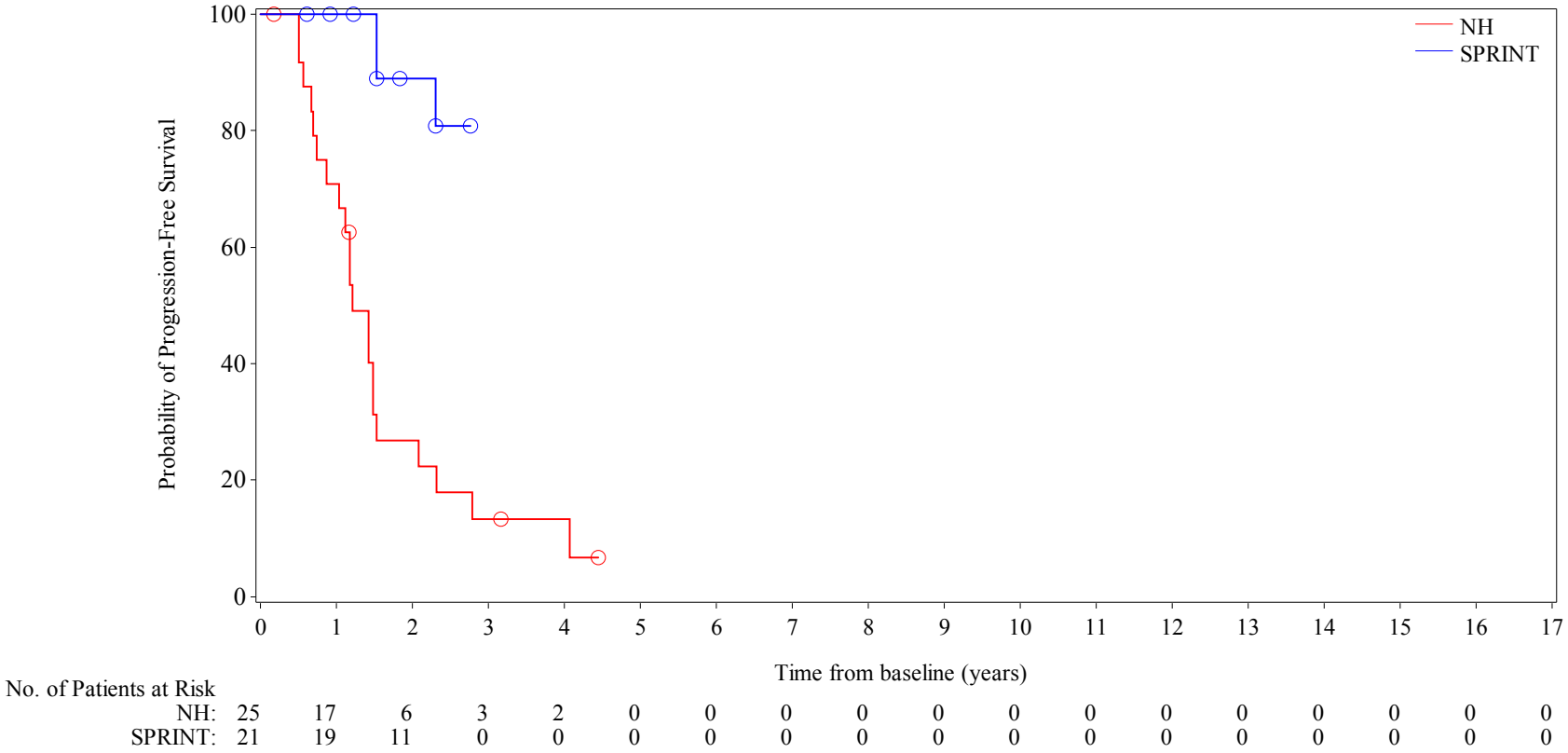
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.1.2 Progression-free Survival (PFS) Kaplan-Meier plot - Gender = Female
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



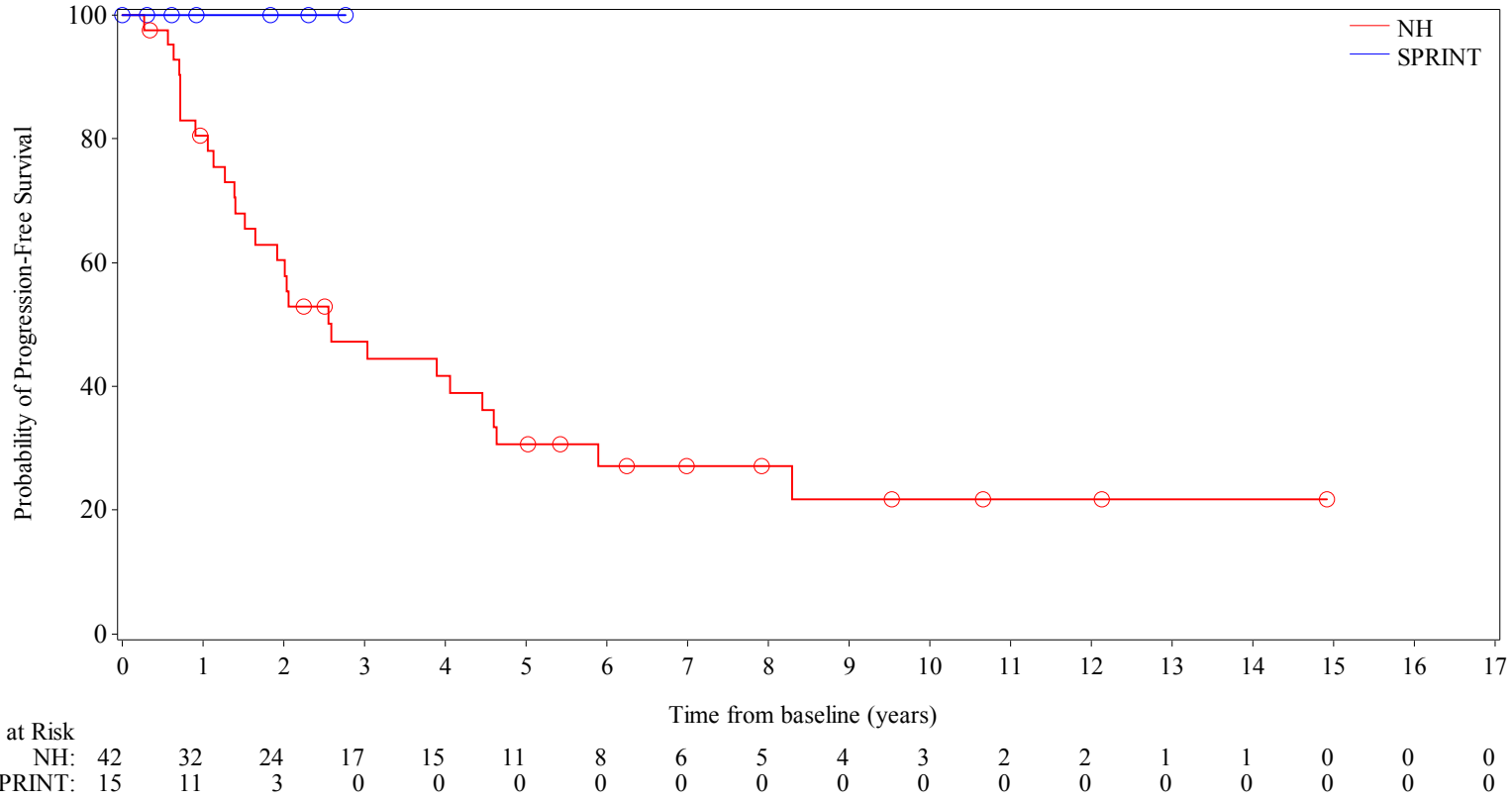
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.1.3 Progression-free Survival (PFS) Kaplan-Meier plot - PN status at enrollment = Progressive
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



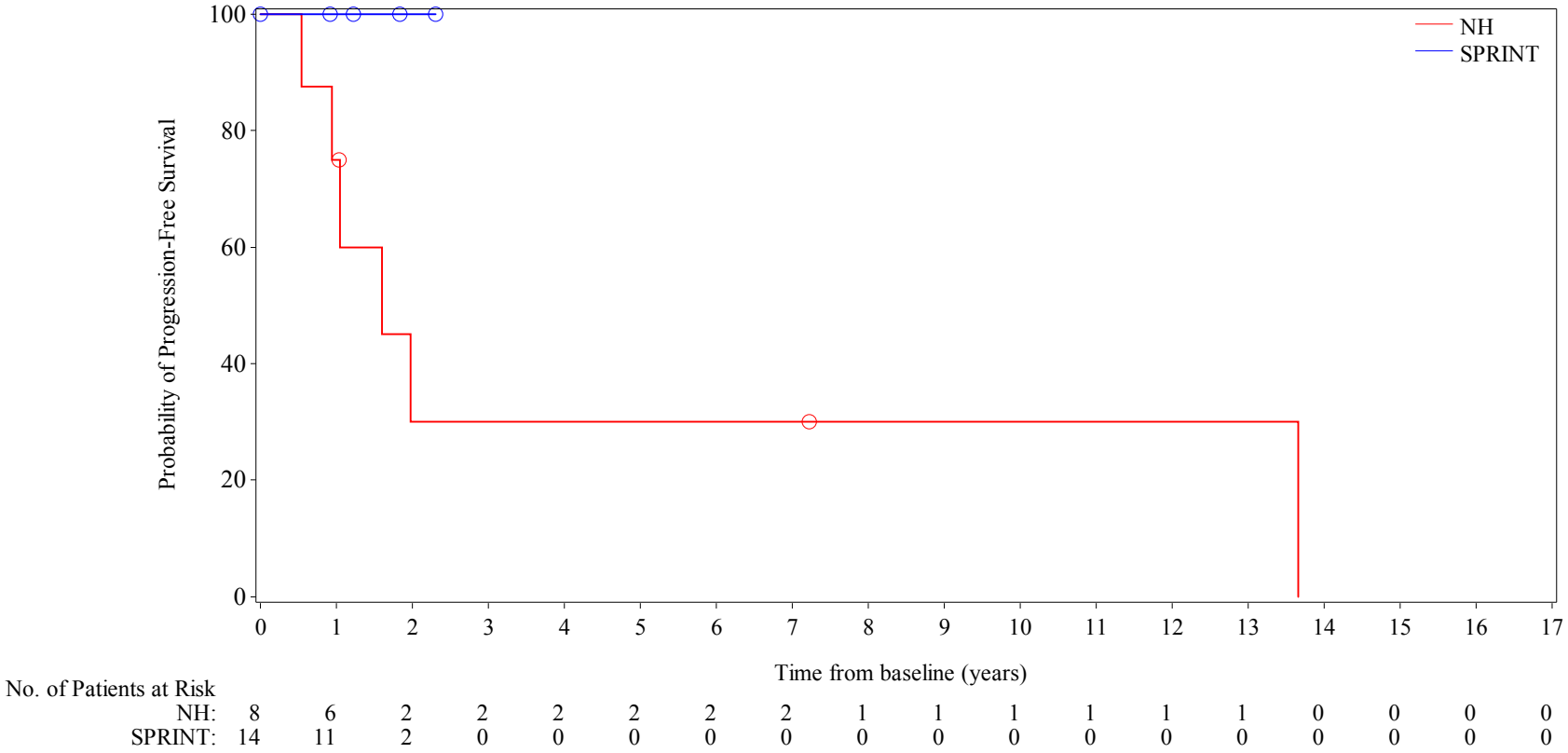
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.1.4 Progression-free Survival (PFS) Kaplan-Meier plot - PN status at enrollment = Non-progressive
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



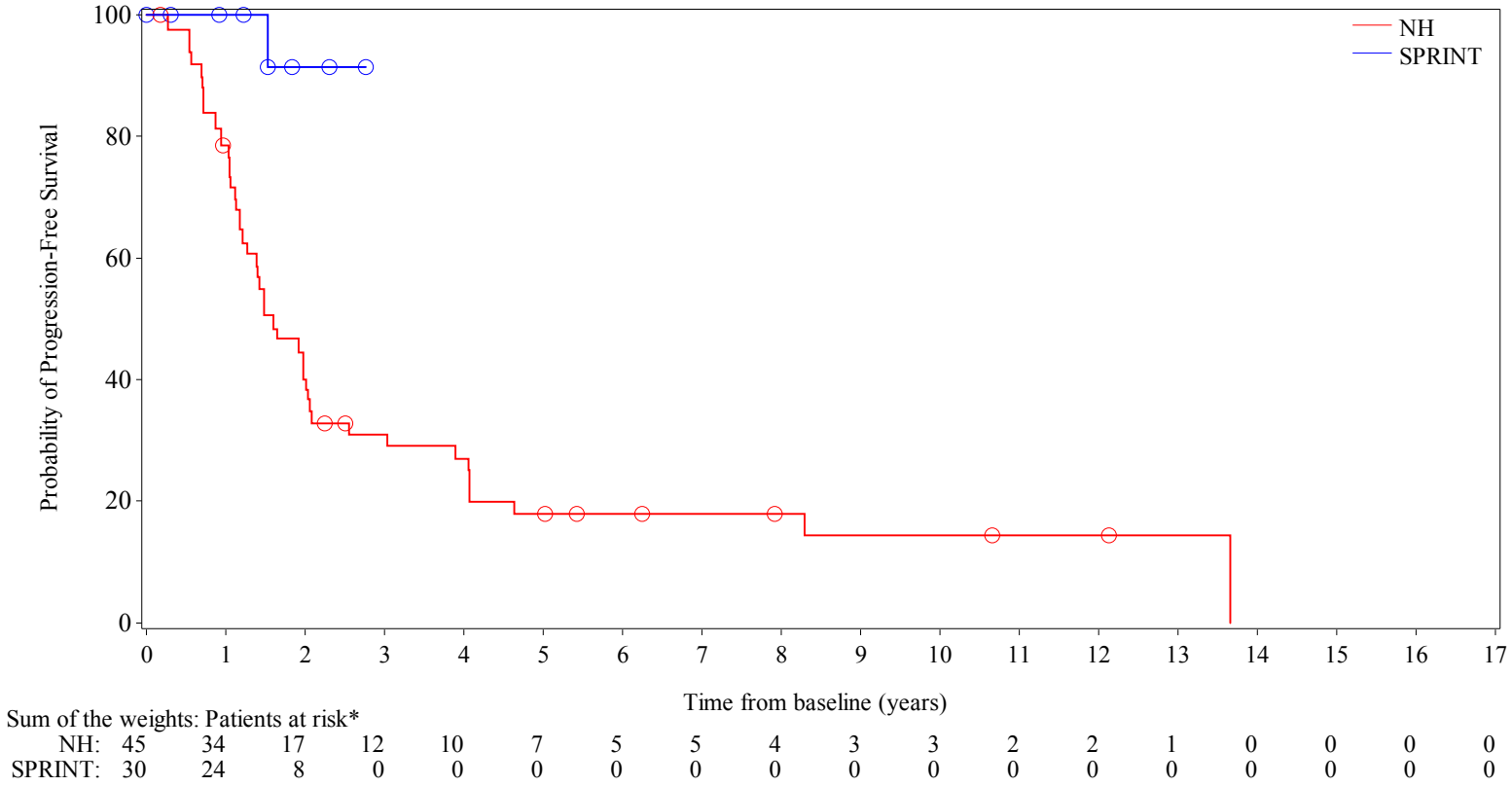
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.1.5 Progression-free Survival (PFS) Kaplan-Meier plot - PN status at enrollment = Unknown
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



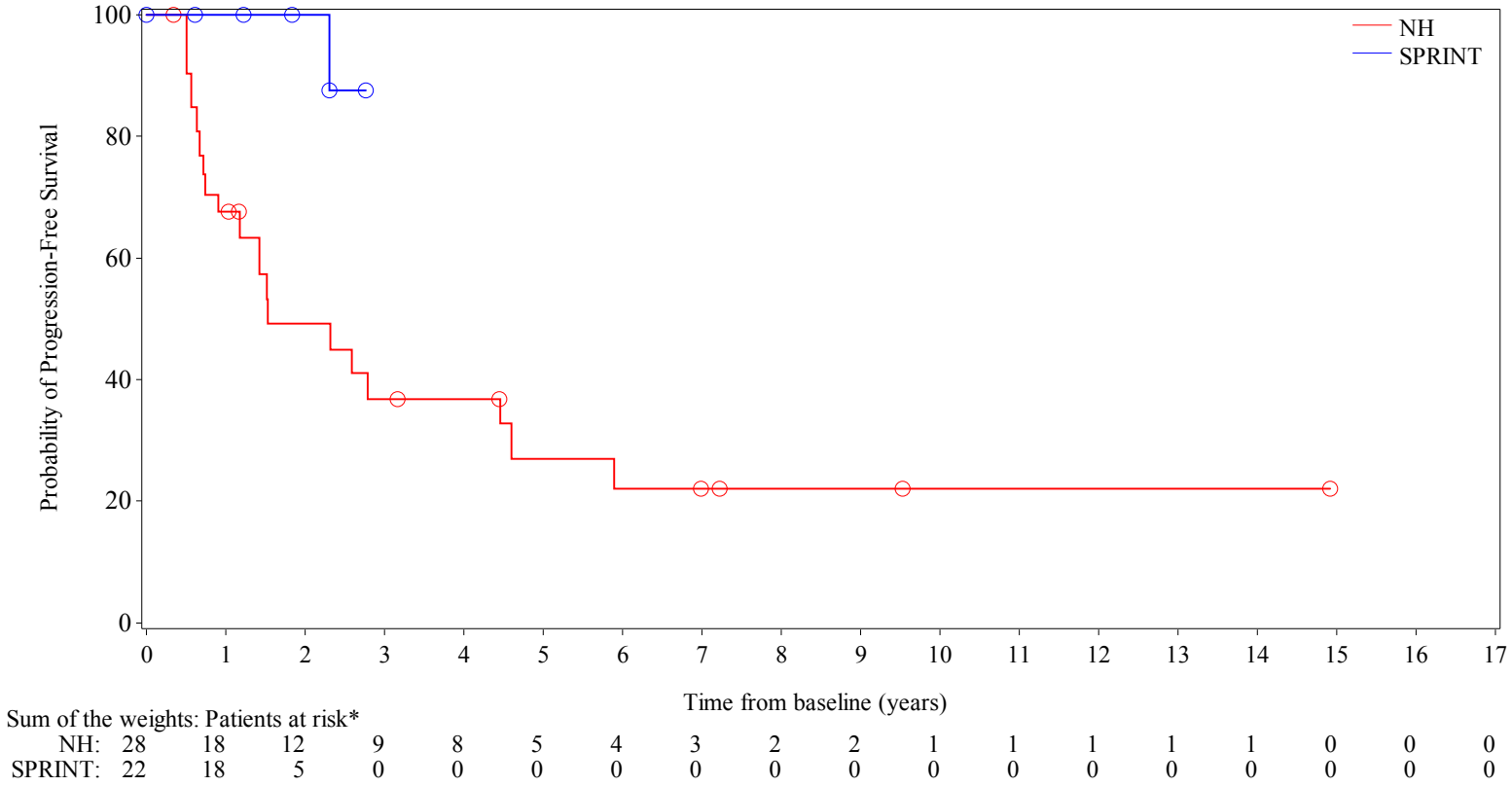
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.2.1 Progression-free Survival (PFS) Kaplan-Meier plot (weighting by the stabilized weights) - Gender = Male
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



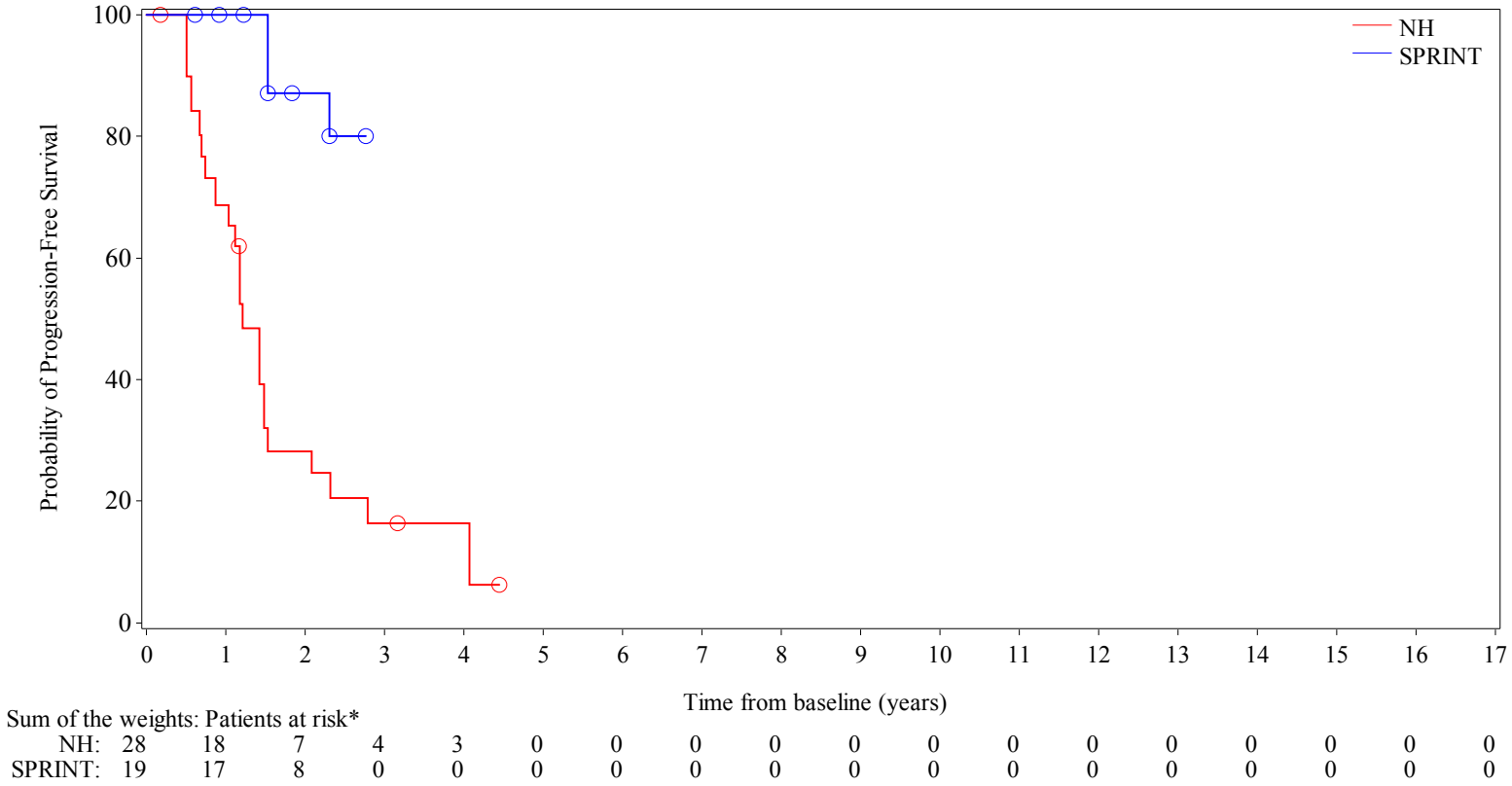
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.2.2 Progression-free Survival (PFS) Kaplan-Meier plot (weighting by the stabilized weights) - Gender = Female
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



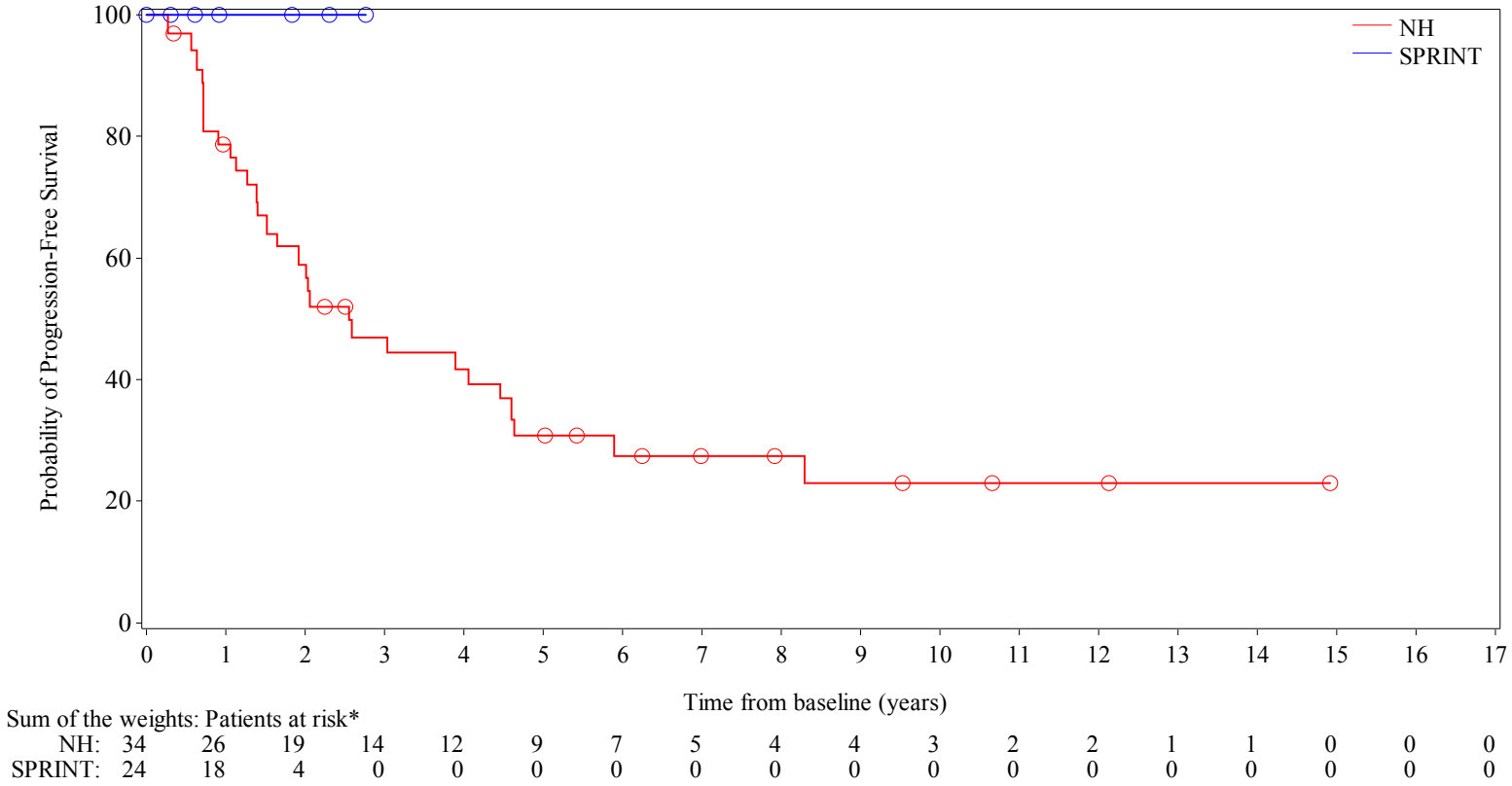
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.2.3 Progression-free Survival (PFS) K-M plot (weighting by the stabilized weights) - PN status at enrol.= Progressive
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



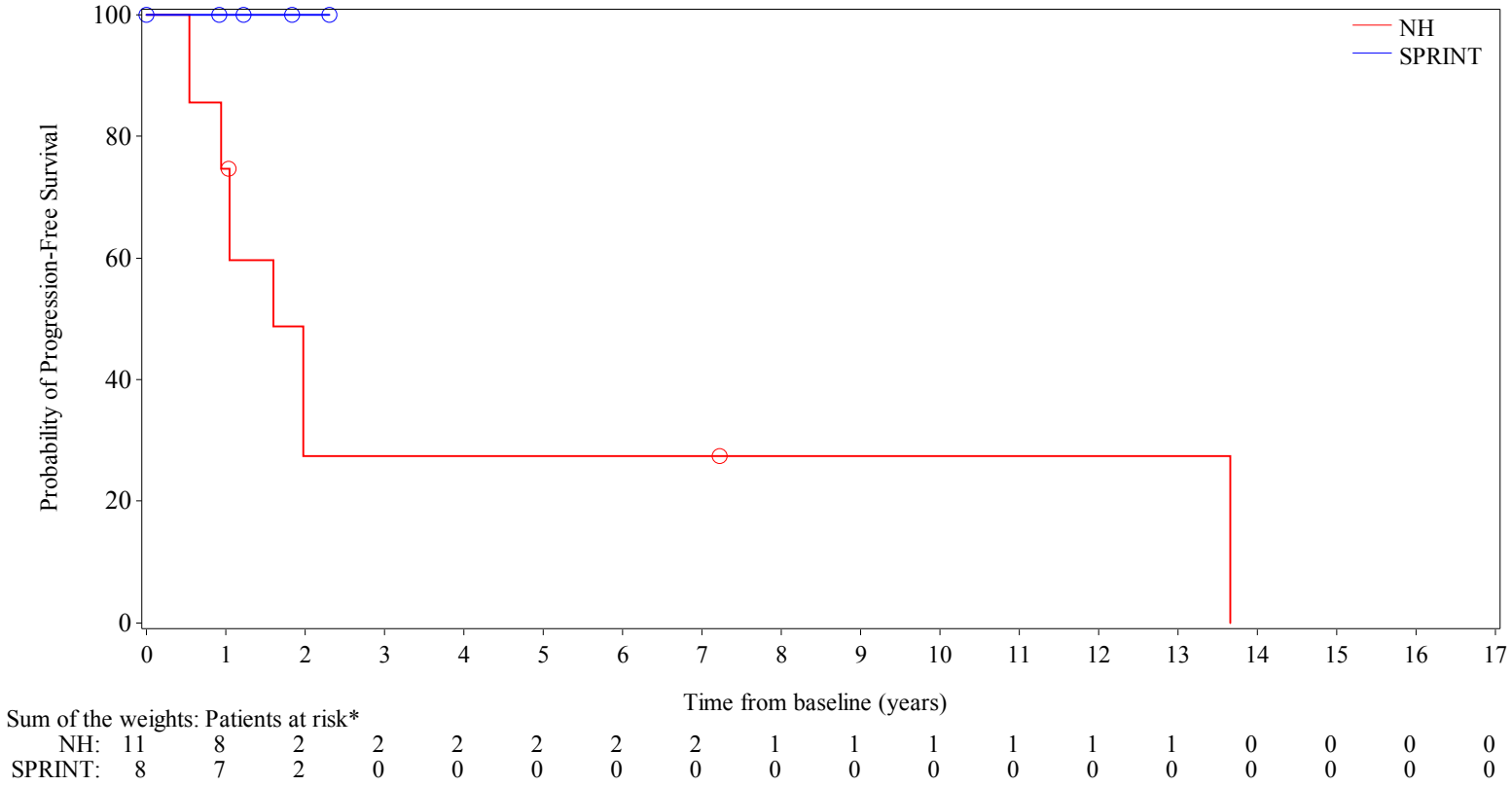
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.2.4 Progression-free Survival (PFS) K-M plot (weighting by the stabilized weights) - PN status at enrol.= Non-progr.
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



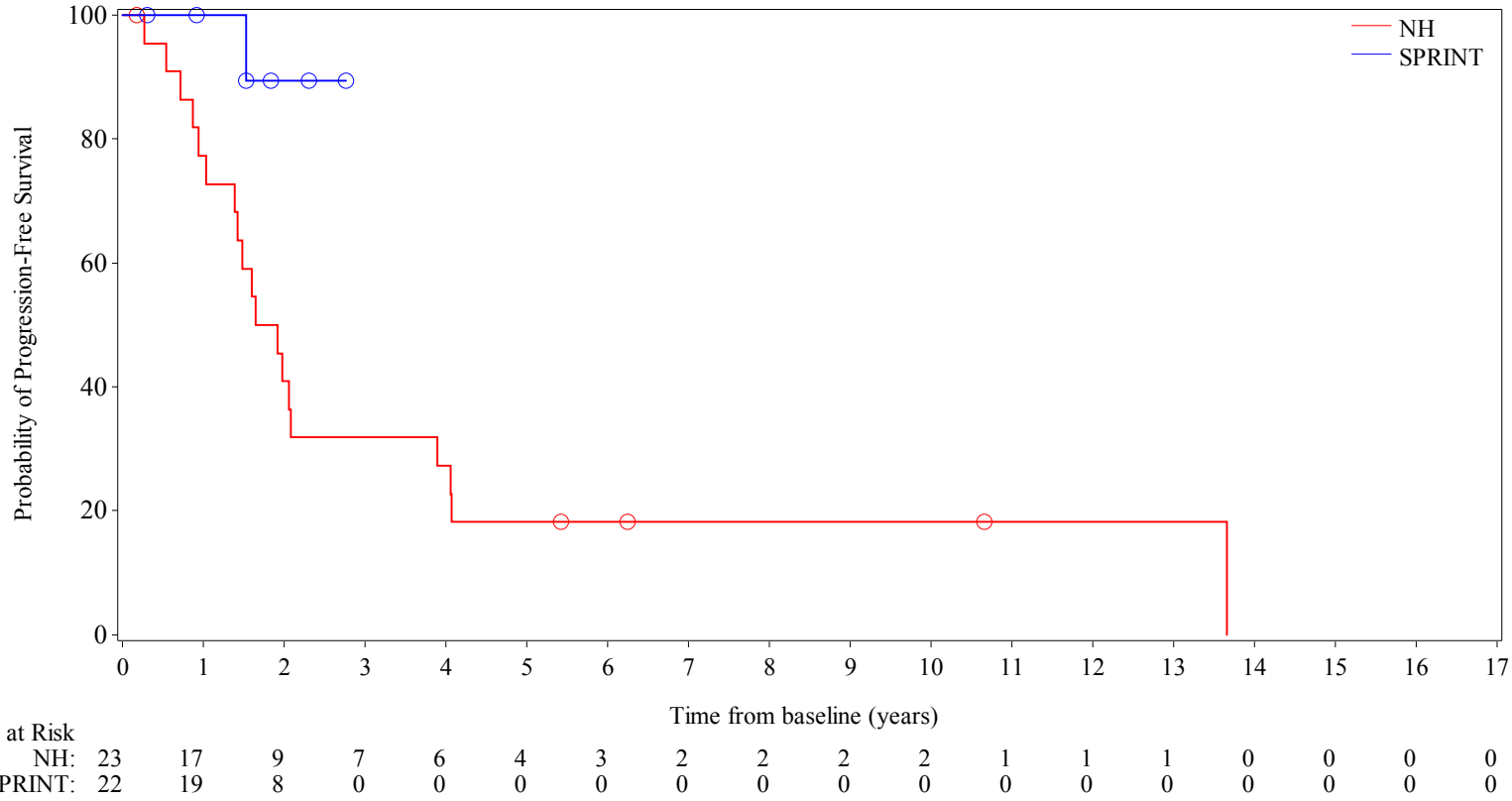
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.2.5 Progression-free Survival (PFS) K-M plot (weighting by the stabilized weights) - PN status at enrol.= Unknown
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



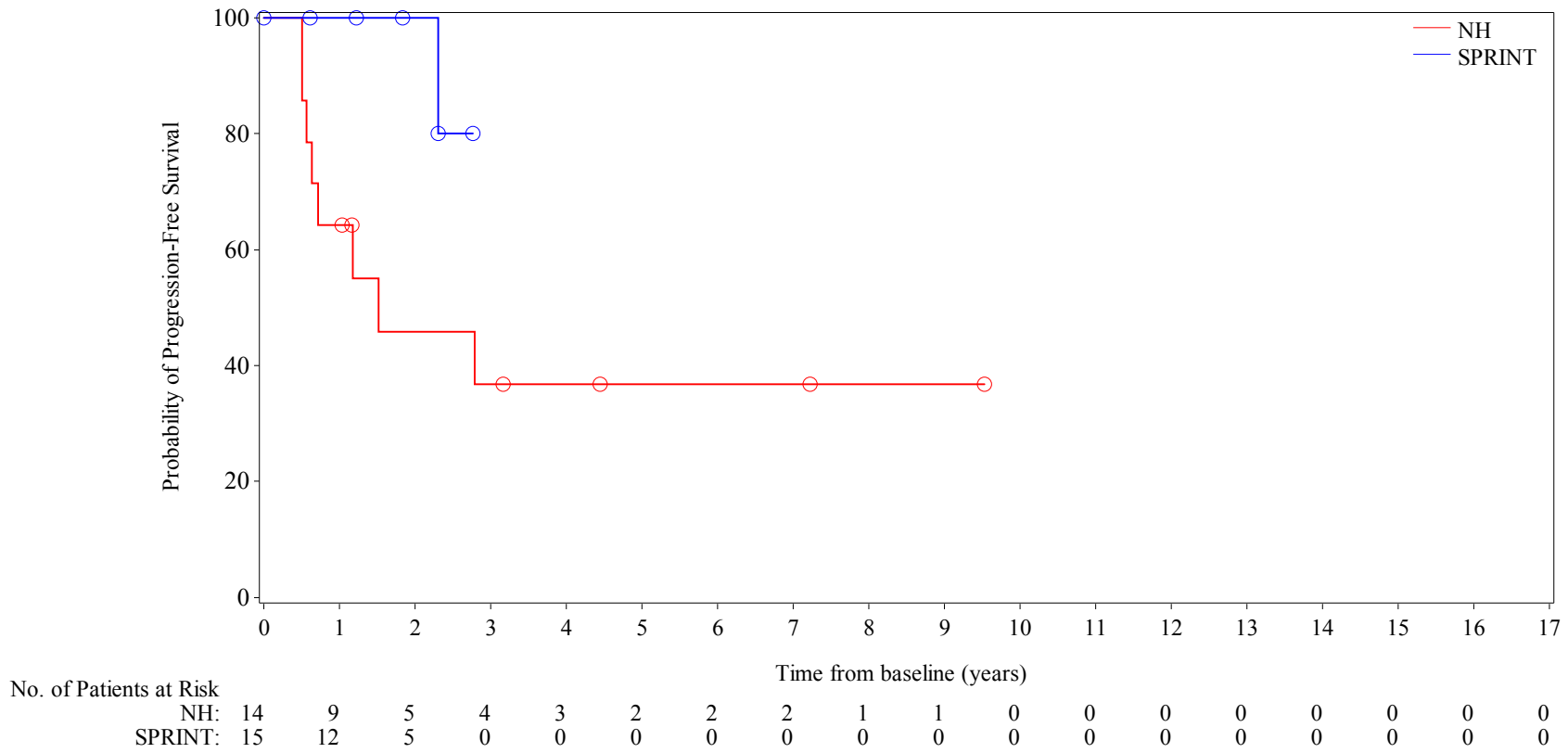
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.3.1 Progression-free Survival (PFS) Kaplan-Meier plot (post 1:1 matching) - Gender = Male
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



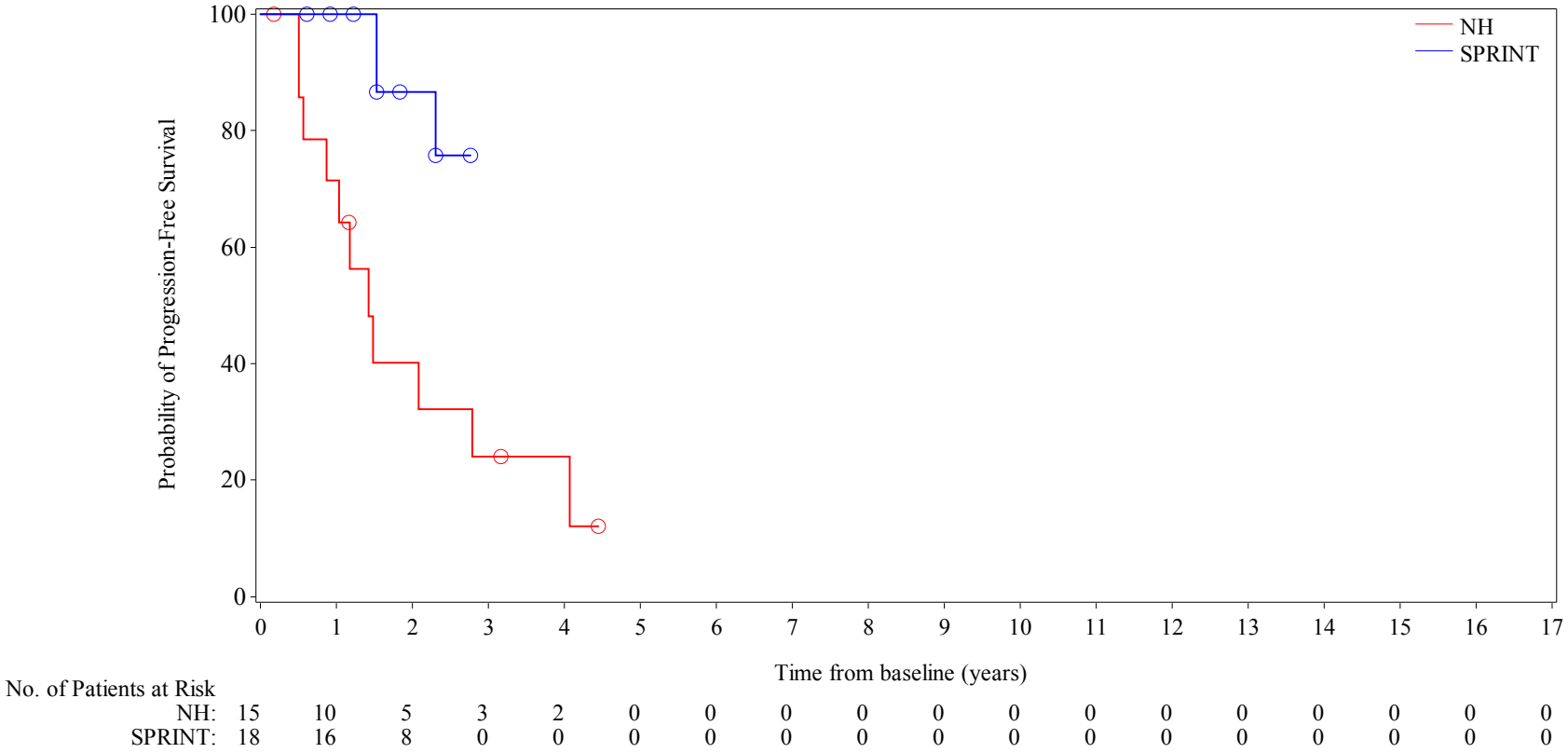
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.3.2 Progression-free Survival (PFS) Kaplan-Meier plot (post 1:1 matching) - Gender = Female
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



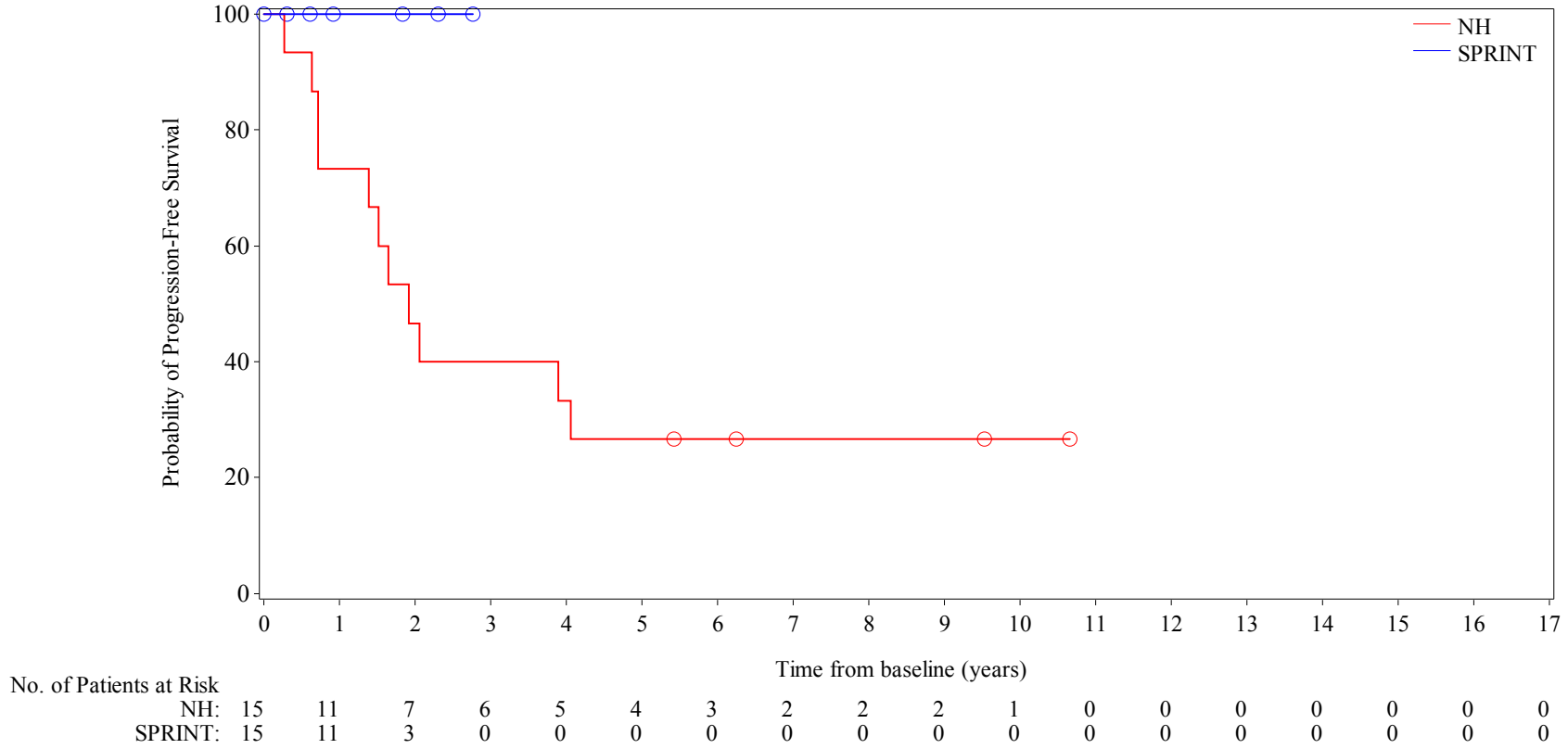
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.3.3 Progression-free Survival (PFS) Kaplan-Meier plot (post 1:1 matching) - PN status at enrollment = Progressive
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



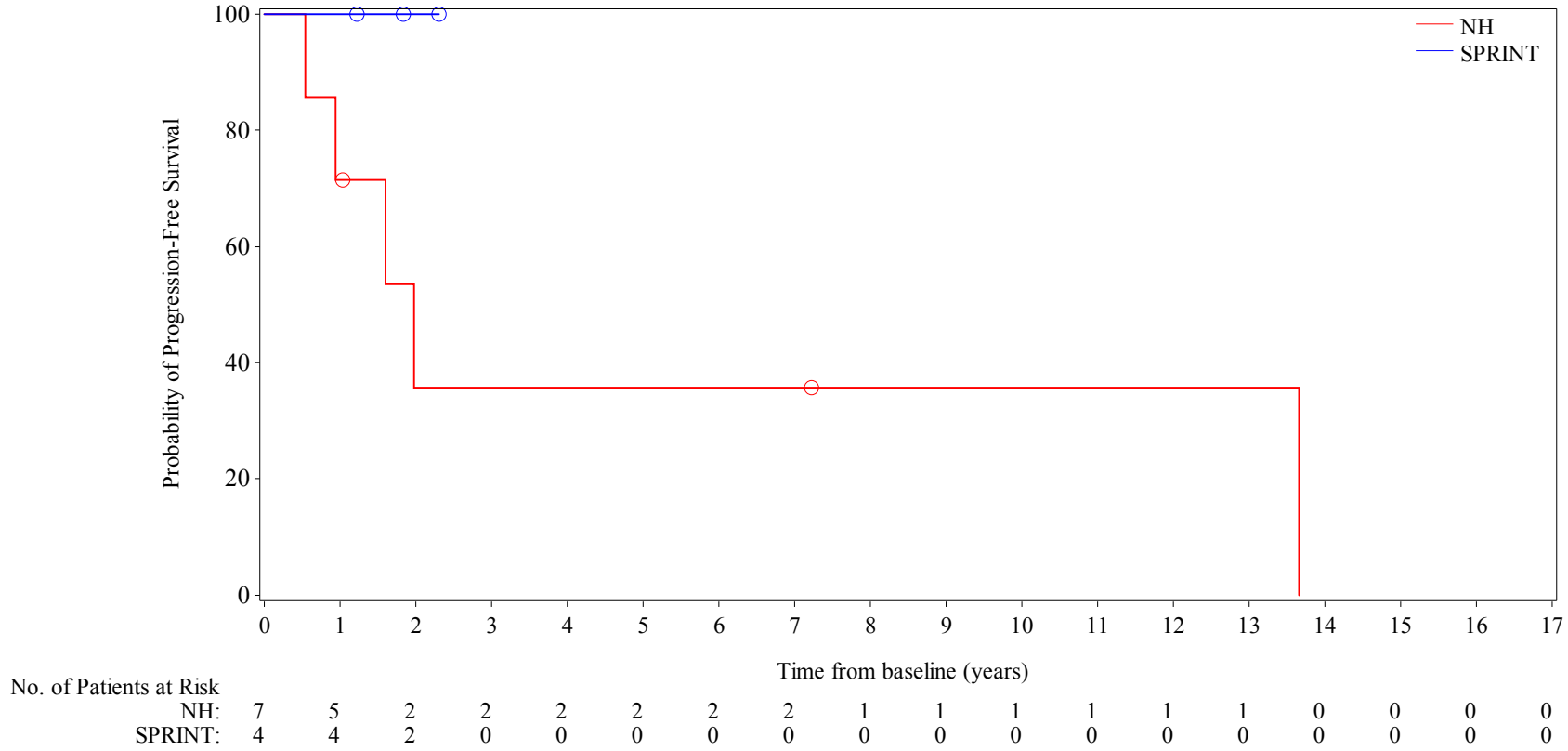
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.3.4 Progression-free Survival (PFS) Kaplan-Meier plot (post 1:1 matching) - PN status at enrollment = Non-progressive
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



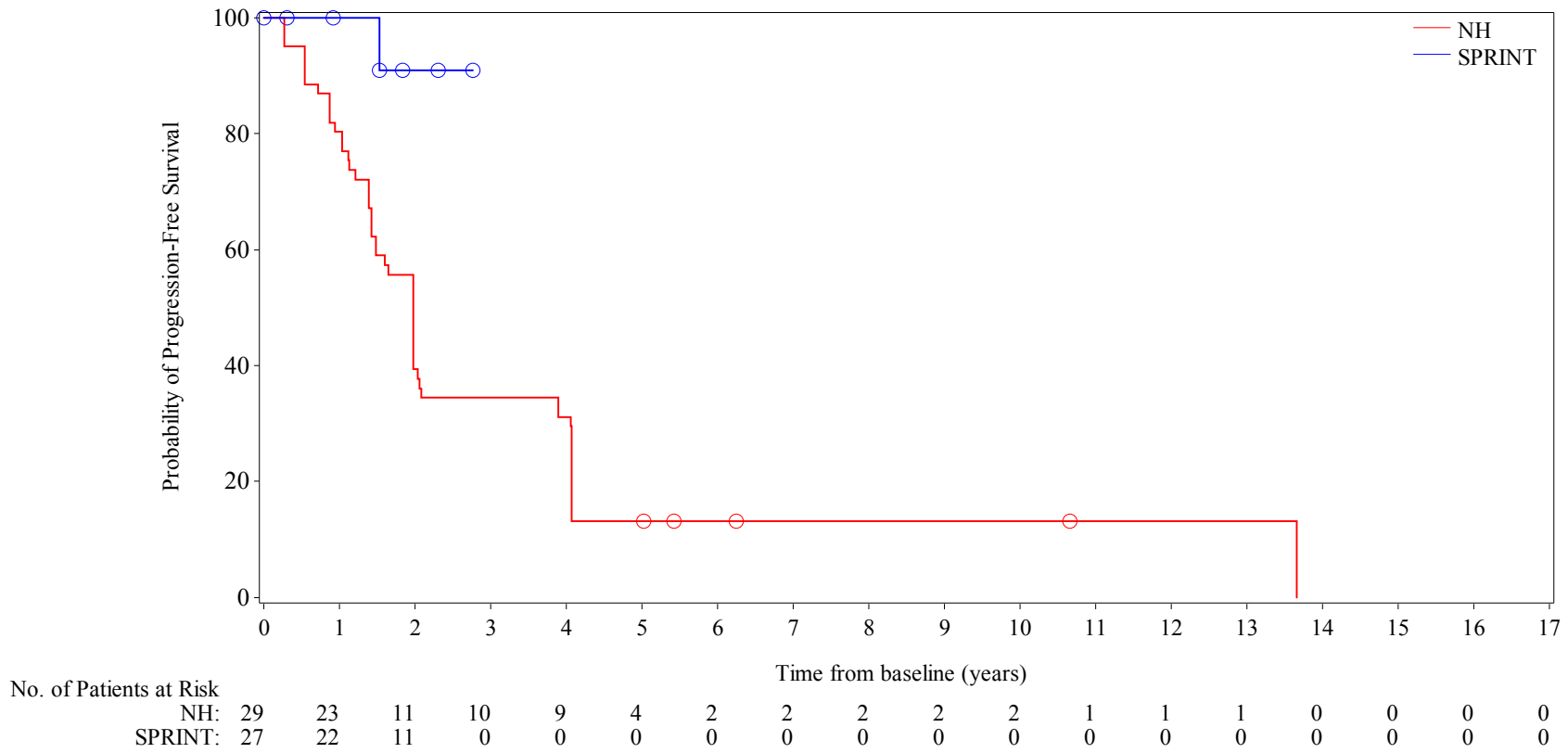
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.3.5 Progression-free Survival (PFS) Kaplan-Meier plot (post 1:1 matching) - PN status at enrollment = Unknown
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



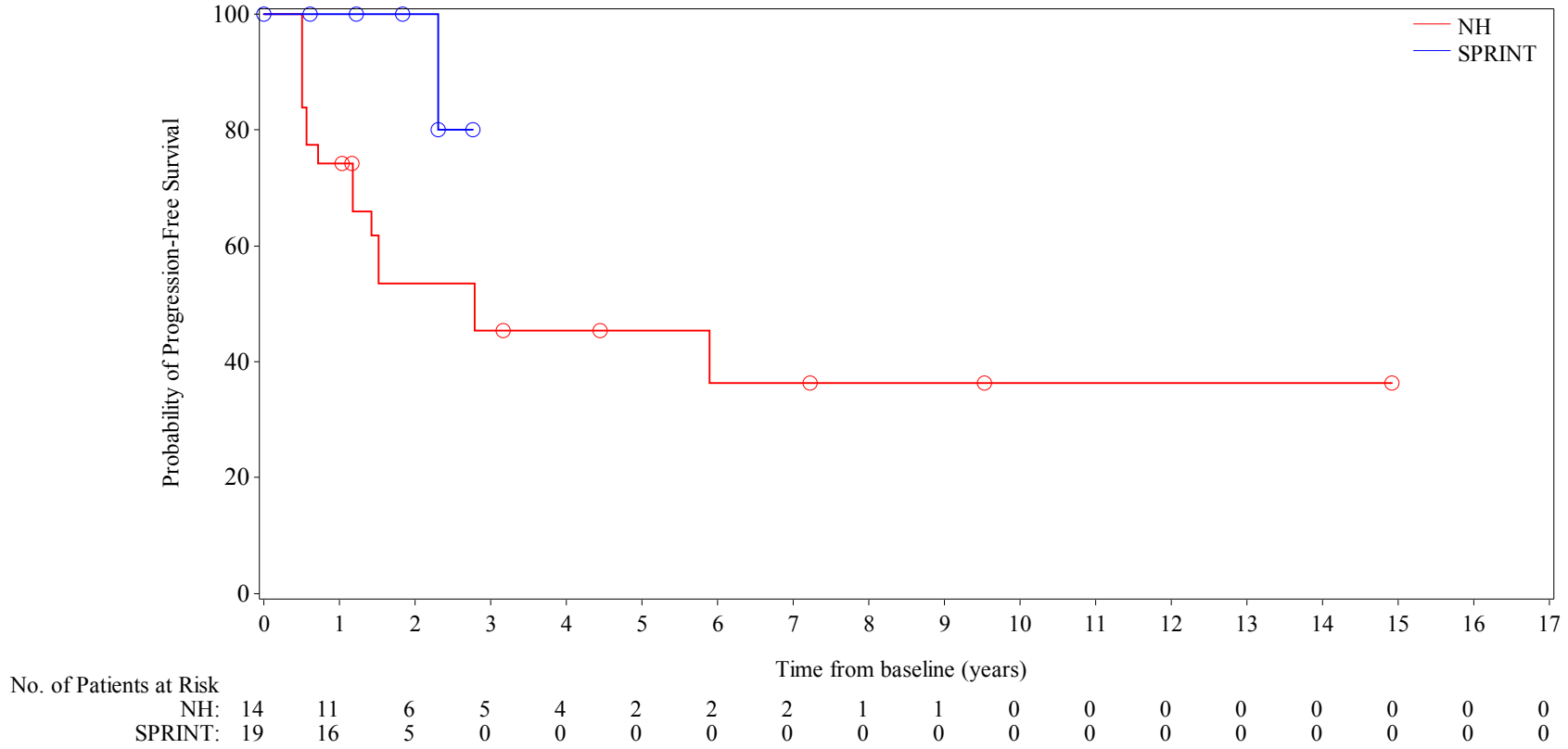
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.4.1 Progression-free Survival (PFS) Kaplan-Meier plot (post 1:2 matching with replacement) - Gender = Male
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.4.2 Progression-free Survival (PFS) Kaplan-Meier plot (post 1:2 matching with replacement) - Gender = Female
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
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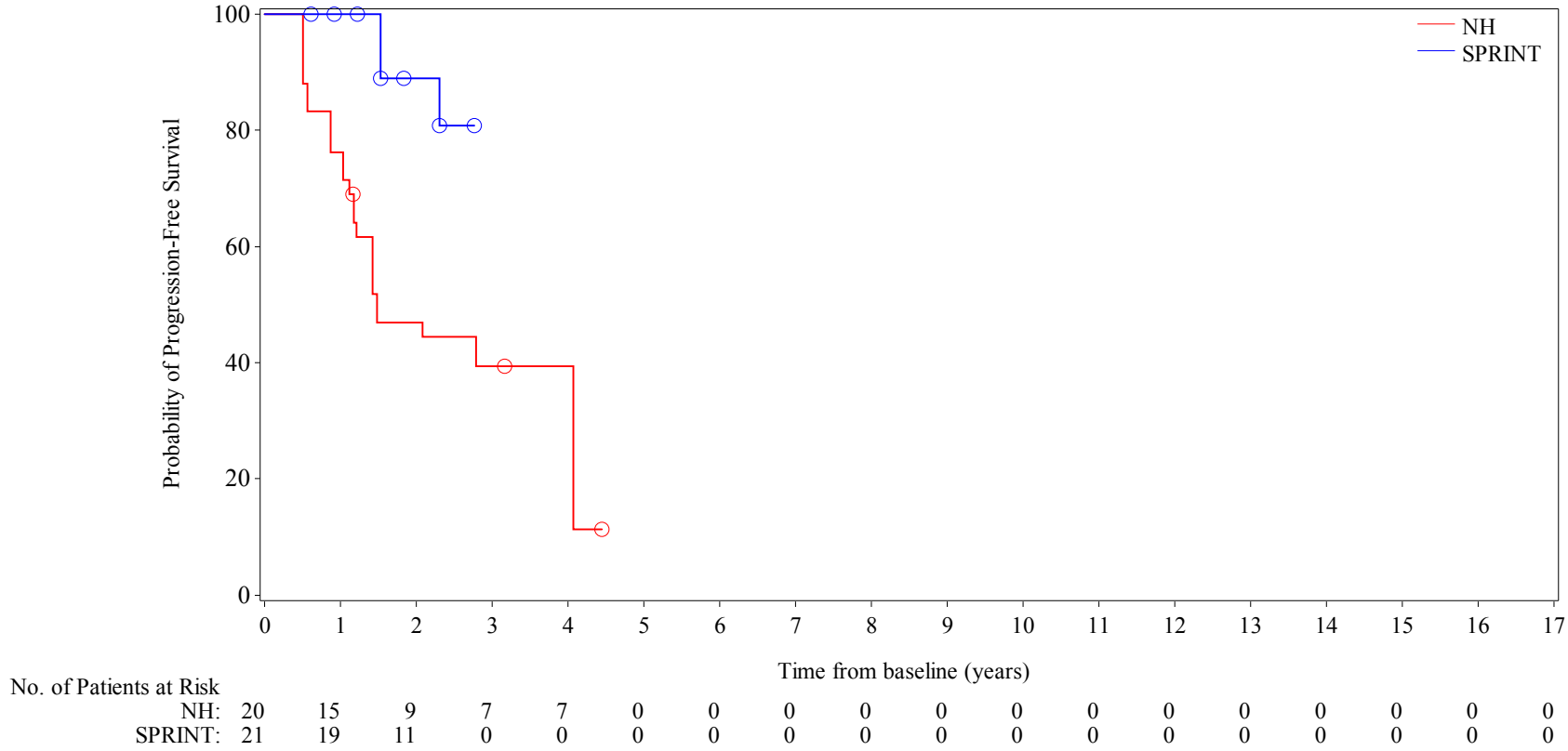
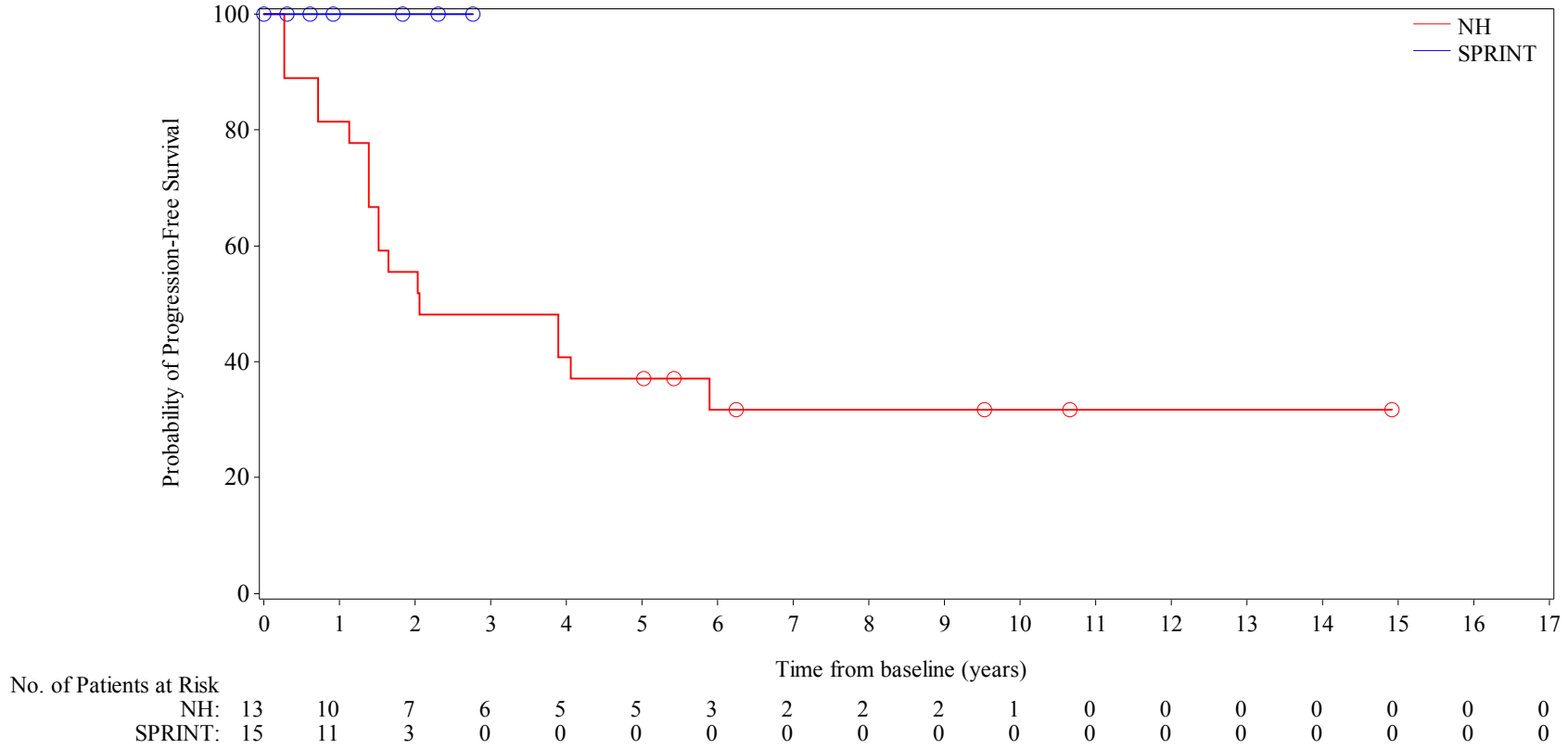
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.4.3 Progression-free Survival (PFS) K-M plot (post 1:2 matching with replacement) - PN status at enrol. = Progressive
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



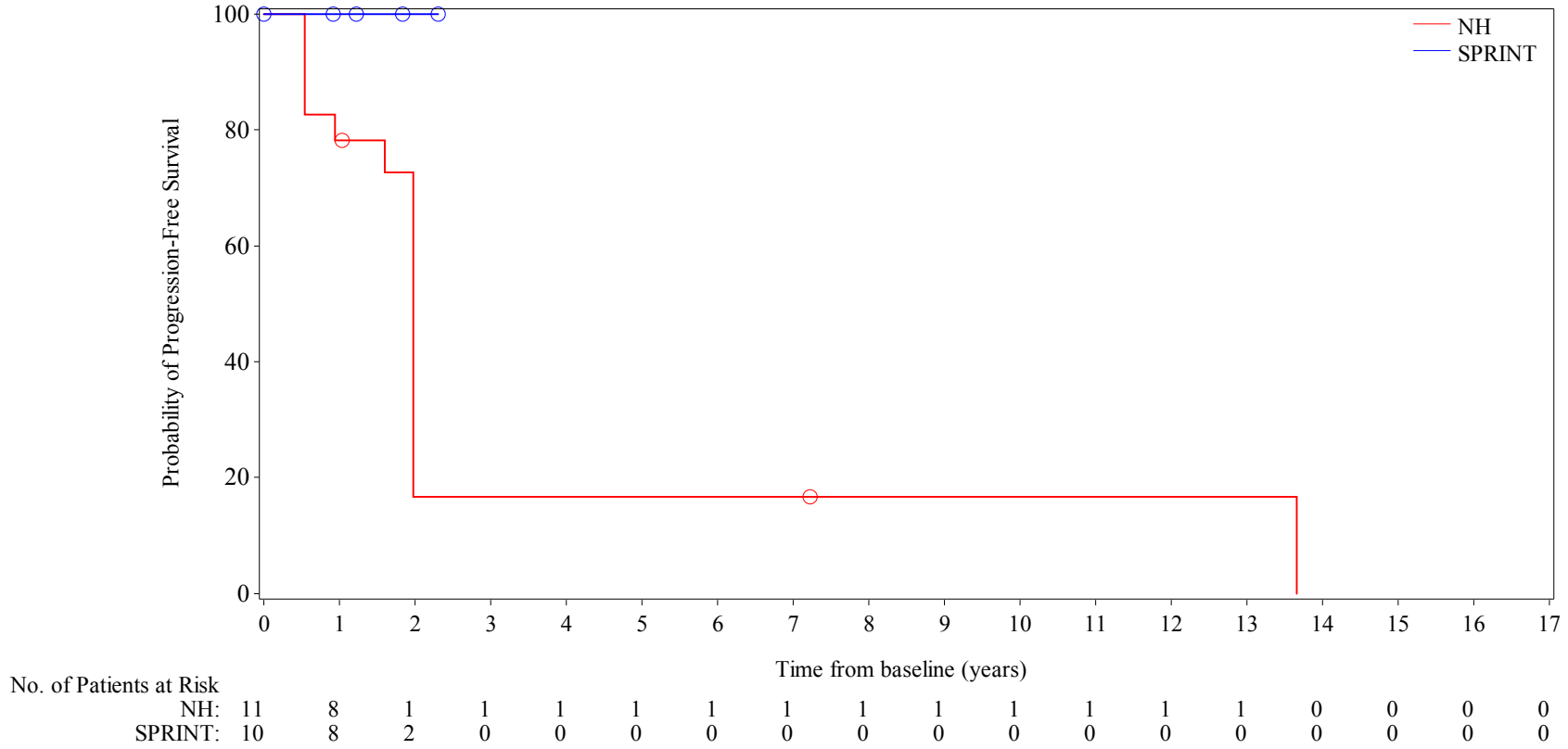
SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.4.4 Progression-free Survival (PFS) K-M plot (post 1:2 matching with replacement) - PN status at enrol. = Non-progr.
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Figure 1.12.4.5 Progression-free Survival (PFS) K-M plot (post 1:2 matching with replacement) - PN status at enrollment = Unknown
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018, Natural History Data as of 19th Feb 2019



SPRINT: PFS is defined as the time from study treatment initiation to the pre-cycle of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last evaluable MRI assessment. PFS in cycles converted to years: No. of cycles * 28/ 365.25.
NH: PFS is defined as the time from first MRI assessment to the date of documented progression or death in the absence of disease progression. Patients not known to have progressed or died at the time of analysis are censored at the last available MRI assessment date or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
The values at the base of the figure indicate number of patients at risk. Dots represent censored observations.

Table 2.1.1 General PN symptoms responder analyses - Patients with Improvement by >= 0.6 pts (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=50) [a] Not improved n/N (%) [b]	Improved by >= 0.6 points n/N (%) [b]
Item 1.Fatigue/feeling tired	Pre-cycle 3 (N=49)	34/49 (69,4)	15/49 (30,6)
	Pre-cycle 5 (N=48)	30/48 (62,5)	18/48 (37,5)
	Pre-cycle 9 (N=47)	30/47 (63,8)	17/47 (36,2)
	Pre-cycle 13 (N=44)	27/44 (61,4)	17/44 (38,6)
	Pre-cycle 25 (N=34)	20/34 (58,8)	14/34 (41,2)
	Pre-cycle 37 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	Overall (N=49)	26/49 (53,1)	23/49 (46,9)
Item 2.Sleep problems	Pre-cycle 3 (N=49)	29/49 (59,2)	20/49 (40,8)
	Pre-cycle 5 (N=48)	30/48 (62,5)	18/48 (37,5)
	Pre-cycle 9 (N=47)	28/47 (59,6)	19/47 (40,4)
	Pre-cycle 13 (N=44)	27/44 (61,4)	17/44 (38,6)
	Pre-cycle 25 (N=34)	17/34 (50,0)	17/34 (50,0)
	Pre-cycle 37 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	Overall (N=49)	25/49 (51,0)	24/49 (49,0)
Item 3.Less appetite	Pre-cycle 3 (N=49)	36/49 (73,5)	13/49 (26,5)
	Pre-cycle 5 (N=48)	35/48 (72,9)	13/48 (27,1)
	Pre-cycle 9 (N=47)	36/47 (76,6)	11/47 (23,4)
	Pre-cycle 13 (N=44)	34/44 (77,3)	10/44 (22,7)
	Pre-cycle 25 (N=34)	25/34 (73,5)	9/34 (26,5)
	Pre-cycle 37 (N=5)	1/ 5 (20,0)	4/ 5 (80,0)
	Overall (N=49)	33/49 (67,3)	16/49 (32,7)
Item 4.More appetite	Pre-cycle 3 (N=49)	41/49 (83,7)	8/49 (16,3)
	Pre-cycle 5 (N=48)	42/48 (87,5)	6/48 (12,5)
	Pre-cycle 9 (N=47)	39/47 (83,0)	8/47 (17,0)
	Pre-cycle 13 (N=44)	34/44 (77,3)	10/44 (22,7)
	Pre-cycle 25 (N=34)	28/34 (82,4)	6/34 (17,6)
	Pre-cycle 37 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	Overall (N=49)	37/49 (75,5)	12/49 (24,5)
Item 5.Headaches	Pre-cycle 3 (N=49)	35/49 (71,4)	14/49 (28,6)
	Pre-cycle 5 (N=48)	33/48 (68,8)	15/48 (31,3)
	Pre-cycle 9 (N=47)	31/47 (66,0)	16/47 (34,0)
	Pre-cycle 13 (N=44)	28/44 (63,6)	16/44 (36,4)
	Pre-cycle 25 (N=34)	24/34 (70,6)	10/34 (29,4)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	30/49 (61,2)	19/49 (38,8)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.1 General PN symptoms responder analyses - Patients with Improvement by >= 0.6 pts (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 6.Vision changes	Pre-cycle 3 (N=49)	44/49 (89,8)	5/49 (10,2)
	Pre-cycle 5 (N=48)	42/48 (87,5)	6/48 (12,5)
	Pre-cycle 9 (N=47)	42/47 (89,4)	5/47 (10,6)
	Pre-cycle 13 (N=44)	39/44 (88,6)	5/44 (11,4)
	Pre-cycle 25 (N=34)	31/34 (91,2)	3/34 (8,8)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	43/49 (87,8)	6/49 (12,2)
Item 7.Decreased hearing	Pre-cycle 3 (N=49)	46/49 (93,9)	3/49 (6,1)
	Pre-cycle 5 (N=48)	45/48 (93,8)	3/48 (6,3)
	Pre-cycle 9 (N=47)	44/47 (93,6)	3/47 (6,4)
	Pre-cycle 13 (N=44)	41/44 (93,2)	3/44 (6,8)
	Pre-cycle 25 (N=34)	31/34 (91,2)	3/34 (8,8)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	46/49 (93,9)	3/49 (6,1)
Item 8.Mouth sores	Pre-cycle 3 (N=49)	45/49 (91,8)	4/49 (8,2)
	Pre-cycle 5 (N=48)	43/48 (89,6)	5/48 (10,4)
	Pre-cycle 9 (N=47)	43/47 (91,5)	4/47 (8,5)
	Pre-cycle 13 (N=44)	39/44 (88,6)	5/44 (11,4)
	Pre-cycle 25 (N=34)	29/34 (85,3)	5/34 (14,7)
	Pre-cycle 37 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	Overall (N=49)	44/49 (89,8)	5/49 (10,2)
Item 9.Trouble swallowing	Pre-cycle 3 (N=49)	44/49 (89,8)	5/49 (10,2)
	Pre-cycle 5 (N=48)	43/48 (89,6)	5/48 (10,4)
	Pre-cycle 9 (N=47)	42/47 (89,4)	5/47 (10,6)
	Pre-cycle 13 (N=44)	39/44 (88,6)	5/44 (11,4)
	Pre-cycle 25 (N=34)	30/34 (88,2)	4/34 (11,8)
	Pre-cycle 37 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	Overall (N=49)	44/49 (89,8)	5/49 (10,2)
Item 10.Choking	Pre-cycle 3 (N=49)	43/49 (87,8)	6/49 (12,2)
	Pre-cycle 5 (N=48)	41/48 (85,4)	7/48 (14,6)
	Pre-cycle 9 (N=47)	41/47 (87,2)	6/47 (12,8)
	Pre-cycle 13 (N=44)	38/44 (86,4)	6/44 (13,6)
	Pre-cycle 25 (N=34)	29/34 (85,3)	5/34 (14,7)
	Pre-cycle 37 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	Overall (N=49)	42/49 (85,7)	7/49 (14,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.1 General PN symptoms responder analyses - Patients with Improvement by >= 0.6 pts (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=50) [a] Not improved n/N (%) [b]	Improved by >= 0.6 points n/N (%) [b]
Item 11.Snoring	Pre-cycle 3 (N=49)	35/49 (71,4)	14/49 (28,6)
	Pre-cycle 5 (N=48)	36/48 (75,0)	12/48 (25,0)
	Pre-cycle 9 (N=47)	31/47 (66,0)	16/47 (34,0)
	Pre-cycle 13 (N=44)	29/44 (65,9)	15/44 (34,1)
	Pre-cycle 25 (N=34)	21/34 (61,8)	13/34 (38,2)
	Pre-cycle 37 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	Overall (N=49)	31/49 (63,3)	18/49 (36,7)
Item 12.Frequent awakenings at night	Pre-cycle 3 (N=49)	33/49 (67,3)	16/49 (32,7)
	Pre-cycle 5 (N=48)	32/48 (66,7)	16/48 (33,3)
	Pre-cycle 9 (N=47)	30/47 (63,8)	17/47 (36,2)
	Pre-cycle 13 (N=44)	27/44 (61,4)	17/44 (38,6)
	Pre-cycle 25 (N=34)	18/34 (52,9)	16/34 (47,1)
	Pre-cycle 37 (N=5)	1/ 5 (20,0)	4/ 5 (80,0)
	Overall (N=49)	29/49 (59,2)	20/49 (40,8)
Item 13.Cough	Pre-cycle 3 (N=49)	31/49 (63,3)	18/49 (36,7)
	Pre-cycle 5 (N=48)	28/48 (58,3)	20/48 (41,7)
	Pre-cycle 9 (N=47)	36/47 (76,6)	11/47 (23,4)
	Pre-cycle 13 (N=44)	27/44 (61,4)	17/44 (38,6)
	Pre-cycle 25 (N=34)	22/34 (64,7)	12/34 (35,3)
	Pre-cycle 37 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	Overall (N=49)	25/49 (51,0)	24/49 (49,0)
Item 14.Wheezing	Pre-cycle 3 (N=49)	43/49 (87,8)	6/49 (12,2)
	Pre-cycle 5 (N=48)	42/48 (87,5)	6/48 (12,5)
	Pre-cycle 9 (N=47)	41/47 (87,2)	6/47 (12,8)
	Pre-cycle 13 (N=44)	39/44 (88,6)	5/44 (11,4)
	Pre-cycle 25 (N=34)	31/34 (91,2)	3/34 (8,8)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	43/49 (87,8)	6/49 (12,2)
Item 15.Difficulty breathing	Pre-cycle 3 (N=49)	44/49 (89,8)	5/49 (10,2)
	Pre-cycle 5 (N=48)	45/48 (93,8)	3/48 (6,3)
	Pre-cycle 9 (N=47)	41/47 (87,2)	6/47 (12,8)
	Pre-cycle 13 (N=44)	41/44 (93,2)	3/44 (6,8)
	Pre-cycle 25 (N=34)	30/34 (88,2)	4/34 (11,8)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	43/49 (87,8)	6/49 (12,2)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.1 General PN symptoms responder analyses - Patients with Improvement by >= 0.6 pts (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	Pre-cycle 3 (N=49)	47/49 (95,9)	2/49 (4,1)
	Pre-cycle 5 (N=48)	46/48 (95,8)	2/48 (4,2)
	Pre-cycle 9 (N=47)	46/47 (97,9)	1/47 (2,1)
	Pre-cycle 13 (N=44)	43/44 (97,7)	1/44 (2,3)
	Pre-cycle 25 (N=34)	33/34 (97,1)	1/34 (2,9)
	Pre-cycle 37 (N=5)	5/ 5 (100,0)	0
	Overall (N=49)	47/49 (95,9)	2/49 (4,1)
Item 17.Palpitations/fluttering	Pre-cycle 3 (N=49)	46/49 (93,9)	3/49 (6,1)
	Pre-cycle 5 (N=48)	45/48 (93,8)	3/48 (6,3)
	Pre-cycle 9 (N=47)	44/47 (93,6)	3/47 (6,4)
	Pre-cycle 13 (N=44)	41/44 (93,2)	3/44 (6,8)
	Pre-cycle 25 (N=34)	32/34 (94,1)	2/34 (5,9)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	45/49 (91,8)	4/49 (8,2)
Item 18.Shortness of breath with activity	Pre-cycle 3 (N=49)	37/49 (75,5)	12/49 (24,5)
	Pre-cycle 5 (N=48)	38/48 (79,2)	10/48 (20,8)
	Pre-cycle 9 (N=47)	37/47 (78,7)	10/47 (21,3)
	Pre-cycle 13 (N=44)	35/44 (79,5)	9/44 (20,5)
	Pre-cycle 25 (N=34)	26/34 (76,5)	8/34 (23,5)
	Pre-cycle 37 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	Overall (N=49)	35/49 (71,4)	14/49 (28,6)
Item 19.Shortness of breath at rest	Pre-cycle 3 (N=49)	46/49 (93,9)	3/49 (6,1)
	Pre-cycle 5 (N=48)	45/48 (93,8)	3/48 (6,3)
	Pre-cycle 9 (N=47)	44/47 (93,6)	3/47 (6,4)
	Pre-cycle 13 (N=44)	42/44 (95,5)	2/44 (4,5)
	Pre-cycle 25 (N=34)	32/34 (94,1)	2/34 (5,9)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	46/49 (93,9)	3/49 (6,1)
Item 20.Swelling in hands/feet	Pre-cycle 3 (N=49)	48/49 (98,0)	1/49 (2,0)
	Pre-cycle 5 (N=48)	47/48 (97,9)	1/48 (2,1)
	Pre-cycle 9 (N=47)	46/47 (97,9)	1/47 (2,1)
	Pre-cycle 13 (N=44)	44/44 (100,0)	0
	Pre-cycle 25 (N=34)	34/34 (100,0)	0
	Pre-cycle 37 (N=5)	5/ 5 (100,0)	0
	Overall (N=49)	48/49 (98,0)	1/49 (2,0)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.1 General PN symptoms responder analyses - Patients with Improvement by >= 0.6 pts (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 21.Abdominal pain	Pre-cycle 3 (N=49)	42/49 (85,7)	7/49 (14,3)
	Pre-cycle 5 (N=48)	42/48 (87,5)	6/48 (12,5)
	Pre-cycle 9 (N=47)	41/47 (87,2)	6/47 (12,8)
	Pre-cycle 13 (N=44)	34/44 (77,3)	10/44 (22,7)
	Pre-cycle 25 (N=34)	26/34 (76,5)	8/34 (23,5)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	34/49 (69,4)	15/49 (30,6)
Item 22.Heartburn	Pre-cycle 3 (N=49)	46/49 (93,9)	3/49 (6,1)
	Pre-cycle 5 (N=48)	45/48 (93,8)	3/48 (6,3)
	Pre-cycle 9 (N=47)	45/47 (95,7)	2/47 (4,3)
	Pre-cycle 13 (N=44)	42/44 (95,5)	2/44 (4,5)
	Pre-cycle 25 (N=34)	33/34 (97,1)	1/34 (2,9)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	46/49 (93,9)	3/49 (6,1)
Item 23.Nausea	Pre-cycle 3 (N=49)	42/49 (85,7)	7/49 (14,3)
	Pre-cycle 5 (N=48)	43/48 (89,6)	5/48 (10,4)
	Pre-cycle 9 (N=47)	41/47 (87,2)	6/47 (12,8)
	Pre-cycle 13 (N=44)	36/44 (81,8)	8/44 (18,2)
	Pre-cycle 25 (N=34)	32/34 (94,1)	2/34 (5,9)
	Pre-cycle 37 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	Overall (N=49)	38/49 (77,6)	11/49 (22,4)
Item 24.Vomiting	Pre-cycle 3 (N=49)	45/49 (91,8)	4/49 (8,2)
	Pre-cycle 5 (N=48)	44/48 (91,7)	4/48 (8,3)
	Pre-cycle 9 (N=47)	45/47 (95,7)	2/47 (4,3)
	Pre-cycle 13 (N=44)	41/44 (93,2)	3/44 (6,8)
	Pre-cycle 25 (N=34)	32/34 (94,1)	2/34 (5,9)
	Pre-cycle 37 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	Overall (N=49)	43/49 (87,8)	6/49 (12,2)
Item 25.Diarrhea	Pre-cycle 3 (N=49)	43/49 (87,8)	6/49 (12,2)
	Pre-cycle 5 (N=48)	43/48 (89,6)	5/48 (10,4)
	Pre-cycle 9 (N=47)	41/47 (87,2)	6/47 (12,8)
	Pre-cycle 13 (N=44)	39/44 (88,6)	5/44 (11,4)
	Pre-cycle 25 (N=34)	28/34 (82,4)	6/34 (17,6)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	38/49 (77,6)	11/49 (22,4)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.1 General PN symptoms responder analyses - Patients with Improvement by >= 0.6 pts (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 26.Constipation	Pre-cycle 3 (N=49)	42/49 (85,7)	7/49 (14,3)
	Pre-cycle 5 (N=48)	41/48 (85,4)	7/48 (14,6)
	Pre-cycle 9 (N=47)	41/47 (87,2)	6/47 (12,8)
	Pre-cycle 13 (N=44)	39/44 (88,6)	5/44 (11,4)
	Pre-cycle 25 (N=34)	31/34 (91,2)	3/34 (8,8)
	Pre-cycle 37 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	Overall (N=49)	38/49 (77,6)	11/49 (22,4)
Item 27.Stool incontinence	Pre-cycle 3 (N=49)	45/49 (91,8)	4/49 (8,2)
	Pre-cycle 5 (N=48)	46/48 (95,8)	2/48 (4,2)
	Pre-cycle 9 (N=47)	44/47 (93,6)	3/47 (6,4)
	Pre-cycle 13 (N=44)	40/44 (90,9)	4/44 (9,1)
	Pre-cycle 25 (N=34)	31/34 (91,2)	3/34 (8,8)
	Pre-cycle 37 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	Overall (N=49)	44/49 (89,8)	5/49 (10,2)
Item 28.Pain with urination	Pre-cycle 3 (N=49)	45/49 (91,8)	4/49 (8,2)
	Pre-cycle 5 (N=48)	45/48 (93,8)	3/48 (6,3)
	Pre-cycle 9 (N=47)	44/47 (93,6)	3/47 (6,4)
	Pre-cycle 13 (N=44)	40/44 (90,9)	4/44 (9,1)
	Pre-cycle 25 (N=34)	33/34 (97,1)	1/34 (2,9)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	45/49 (91,8)	4/49 (8,2)
Item 29.Increased urinary frequency/urgency	Pre-cycle 3 (N=49)	41/49 (83,7)	8/49 (16,3)
	Pre-cycle 5 (N=48)	41/48 (85,4)	7/48 (14,6)
	Pre-cycle 9 (N=47)	41/47 (87,2)	6/47 (12,8)
	Pre-cycle 13 (N=44)	38/44 (86,4)	6/44 (13,6)
	Pre-cycle 25 (N=34)	30/34 (88,2)	4/34 (11,8)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	40/49 (81,6)	9/49 (18,4)
Item 30.Difficulty beginning urination	Pre-cycle 3 (N=49)	45/49 (91,8)	4/49 (8,2)
	Pre-cycle 5 (N=48)	44/48 (91,7)	4/48 (8,3)
	Pre-cycle 9 (N=47)	45/47 (95,7)	2/47 (4,3)
	Pre-cycle 13 (N=44)	41/44 (93,2)	3/44 (6,8)
	Pre-cycle 25 (N=33)	31/33 (93,9)	2/33 (6,1)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	43/49 (87,8)	6/49 (12,2)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.1 General PN symptoms responder analyses - Patients with Improvement by >= 0.6 pts (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	Pre-cycle 3 (N=48)	41/48 (85,4)	7/48 (14,6)
	Pre-cycle 5 (N=47)	40/47 (85,1)	7/47 (14,9)
	Pre-cycle 9 (N=47)	40/47 (85,1)	7/47 (14,9)
	Pre-cycle 13 (N=44)	38/44 (86,4)	6/44 (13,6)
	Pre-cycle 25 (N=33)	31/33 (93,9)	2/33 (6,1)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	41/49 (83,7)	8/49 (16,3)
Item 32.Weakness	Pre-cycle 3 (N=49)	35/49 (71,4)	14/49 (28,6)
	Pre-cycle 5 (N=48)	32/48 (66,7)	16/48 (33,3)
	Pre-cycle 9 (N=47)	33/47 (70,2)	14/47 (29,8)
	Pre-cycle 13 (N=44)	29/44 (65,9)	15/44 (34,1)
	Pre-cycle 25 (N=34)	23/34 (67,6)	11/34 (32,4)
	Pre-cycle 37 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	Overall (N=49)	33/49 (67,3)	16/49 (32,7)
Item 33.Muscle pain	Pre-cycle 3 (N=49)	30/49 (61,2)	19/49 (38,8)
	Pre-cycle 5 (N=48)	28/48 (58,3)	20/48 (41,7)
	Pre-cycle 9 (N=47)	29/47 (61,7)	18/47 (38,3)
	Pre-cycle 13 (N=44)	28/44 (63,6)	16/44 (36,4)
	Pre-cycle 25 (N=34)	22/34 (64,7)	12/34 (35,3)
	Pre-cycle 37 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	Overall (N=49)	28/49 (57,1)	21/49 (42,9)
Item 34.Dizziness	Pre-cycle 3 (N=49)	47/49 (95,9)	2/49 (4,1)
	Pre-cycle 5 (N=48)	45/48 (93,8)	3/48 (6,3)
	Pre-cycle 9 (N=47)	45/47 (95,7)	2/47 (4,3)
	Pre-cycle 13 (N=44)	40/44 (90,9)	4/44 (9,1)
	Pre-cycle 25 (N=34)	32/34 (94,1)	2/34 (5,9)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	45/49 (91,8)	4/49 (8,2)
Item 35.Numbness	Pre-cycle 3 (N=49)	44/49 (89,8)	5/49 (10,2)
	Pre-cycle 5 (N=48)	45/48 (93,8)	3/48 (6,3)
	Pre-cycle 9 (N=47)	42/47 (89,4)	5/47 (10,6)
	Pre-cycle 13 (N=44)	41/44 (93,2)	3/44 (6,8)
	Pre-cycle 25 (N=34)	32/34 (94,1)	2/34 (5,9)
	Pre-cycle 37 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=49)	44/49 (89,8)	5/49 (10,2)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.1 General PN symptoms responder analyses - Patients with Improvement by >= 0.6 pts (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	Pre-cycle 3 (N=49)	41/49 (83,7)	8/49 (16,3)
	Pre-cycle 5 (N=48)	42/48 (87,5)	6/48 (12,5)
	Pre-cycle 9 (N=47)	41/47 (87,2)	6/47 (12,8)
	Pre-cycle 13 (N=44)	38/44 (86,4)	6/44 (13,6)
	Pre-cycle 25 (N=34)	30/34 (88,2)	4/34 (11,8)
	Pre-cycle 37 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	Overall (N=49)	40/49 (81,6)	9/49 (18,4)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.1 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 1.Fatigue/feeling tired	Pre-cycle 3 (N=30)	22/30 (73,3)	8/30 (26,7)
	Pre-cycle 5 (N=29)	20/29 (69,0)	9/29 (31,0)
	Pre-cycle 9 (N=28)	18/28 (64,3)	10/28 (35,7)
	Pre-cycle 13 (N=27)	18/27 (66,7)	9/27 (33,3)
	Pre-cycle 25 (N=19)	13/19 (68,4)	6/19 (31,6)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=30)	17/30 (56,7)	13/30 (43,3)
Item 2.Sleep problems	Pre-cycle 3 (N=30)	19/30 (63,3)	11/30 (36,7)
	Pre-cycle 5 (N=29)	18/29 (62,1)	11/29 (37,9)
	Pre-cycle 9 (N=28)	19/28 (67,9)	9/28 (32,1)
	Pre-cycle 13 (N=27)	19/27 (70,4)	8/27 (29,6)
	Pre-cycle 25 (N=19)	10/19 (52,6)	9/19 (47,4)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=30)	19/30 (63,3)	11/30 (36,7)
Item 3.Less appetite	Pre-cycle 3 (N=30)	23/30 (76,7)	7/30 (23,3)
	Pre-cycle 5 (N=29)	22/29 (75,9)	7/29 (24,1)
	Pre-cycle 9 (N=28)	24/28 (85,7)	4/28 (14,3)
	Pre-cycle 13 (N=27)	24/27 (88,9)	3/27 (11,1)
	Pre-cycle 25 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 37 (N=4)	1/ 4 (25,0)	3/ 4 (75,0)
	Overall (N=30)	22/30 (73,3)	8/30 (26,7)
Item 4.More appetite	Pre-cycle 3 (N=30)	26/30 (86,7)	4/30 (13,3)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	24/28 (85,7)	4/28 (14,3)
	Pre-cycle 13 (N=27)	22/27 (81,5)	5/27 (18,5)
	Pre-cycle 25 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=30)	23/30 (76,7)	7/30 (23,3)
Item 5.Headaches	Pre-cycle 3 (N=30)	22/30 (73,3)	8/30 (26,7)
	Pre-cycle 5 (N=29)	20/29 (69,0)	9/29 (31,0)
	Pre-cycle 9 (N=28)	20/28 (71,4)	8/28 (28,6)
	Pre-cycle 13 (N=27)	18/27 (66,7)	9/27 (33,3)
	Pre-cycle 25 (N=19)	13/19 (68,4)	6/19 (31,6)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=30)	19/30 (63,3)	11/30 (36,7)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.1 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 6.Vision changes	Pre-cycle 3 (N=30)	27/30 (90,0)	3/30 (10,0)
	Pre-cycle 5 (N=29)	26/29 (89,7)	3/29 (10,3)
	Pre-cycle 9 (N=28)	26/28 (92,9)	2/28 (7,1)
	Pre-cycle 13 (N=27)	25/27 (92,6)	2/27 (7,4)
	Pre-cycle 25 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	27/30 (90,0)	3/30 (10,0)
Item 7.Decreased hearing	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	26/28 (92,9)	2/28 (7,1)
	Pre-cycle 13 (N=27)	25/27 (92,6)	2/27 (7,4)
	Pre-cycle 25 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)
Item 8.Mouth sores	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	26/29 (89,7)	3/29 (10,3)
	Pre-cycle 9 (N=28)	26/28 (92,9)	2/28 (7,1)
	Pre-cycle 13 (N=27)	24/27 (88,9)	3/27 (11,1)
	Pre-cycle 25 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=30)	27/30 (90,0)	3/30 (10,0)
Item 9.Trouble swallowing	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	26/28 (92,9)	2/28 (7,1)
	Pre-cycle 13 (N=27)	25/27 (92,6)	2/27 (7,4)
	Pre-cycle 25 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)
Item 10.Choking	Pre-cycle 3 (N=30)	27/30 (90,0)	3/30 (10,0)
	Pre-cycle 5 (N=29)	26/29 (89,7)	3/29 (10,3)
	Pre-cycle 9 (N=28)	26/28 (92,9)	2/28 (7,1)
	Pre-cycle 13 (N=27)	24/27 (88,9)	3/27 (11,1)
	Pre-cycle 25 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=30)	27/30 (90,0)	3/30 (10,0)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.1 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 11.Snoring	Pre-cycle 3 (N=30)	22/30 (73,3)	8/30 (26,7)
	Pre-cycle 5 (N=29)	23/29 (79,3)	6/29 (20,7)
	Pre-cycle 9 (N=28)	20/28 (71,4)	8/28 (28,6)
	Pre-cycle 13 (N=27)	20/27 (74,1)	7/27 (25,9)
	Pre-cycle 25 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=30)	20/30 (66,7)	10/30 (33,3)
Item 12.Frequent awakenings at night	Pre-cycle 3 (N=30)	21/30 (70,0)	9/30 (30,0)
	Pre-cycle 5 (N=29)	20/29 (69,0)	9/29 (31,0)
	Pre-cycle 9 (N=28)	19/28 (67,9)	9/28 (32,1)
	Pre-cycle 13 (N=27)	17/27 (63,0)	10/27 (37,0)
	Pre-cycle 25 (N=19)	9/19 (47,4)	10/19 (52,6)
	Pre-cycle 37 (N=4)	1/ 4 (25,0)	3/ 4 (75,0)
	Overall (N=30)	19/30 (63,3)	11/30 (36,7)
Item 13.Cough	Pre-cycle 3 (N=30)	20/30 (66,7)	10/30 (33,3)
	Pre-cycle 5 (N=29)	18/29 (62,1)	11/29 (37,9)
	Pre-cycle 9 (N=28)	25/28 (89,3)	3/28 (10,7)
	Pre-cycle 13 (N=27)	19/27 (70,4)	8/27 (29,6)
	Pre-cycle 25 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=30)	17/30 (56,7)	13/30 (43,3)
Item 14.Wheezing	Pre-cycle 3 (N=30)	27/30 (90,0)	3/30 (10,0)
	Pre-cycle 5 (N=29)	26/29 (89,7)	3/29 (10,3)
	Pre-cycle 9 (N=28)	25/28 (89,3)	3/28 (10,7)
	Pre-cycle 13 (N=27)	25/27 (92,6)	2/27 (7,4)
	Pre-cycle 25 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=30)	27/30 (90,0)	3/30 (10,0)
Item 15.Difficulty breathing	Pre-cycle 3 (N=30)	27/30 (90,0)	3/30 (10,0)
	Pre-cycle 5 (N=29)	29/29 (100,0)	0
	Pre-cycle 9 (N=28)	25/28 (89,3)	3/28 (10,7)
	Pre-cycle 13 (N=27)	27/27 (100,0)	0
	Pre-cycle 25 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	27/30 (90,0)	3/30 (10,0)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.1 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	27/28 (96,4)	1/28 (3,6)
	Pre-cycle 13 (N=27)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)
Item 17.Palpitations/fluttering	Pre-cycle 3 (N=30)	29/30 (96,7)	1/30 (3,3)
	Pre-cycle 5 (N=29)	28/29 (96,6)	1/29 (3,4)
	Pre-cycle 9 (N=28)	28/28 (100,0)	0
	Pre-cycle 13 (N=27)	27/27 (100,0)	0
	Pre-cycle 25 (N=19)	19/19 (100,0)	0
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	29/30 (96,7)	1/30 (3,3)
Item 18.Shortness of breath with activity	Pre-cycle 3 (N=30)	23/30 (76,7)	7/30 (23,3)
	Pre-cycle 5 (N=29)	23/29 (79,3)	6/29 (20,7)
	Pre-cycle 9 (N=28)	23/28 (82,1)	5/28 (17,9)
	Pre-cycle 13 (N=27)	22/27 (81,5)	5/27 (18,5)
	Pre-cycle 25 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=30)	21/30 (70,0)	9/30 (30,0)
Item 19.Shortness of breath at rest	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	26/28 (92,9)	2/28 (7,1)
	Pre-cycle 13 (N=27)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)
Item 20.Swelling in hands/feet	Pre-cycle 3 (N=30)	30/30 (100,0)	0
	Pre-cycle 5 (N=29)	29/29 (100,0)	0
	Pre-cycle 9 (N=28)	28/28 (100,0)	0
	Pre-cycle 13 (N=27)	27/27 (100,0)	0
	Pre-cycle 25 (N=19)	19/19 (100,0)	0
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	30/30 (100,0)	0

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.1 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 21.Abdominal pain	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	26/28 (92,9)	2/28 (7,1)
	Pre-cycle 13 (N=27)	22/27 (81,5)	5/27 (18,5)
	Pre-cycle 25 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	23/30 (76,7)	7/30 (23,3)
Item 22.Heartburn	Pre-cycle 3 (N=30)	29/30 (96,7)	1/30 (3,3)
	Pre-cycle 5 (N=29)	28/29 (96,6)	1/29 (3,4)
	Pre-cycle 9 (N=28)	27/28 (96,4)	1/28 (3,6)
	Pre-cycle 13 (N=27)	27/27 (100,0)	0
	Pre-cycle 25 (N=19)	19/19 (100,0)	0
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	29/30 (96,7)	1/30 (3,3)
Item 23.Nausea	Pre-cycle 3 (N=30)	26/30 (86,7)	4/30 (13,3)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	26/28 (92,9)	2/28 (7,1)
	Pre-cycle 13 (N=27)	24/27 (88,9)	3/27 (11,1)
	Pre-cycle 25 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=30)	25/30 (83,3)	5/30 (16,7)
Item 24.Vomiting	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	27/28 (96,4)	1/28 (3,6)
	Pre-cycle 13 (N=27)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=30)	26/30 (86,7)	4/30 (13,3)
Item 25.Diarrhea	Pre-cycle 3 (N=30)	26/30 (86,7)	4/30 (13,3)
	Pre-cycle 5 (N=29)	25/29 (86,2)	4/29 (13,8)
	Pre-cycle 9 (N=28)	26/28 (92,9)	2/28 (7,1)
	Pre-cycle 13 (N=27)	25/27 (92,6)	2/27 (7,4)
	Pre-cycle 25 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	24/30 (80,0)	6/30 (20,0)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.1 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 26.Constipation	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	26/29 (89,7)	3/29 (10,3)
	Pre-cycle 9 (N=28)	24/28 (85,7)	4/28 (14,3)
	Pre-cycle 13 (N=27)	24/27 (88,9)	3/27 (11,1)
	Pre-cycle 25 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=30)	25/30 (83,3)	5/30 (16,7)
Item 27.Stool incontinence	Pre-cycle 3 (N=30)	26/30 (86,7)	4/30 (13,3)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	25/28 (89,3)	3/28 (10,7)
	Pre-cycle 13 (N=27)	23/27 (85,2)	4/27 (14,8)
	Pre-cycle 25 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=30)	25/30 (83,3)	5/30 (16,7)
Item 28.Pain with urination	Pre-cycle 3 (N=30)	29/30 (96,7)	1/30 (3,3)
	Pre-cycle 5 (N=29)	29/29 (100,0)	0
	Pre-cycle 9 (N=28)	27/28 (96,4)	1/28 (3,6)
	Pre-cycle 13 (N=27)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=19)	19/19 (100,0)	0
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	29/30 (96,7)	1/30 (3,3)
Item 29.Increased urinary frequency/urgency	Pre-cycle 3 (N=30)	25/30 (83,3)	5/30 (16,7)
	Pre-cycle 5 (N=29)	24/29 (82,8)	5/29 (17,2)
	Pre-cycle 9 (N=28)	24/28 (85,7)	4/28 (14,3)
	Pre-cycle 13 (N=27)	24/27 (88,9)	3/27 (11,1)
	Pre-cycle 25 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	25/30 (83,3)	5/30 (16,7)
Item 30.Difficulty beginning urination	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	27/28 (96,4)	1/28 (3,6)
	Pre-cycle 13 (N=27)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=18)	18/18 (100,0)	0
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	27/30 (90,0)	3/30 (10,0)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.1 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	Pre-cycle 3 (N=29)	25/29 (86,2)	4/29 (13,8)
	Pre-cycle 5 (N=28)	24/28 (85,7)	4/28 (14,3)
	Pre-cycle 9 (N=28)	24/28 (85,7)	4/28 (14,3)
	Pre-cycle 13 (N=27)	24/27 (88,9)	3/27 (11,1)
	Pre-cycle 25 (N=18)	18/18 (100,0)	0
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	25/30 (83,3)	5/30 (16,7)
Item 32.Weakness	Pre-cycle 3 (N=30)	23/30 (76,7)	7/30 (23,3)
	Pre-cycle 5 (N=29)	21/29 (72,4)	8/29 (27,6)
	Pre-cycle 9 (N=28)	22/28 (78,6)	6/28 (21,4)
	Pre-cycle 13 (N=27)	19/27 (70,4)	8/27 (29,6)
	Pre-cycle 25 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=30)	22/30 (73,3)	8/30 (26,7)
Item 33.Muscle pain	Pre-cycle 3 (N=30)	21/30 (70,0)	9/30 (30,0)
	Pre-cycle 5 (N=29)	20/29 (69,0)	9/29 (31,0)
	Pre-cycle 9 (N=28)	20/28 (71,4)	8/28 (28,6)
	Pre-cycle 13 (N=27)	20/27 (74,1)	7/27 (25,9)
	Pre-cycle 25 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=30)	20/30 (66,7)	10/30 (33,3)
Item 34.Dizziness	Pre-cycle 3 (N=30)	29/30 (96,7)	1/30 (3,3)
	Pre-cycle 5 (N=29)	28/29 (96,6)	1/29 (3,4)
	Pre-cycle 9 (N=28)	27/28 (96,4)	1/28 (3,6)
	Pre-cycle 13 (N=27)	25/27 (92,6)	2/27 (7,4)
	Pre-cycle 25 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)
Item 35.Numbness	Pre-cycle 3 (N=30)	29/30 (96,7)	1/30 (3,3)
	Pre-cycle 5 (N=29)	29/29 (100,0)	0
	Pre-cycle 9 (N=28)	27/28 (96,4)	1/28 (3,6)
	Pre-cycle 13 (N=27)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=19)	19/19 (100,0)	0
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=30)	29/30 (96,7)	1/30 (3,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.1 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	Pre-cycle 3 (N=30)	27/30 (90,0)	3/30 (10,0)
	Pre-cycle 5 (N=29)	27/29 (93,1)	2/29 (6,9)
	Pre-cycle 9 (N=28)	25/28 (89,3)	3/28 (10,7)
	Pre-cycle 13 (N=27)	24/27 (88,9)	3/27 (11,1)
	Pre-cycle 25 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=30)	26/30 (86,7)	4/30 (13,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.2 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 1.Fatigue/feeling tired	Pre-cycle 3 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 5 (N=19)	10/19 (52,6)	9/19 (47,4)
	Pre-cycle 9 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 13 (N=17)	9/17 (52,9)	8/17 (47,1)
	Pre-cycle 25 (N=15)	7/15 (46,7)	8/15 (53,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	9/19 (47,4)	10/19 (52,6)
Item 2.Sleep problems	Pre-cycle 3 (N=19)	10/19 (52,6)	9/19 (47,4)
	Pre-cycle 5 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 9 (N=19)	9/19 (47,4)	10/19 (52,6)
	Pre-cycle 13 (N=17)	8/17 (47,1)	9/17 (52,9)
	Pre-cycle 25 (N=15)	7/15 (46,7)	8/15 (53,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	6/19 (31,6)	13/19 (68,4)
Item 3.Less appetite	Pre-cycle 3 (N=19)	13/19 (68,4)	6/19 (31,6)
	Pre-cycle 5 (N=19)	13/19 (68,4)	6/19 (31,6)
	Pre-cycle 9 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 13 (N=17)	10/17 (58,8)	7/17 (41,2)
	Pre-cycle 25 (N=15)	10/15 (66,7)	5/15 (33,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	11/19 (57,9)	8/19 (42,1)
Item 4.More appetite	Pre-cycle 3 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 5 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 9 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 13 (N=17)	12/17 (70,6)	5/17 (29,4)
	Pre-cycle 25 (N=15)	12/15 (80,0)	3/15 (20,0)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	14/19 (73,7)	5/19 (26,3)
Item 5.Headaches	Pre-cycle 3 (N=19)	13/19 (68,4)	6/19 (31,6)
	Pre-cycle 5 (N=19)	13/19 (68,4)	6/19 (31,6)
	Pre-cycle 9 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 13 (N=17)	10/17 (58,8)	7/17 (41,2)
	Pre-cycle 25 (N=15)	11/15 (73,3)	4/15 (26,7)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=19)	11/19 (57,9)	8/19 (42,1)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.2 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 6.Vision changes	Pre-cycle 3 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 5 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 9 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)
Item 7.Decreased hearing	Pre-cycle 3 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 5 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 9 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 13 (N=17)	16/17 (94,1)	1/17 (5,9)
	Pre-cycle 25 (N=15)	14/15 (93,3)	1/15 (6,7)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	18/19 (94,7)	1/19 (5,3)
Item 8.Mouth sores	Pre-cycle 3 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 5 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 9 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 13 (N=17)	15/17 (88,2)	2/17 (11,8)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=19)	17/19 (89,5)	2/19 (10,5)
Item 9.Trouble swallowing	Pre-cycle 3 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 5 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 9 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)
Item 10.Choking	Pre-cycle 3 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 5 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 9 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	15/19 (78,9)	4/19 (21,1)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.2 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 11.Snoring	Pre-cycle 3 (N=19)	13/19 (68,4)	6/19 (31,6)
	Pre-cycle 5 (N=19)	13/19 (68,4)	6/19 (31,6)
	Pre-cycle 9 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 13 (N=17)	9/17 (52,9)	8/17 (47,1)
	Pre-cycle 25 (N=15)	9/15 (60,0)	6/15 (40,0)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	11/19 (57,9)	8/19 (42,1)
Item 12.Frequent awakenings at night	Pre-cycle 3 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 5 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 9 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 13 (N=17)	10/17 (58,8)	7/17 (41,2)
	Pre-cycle 25 (N=15)	9/15 (60,0)	6/15 (40,0)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	10/19 (52,6)	9/19 (47,4)
Item 13.Cough	Pre-cycle 3 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 5 (N=19)	10/19 (52,6)	9/19 (47,4)
	Pre-cycle 9 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 13 (N=17)	8/17 (47,1)	9/17 (52,9)
	Pre-cycle 25 (N=15)	10/15 (66,7)	5/15 (33,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	8/19 (42,1)	11/19 (57,9)
Item 14.Wheezing	Pre-cycle 3 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 5 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 9 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)
Item 15.Difficulty breathing	Pre-cycle 3 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 5 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 9 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.2 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	Pre-cycle 3 (N=19)	19/19 (100,0)	0
	Pre-cycle 5 (N=19)	19/19 (100,0)	0
	Pre-cycle 9 (N=19)	19/19 (100,0)	0
	Pre-cycle 13 (N=17)	17/17 (100,0)	0
	Pre-cycle 25 (N=15)	15/15 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=19)	19/19 (100,0)	0
Item 17.Palpitations/fluttering	Pre-cycle 3 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 5 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 9 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)
Item 18.Shortness of breath with activity	Pre-cycle 3 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 5 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 9 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 13 (N=17)	13/17 (76,5)	4/17 (23,5)
	Pre-cycle 25 (N=15)	12/15 (80,0)	3/15 (20,0)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	14/19 (73,7)	5/19 (26,3)
Item 19.Shortness of breath at rest	Pre-cycle 3 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 5 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 9 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 13 (N=17)	16/17 (94,1)	1/17 (5,9)
	Pre-cycle 25 (N=15)	14/15 (93,3)	1/15 (6,7)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	18/19 (94,7)	1/19 (5,3)
Item 20.Swelling in hands/feet	Pre-cycle 3 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 5 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 9 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 13 (N=17)	17/17 (100,0)	0
	Pre-cycle 25 (N=15)	15/15 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=19)	18/19 (94,7)	1/19 (5,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.2 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 21.Abdominal pain	Pre-cycle 3 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 5 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 9 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 13 (N=17)	12/17 (70,6)	5/17 (29,4)
	Pre-cycle 25 (N=15)	10/15 (66,7)	5/15 (33,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	11/19 (57,9)	8/19 (42,1)
Item 22.Heartburn	Pre-cycle 3 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 5 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 9 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 13 (N=17)	15/17 (88,2)	2/17 (11,8)
	Pre-cycle 25 (N=15)	14/15 (93,3)	1/15 (6,7)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	17/19 (89,5)	2/19 (10,5)
Item 23.Nausea	Pre-cycle 3 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 5 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 9 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 13 (N=17)	12/17 (70,6)	5/17 (29,4)
	Pre-cycle 25 (N=15)	14/15 (93,3)	1/15 (6,7)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	13/19 (68,4)	6/19 (31,6)
Item 24.Vomiting	Pre-cycle 3 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 5 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 9 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 13 (N=17)	15/17 (88,2)	2/17 (11,8)
	Pre-cycle 25 (N=15)	15/15 (100,0)	0
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	17/19 (89,5)	2/19 (10,5)
Item 25.Diarrhea	Pre-cycle 3 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 5 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 9 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	12/15 (80,0)	3/15 (20,0)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	14/19 (73,7)	5/19 (26,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.2 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 26.Constipation	Pre-cycle 3 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 5 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 9 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 13 (N=17)	15/17 (88,2)	2/17 (11,8)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	13/19 (68,4)	6/19 (31,6)
Item 27.Stool incontinence	Pre-cycle 3 (N=19)	19/19 (100,0)	0
	Pre-cycle 5 (N=19)	19/19 (100,0)	0
	Pre-cycle 9 (N=19)	19/19 (100,0)	0
	Pre-cycle 13 (N=17)	17/17 (100,0)	0
	Pre-cycle 25 (N=15)	15/15 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=19)	19/19 (100,0)	0
Item 28.Pain with urination	Pre-cycle 3 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 5 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 9 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	14/15 (93,3)	1/15 (6,7)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)
Item 29.Increased urinary frequency/urgency	Pre-cycle 3 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 5 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 9 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	12/15 (80,0)	3/15 (20,0)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	15/19 (78,9)	4/19 (21,1)
Item 30.Difficulty beginning urination	Pre-cycle 3 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 5 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 9 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 13 (N=17)	15/17 (88,2)	2/17 (11,8)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.2 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	Pre-cycle 3 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 5 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 9 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)
Item 32.Weakness	Pre-cycle 3 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 5 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 9 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 13 (N=17)	10/17 (58,8)	7/17 (41,2)
	Pre-cycle 25 (N=15)	8/15 (53,3)	7/15 (46,7)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	11/19 (57,9)	8/19 (42,1)
Item 33.Muscle pain	Pre-cycle 3 (N=19)	9/19 (47,4)	10/19 (52,6)
	Pre-cycle 5 (N=19)	8/19 (42,1)	11/19 (57,9)
	Pre-cycle 9 (N=19)	9/19 (47,4)	10/19 (52,6)
	Pre-cycle 13 (N=17)	8/17 (47,1)	9/17 (52,9)
	Pre-cycle 25 (N=15)	6/15 (40,0)	9/15 (60,0)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	8/19 (42,1)	11/19 (57,9)
Item 34.Dizziness	Pre-cycle 3 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 5 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 9 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 13 (N=17)	15/17 (88,2)	2/17 (11,8)
	Pre-cycle 25 (N=15)	14/15 (93,3)	1/15 (6,7)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	17/19 (89,5)	2/19 (10,5)
Item 35.Numbness	Pre-cycle 3 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 5 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 9 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 13 (N=17)	15/17 (88,2)	2/17 (11,8)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	15/19 (78,9)	4/19 (21,1)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.2 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	Pre-cycle 3 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 5 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 9 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	12/15 (80,0)	3/15 (20,0)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=19)	14/19 (73,7)	5/19 (26,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.3 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 1.Fatigue/feeling tired	Pre-cycle 3 (N=21)	12/21 (57,1)	9/21 (42,9)
	Pre-cycle 5 (N=21)	11/21 (52,4)	10/21 (47,6)
	Pre-cycle 9 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 13 (N=19)	10/19 (52,6)	9/19 (47,4)
	Pre-cycle 25 (N=12)	6/12 (50,0)	6/12 (50,0)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	9/21 (42,9)	12/21 (57,1)
Item 2.Sleep problems	Pre-cycle 3 (N=21)	10/21 (47,6)	11/21 (52,4)
	Pre-cycle 5 (N=21)	10/21 (47,6)	11/21 (52,4)
	Pre-cycle 9 (N=21)	12/21 (57,1)	9/21 (42,9)
	Pre-cycle 13 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 25 (N=12)	3/12 (25,0)	9/12 (75,0)
	Pre-cycle 37 (N=4)	1/ 4 (25,0)	3/ 4 (75,0)
	Overall (N=21)	9/21 (42,9)	12/21 (57,1)
Item 3.Less appetite	Pre-cycle 3 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 5 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 9 (N=21)	15/21 (71,4)	6/21 (28,6)
	Pre-cycle 13 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 25 (N=12)	6/12 (50,0)	6/12 (50,0)
	Pre-cycle 37 (N=4)	0	4/ 4 (100,0)
	Overall (N=21)	12/21 (57,1)	9/21 (42,9)
Item 4.More appetite	Pre-cycle 3 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 5 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 9 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 13 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	16/21 (76,2)	5/21 (23,8)
Item 5.Headaches	Pre-cycle 3 (N=21)	14/21 (66,7)	7/21 (33,3)
	Pre-cycle 5 (N=21)	15/21 (71,4)	6/21 (28,6)
	Pre-cycle 9 (N=21)	15/21 (71,4)	6/21 (28,6)
	Pre-cycle 13 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	13/21 (61,9)	8/21 (38,1)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.3 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 6.Vision changes	Pre-cycle 3 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 5 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 9 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 13 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	18/21 (85,7)	3/21 (14,3)
Item 7.Decreased hearing	Pre-cycle 3 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 5 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 9 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	19/21 (90,5)	2/21 (9,5)
Item 8.Mouth sores	Pre-cycle 3 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 5 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 9 (N=21)	21/21 (100,0)	0
	Pre-cycle 13 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	20/21 (95,2)	1/21 (4,8)
Item 9.Trouble swallowing	Pre-cycle 3 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 5 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 9 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 13 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 25 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=21)	18/21 (85,7)	3/21 (14,3)
Item 10.Choking	Pre-cycle 3 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 5 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 9 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 13 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 37 (N=4)	1/ 4 (25,0)	3/ 4 (75,0)
	Overall (N=21)	17/21 (81,0)	4/21 (19,0)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.3 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 11.Snoring	Pre-cycle 3 (N=21)	14/21 (66,7)	7/21 (33,3)
	Pre-cycle 5 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 9 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 13 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 25 (N=12)	5/12 (41,7)	7/12 (58,3)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=21)	11/21 (52,4)	10/21 (47,6)
Item 12.Frequent awakenings at night	Pre-cycle 3 (N=21)	12/21 (57,1)	9/21 (42,9)
	Pre-cycle 5 (N=21)	11/21 (52,4)	10/21 (47,6)
	Pre-cycle 9 (N=21)	12/21 (57,1)	9/21 (42,9)
	Pre-cycle 13 (N=19)	10/19 (52,6)	9/19 (47,4)
	Pre-cycle 25 (N=12)	3/12 (25,0)	9/12 (75,0)
	Pre-cycle 37 (N=4)	0	4/ 4 (100,0)
	Overall (N=21)	10/21 (47,6)	11/21 (52,4)
Item 13.Cough	Pre-cycle 3 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 5 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 9 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 13 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 25 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=21)	12/21 (57,1)	9/21 (42,9)
Item 14.Wheezing	Pre-cycle 3 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 5 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 9 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 13 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	16/21 (76,2)	5/21 (23,8)
Item 15.Difficulty breathing	Pre-cycle 3 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 5 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 9 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 13 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	18/21 (85,7)	3/21 (14,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.3 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	Pre-cycle 3 (N=21)	21/21 (100,0)	0
	Pre-cycle 5 (N=21)	21/21 (100,0)	0
	Pre-cycle 9 (N=21)	21/21 (100,0)	0
	Pre-cycle 13 (N=19)	19/19 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	21/21 (100,0)	0
Item 17.Palpitations/fluttering	Pre-cycle 3 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 5 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 9 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 13 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	20/21 (95,2)	1/21 (4,8)
Item 18.Shortness of breath with activity	Pre-cycle 3 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 5 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 9 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=21)	16/21 (76,2)	5/21 (23,8)
Item 19.Shortness of breath at rest	Pre-cycle 3 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 5 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 9 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	19/21 (90,5)	2/21 (9,5)
Item 20.Swelling in hands/feet	Pre-cycle 3 (N=21)	21/21 (100,0)	0
	Pre-cycle 5 (N=21)	21/21 (100,0)	0
	Pre-cycle 9 (N=21)	21/21 (100,0)	0
	Pre-cycle 13 (N=19)	19/19 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	21/21 (100,0)	0

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.3 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 21.Abdominal pain	Pre-cycle 3 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 5 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 9 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 13 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 25 (N=12)	6/12 (50,0)	6/12 (50,0)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	11/21 (52,4)	10/21 (47,6)
Item 22.Heartburn	Pre-cycle 3 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 5 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 9 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	19/21 (90,5)	2/21 (9,5)
Item 23.Nausea	Pre-cycle 3 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 5 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 9 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 13 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=21)	15/21 (71,4)	6/21 (28,6)
Item 24.Vomiting	Pre-cycle 3 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 5 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 9 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 13 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=21)	17/21 (81,0)	4/21 (19,0)
Item 25.Diarrhea	Pre-cycle 3 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 5 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 9 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 13 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	16/21 (76,2)	5/21 (23,8)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.3 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 26.Constipation	Pre-cycle 3 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 5 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 9 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 13 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	18/21 (85,7)	3/21 (14,3)
Item 27.Stool incontinence	Pre-cycle 3 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 5 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 9 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	18/21 (85,7)	3/21 (14,3)
Item 28.Pain with urination	Pre-cycle 3 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 5 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 9 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 13 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	17/21 (81,0)	4/21 (19,0)
Item 29.Increased urinary frequency/urgency	Pre-cycle 3 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 5 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 9 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 13 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	16/21 (76,2)	5/21 (23,8)
Item 30.Difficulty beginning urination	Pre-cycle 3 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 5 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 9 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	18/21 (85,7)	3/21 (14,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.3 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	Pre-cycle 3 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 5 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 9 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 13 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	16/21 (76,2)	5/21 (23,8)
Item 32.Weakness	Pre-cycle 3 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 5 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 9 (N=21)	15/21 (71,4)	6/21 (28,6)
	Pre-cycle 13 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 25 (N=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 37 (N=4)	1/ 4 (25,0)	3/ 4 (75,0)
	Overall (N=21)	13/21 (61,9)	8/21 (38,1)
Item 33.Muscle pain	Pre-cycle 3 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 5 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 9 (N=21)	14/21 (66,7)	7/21 (33,3)
	Pre-cycle 13 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 25 (N=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 37 (N=4)	1/ 4 (25,0)	3/ 4 (75,0)
	Overall (N=21)	12/21 (57,1)	9/21 (42,9)
Item 34.Dizziness	Pre-cycle 3 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 5 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 9 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	19/21 (90,5)	2/21 (9,5)
Item 35.Numbness	Pre-cycle 3 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 5 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 9 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	19/21 (90,5)	2/21 (9,5)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.3 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	Pre-cycle 3 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 5 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 9 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 13 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=21)	17/21 (81,0)	4/21 (19,0)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.4 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 1.Fatigue/feeling tired	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 9 (N=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 13 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 25 (N=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
Item 2.Sleep problems	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 5 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 9 (N=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)
Item 3.Less appetite	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 9 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 13 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)
Item 4.More appetite	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 9 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 13 (N=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
Item 5.Headaches	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 5 (N=14)	9/14 (64,3)	5/14 (35,7)
	Pre-cycle 9 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 13 (N=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 25 (N=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.4 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 6.Vision changes	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 7.Decreased hearing	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 8.Mouth sores	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 9.Trouble swallowing	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=14)	14/14 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0
Item 10.Choking	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.4 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 11.Snoring	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 9 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 13 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 25 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	11/14 (78,6)	3/14 (21,4)
Item 12.Frequent awakenings at night	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 9 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 13 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 25 (N=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)
Item 13.Cough	Pre-cycle 3 (N=14)	7/14 (50,0)	7/14 (50,0)
	Pre-cycle 5 (N=14)	8/14 (57,1)	6/14 (42,9)
	Pre-cycle 9 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 13 (N=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 25 (N=12)	6/12 (50,0)	6/12 (50,0)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)
Item 14.Wheezing	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=14)	14/14 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0
Item 15.Difficulty breathing	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	14/14 (100,0)	0
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.4 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 17.Palpitations/fluttering	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 18.Shortness of breath with activity	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 5 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 9 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 13 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 25 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)
Item 19.Shortness of breath at rest	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 20.Swelling in hands/feet	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.4 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 21.Abdominal pain	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	11/14 (78,6)	3/14 (21,4)
Item 22.Heartburn	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=14)	14/14 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0
Item 23.Nausea	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 24.Vomiting	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 25.Diarrhea	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 25 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.4 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 26.Constipation	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
Item 27.Stool incontinence	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	14/14 (100,0)	0
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	0	1/ 1 (100,0)
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 28.Pain with urination	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=14)	14/14 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0
Item 29.Increased urinary frequency/urgency	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)
Item 30.Difficulty beginning urination	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=11)	11/11 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.4 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	Pre-cycle 3 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=11)	10/11 (90,9)	1/11 (9,1)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 32.Weakness	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 33.Muscle pain	Pre-cycle 3 (N=14)	8/14 (57,1)	6/14 (42,9)
	Pre-cycle 5 (N=14)	8/14 (57,1)	6/14 (42,9)
	Pre-cycle 9 (N=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 13 (N=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
Item 34.Dizziness	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=14)	14/14 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 35.Numbness	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.4 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=1)	1/ 1 (100,0)	0
	Overall (N=14)	11/14 (78,6)	3/14 (21,4)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.5 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 1.Fatigue/feeling tired	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 5 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 9 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 13 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 25 (N=10)	6/10 (60,0)	4/10 (40,0)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
Item 2.Sleep problems	Pre-cycle 3 (N=14)	9/14 (64,3)	5/14 (35,7)
	Pre-cycle 5 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 9 (N=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 13 (N=13)	5/13 (38,5)	8/13 (61,5)
	Pre-cycle 25 (N=10)	5/10 (50,0)	5/10 (50,0)
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)
Item 3.Less appetite	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 25 (N=10)	8/10 (80,0)	2/10 (20,0)
	Overall (N=14)	11/14 (78,6)	3/14 (21,4)
Item 4.More appetite	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	8/10 (80,0)	2/10 (20,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 5.Headaches	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 9 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 13 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 25 (N=10)	7/10 (70,0)	3/10 (30,0)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.5 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 6.Vision changes	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 7.Decreased hearing	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0
Item 8.Mouth sores	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	8/10 (80,0)	2/10 (20,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 9.Trouble swallowing	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 10.Choking	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.5 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 11.Snoring	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 5 (N=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 9 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 13 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 25 (N=10)	7/10 (70,0)	3/10 (30,0)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
Item 12.Frequent awakenings at night	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 5 (N=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 9 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 13 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 25 (N=10)	7/10 (70,0)	3/10 (30,0)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
Item 13.Cough	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 9 (N=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 13 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 25 (N=10)	7/10 (70,0)	3/10 (30,0)
	Overall (N=14)	7/14 (50,0)	7/14 (50,0)
Item 14.Wheezing	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 15.Difficulty breathing	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.5 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0
Item 17.Palpitations/fluttering	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 18.Shortness of breath with activity	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 5 (N=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 9 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 13 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 25 (N=10)	8/10 (80,0)	2/10 (20,0)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
Item 19.Shortness of breath at rest	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0
Item 20.Swelling in hands/feet	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.5 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 21.Abdominal pain	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 22.Heartburn	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 23.Nausea	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	11/14 (78,6)	3/14 (21,4)
Item 24.Vomiting	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0
Item 25.Diarrhea	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.5 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 26.Constipation	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	11/14 (78,6)	3/14 (21,4)
Item 27.Stool incontinence	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 28.Pain with urination	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0
Item 29.Increased urinary frequency/urgency	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	14/14 (100,0)	0
Item 30.Difficulty beginning urination	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	13/13 (100,0)	0
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.5 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 32.Weakness	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 5 (N=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 9 (N=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 13 (N=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 25 (N=10)	5/10 (50,0)	5/10 (50,0)
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
Item 33.Muscle pain	Pre-cycle 3 (N=14)	9/14 (64,3)	5/14 (35,7)
	Pre-cycle 5 (N=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 9 (N=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 13 (N=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 25 (N=10)	5/10 (50,0)	5/10 (50,0)
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
Item 34.Dizziness	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 35.Numbness	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.2.5 General PN symptoms responder analyses (Improvement by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not improved	Improved by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 9 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)

[a] Compared to baseline.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 1: Fatigue/feeling tired, n (%)	Baseline (n=30)	Not at all	11 (36,7)
		A little	14 (46,7)
		Some	3 (10,0)
		Pretty much	1 (3,3)
		A lot	1 (3,3)
	Pre-cycle 3 (n=30)	Not at all	10 (33,3)
		A little	10 (33,3)
		Some	9 (30,0)
		Pretty much	1 (3,3)
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	13 (44,8)
		A little	9 (31,0)
		Some	4 (13,8)
		Pretty much	3 (10,3)
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	13 (46,4)
		A little	10 (35,7)
		Some	4 (14,3)
		Pretty much	1 (3,6)
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	13 (48,1)
		A little	9 (33,3)
		Some	5 (18,5)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	10 (52,6)
		A little	4 (21,1)
		Some	5 (26,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	1 (25,0)
		A little	2 (50,0)
		Some	1 (25,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 2: Sleep problems, n (%)	Baseline (n=30)	Not at all	18 (60,0)
		A little	3 (10,0)
		Some	4 (13,3)
		Pretty much	3 (10,0)
		A lot	2 (6,7)
	Pre-cycle 3 (n=30)	Not at all	19 (63,3)
		A little	7 (23,3)
		Some	4 (13,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	22 (75,9)
		A little	3 (10,3)
		Some	2 (6,9)
		Pretty much	2 (6,9)
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	16 (57,1)
		A little	6 (21,4)
		Some	4 (14,3)
		Pretty much	1 (3,6)
		A lot	1 (3,6)
	Pre-cycle 13 (n=27)	Not at all	20 (74,1)
		A little	2 (7,4)
		Some	2 (7,4)
		Pretty much	1 (3,7)
		A lot	2 (7,4)
	Pre-cycle 25 (n=19)	Not at all	16 (84,2)
		A little	2 (10,5)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	0
		Some	0
		Pretty much	1 (25,0)
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 3: Less appetite, n (%)	Baseline (n=30)	Not at all	22 (73,3)
		A little	3 (10,0)
		Some	1 (3,3)
		Pretty much	3 (10,0)
		A lot	1 (3,3)
	Pre-cycle 3 (n=30)	Not at all	23 (76,7)
		A little	4 (13,3)
		Some	2 (6,7)
		Pretty much	1 (3,3)
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	22 (75,9)
		A little	5 (17,2)
		Some	1 (3,4)
		Pretty much	0
		A lot	1 (3,4)
	Pre-cycle 9 (n=28)	Not at all	19 (67,9)
		A little	3 (10,7)
		Some	5 (17,9)
		Pretty much	1 (3,6)
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	18 (66,7)
		A little	4 (14,8)
		Some	2 (7,4)
		Pretty much	2 (7,4)
		A lot	1 (3,7)
	Pre-cycle 25 (n=19)	Not at all	15 (78,9)
		A little	3 (15,8)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 4: More appetite, n (%)	Baseline (n=30)	Not at all	22 (73,3)
		A little	6 (20,0)
		Some	1 (3,3)
		Pretty much	0
		A lot	1 (3,3)
	Pre-cycle 3 (n=30)	Not at all	13 (43,3)
		A little	8 (26,7)
		Some	5 (16,7)
		Pretty much	3 (10,0)
		A lot	1 (3,3)
	Pre-cycle 5 (n=29)	Not at all	9 (31,0)
		A little	12 (41,4)
		Some	5 (17,2)
		Pretty much	2 (6,9)
		A lot	1 (3,4)
	Pre-cycle 9 (n=28)	Not at all	19 (67,9)
		A little	5 (17,9)
		Some	1 (3,6)
		Pretty much	2 (7,1)
		A lot	1 (3,6)
	Pre-cycle 13 (n=27)	Not at all	18 (66,7)
		A little	3 (11,1)
		Some	5 (18,5)
		Pretty much	0
		A lot	1 (3,7)
	Pre-cycle 25 (n=19)	Not at all	10 (52,6)
		A little	6 (31,6)
		Some	1 (5,3)
		Pretty much	2 (10,5)
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	0
		Some	1 (25,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 5: Headaches, n (%)	Baseline (n=30)	Not at all	18 (60,0)
		A little	7 (23,3)
		Some	5 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	19 (63,3)
		A little	8 (26,7)
		Some	3 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	20 (69,0)
		A little	6 (20,7)
		Some	2 (6,9)
		Pretty much	1 (3,4)
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	15 (53,6)
		A little	10 (35,7)
		Some	3 (10,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	17 (63,0)
		A little	8 (29,6)
		Some	2 (7,4)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	13 (68,4)
		A little	4 (21,1)
		Some	1 (5,3)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	2 (50,0)
		A little	2 (50,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 6: Vision changes, n (%)	Baseline (n=30)	Not at all	27 (90,0)
		A little	3 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	29 (96,7)
		A little	1 (3,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	27 (93,1)
		A little	2 (6,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	27 (96,4)
		A little	1 (3,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	26 (96,3)
		A little	1 (3,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 7: Decreased hearing, n (%)	Baseline (n=30)	Not at all	28 (93,3)
		A little	1 (3,3)
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	29 (96,7)
		A little	0
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	28 (96,6)
		A little	0
		Some	1 (3,4)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	27 (96,4)
		A little	1 (3,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	24 (88,9)
		A little	2 (7,4)
		Some	1 (3,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 8: Mouth sores, n (%)	Baseline (n=30)	Not at all	27 (90,0)
		A little	3 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	25 (83,3)
		A little	4 (13,3)
		Some	0
		Pretty much	1 (3,3)
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	28 (96,6)
		A little	0
		Some	0
		Pretty much	1 (3,4)
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	24 (85,7)
		A little	3 (10,7)
		Some	1 (3,6)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	23 (85,2)
		A little	4 (14,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 9: Trouble swallowing, n (%)	Baseline (n=30)	Not at all	27 (90,0)
		A little	1 (3,3)
		Some	1 (3,3)
		Pretty much	0
		A lot	1 (3,3)
	Pre-cycle 3 (n=30)	Not at all	28 (93,3)
		A little	2 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	27 (93,1)
		A little	2 (6,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	26 (92,9)
		A little	1 (3,6)
		Some	1 (3,6)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	25 (92,6)
		A little	1 (3,7)
		Some	1 (3,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 10: Choking, n (%)	Baseline (n=30)	Not at all	27 (90,0)
		A little	1 (3,3)
		Some	2 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	29 (96,7)
		A little	1 (3,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	29 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	27 (96,4)
		A little	0
		Some	1 (3,6)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	27 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 11: Snoring, n (%)	Baseline (n=30)	Not at all	19 (63,3)
		A little	6 (20,0)
		Some	2 (6,7)
		Pretty much	1 (3,3)
		A lot	2 (6,7)
	Pre-cycle 3 (n=30)	Not at all	22 (73,3)
		A little	7 (23,3)
		Some	0
		Pretty much	1 (3,3)
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	19 (65,5)
		A little	5 (17,2)
		Some	4 (13,8)
		Pretty much	1 (3,4)
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	22 (78,6)
		A little	3 (10,7)
		Some	2 (7,1)
		Pretty much	1 (3,6)
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	19 (70,4)
		A little	4 (14,8)
		Some	4 (14,8)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 12: Frequent awakenings at night, n (%)	Baseline (n=30)	Not at all	17 (56,7)
		A little	6 (20,0)
		Some	4 (13,3)
		Pretty much	2 (6,7)
		A lot	1 (3,3)
	Pre-cycle 3 (n=30)	Not at all	18 (60,0)
		A little	7 (23,3)
		Some	5 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	20 (69,0)
		A little	6 (20,7)
		Some	2 (6,9)
		Pretty much	1 (3,4)
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	21 (75,0)
		A little	4 (14,3)
		Some	1 (3,6)
		Pretty much	1 (3,6)
		A lot	1 (3,6)
	Pre-cycle 13 (n=27)	Not at all	19 (70,4)
		A little	3 (11,1)
		Some	2 (7,4)
		Pretty much	1 (3,7)
		A lot	2 (7,4)
	Pre-cycle 25 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 13: Cough, n (%)	Baseline (n=30)	Not at all	17 (56,7)
		A little	10 (33,3)
		Some	3 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	20 (66,7)
		A little	7 (23,3)
		Some	3 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	19 (65,5)
		A little	9 (31,0)
		Some	0
		Pretty much	0
		A lot	1 (3,4)
	Pre-cycle 9 (n=28)	Not at all	11 (39,3)
		A little	13 (46,4)
		Some	3 (10,7)
		Pretty much	1 (3,6)
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	17 (63,0)
		A little	9 (33,3)
		Some	1 (3,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	14 (73,7)
		A little	4 (21,1)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 14: Wheezing, n (%)	Baseline (n=30)	Not at all	27 (90,0)
		A little	1 (3,3)
		Some	1 (3,3)
		Pretty much	1 (3,3)
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	27 (90,0)
		A little	3 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	26 (89,7)
		A little	3 (10,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	26 (92,9)
		A little	1 (3,6)
		Some	1 (3,6)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	27 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 15: Difficulty breathing, n (%)	Baseline (n=30)	Not at all	27 (90,0)
		A little	3 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	30 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	26 (89,7)
		A little	3 (10,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	28 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	24 (88,9)
		A little	3 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 16: Chest pain, n (%)	Baseline (n=30)	Not at all	28 (93,3)
		A little	1 (3,3)
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	30 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	29 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	27 (96,4)
		A little	1 (3,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	25 (92,6)
		A little	1 (3,7)
		Some	1 (3,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 17: Palpitations/fluttering, n (%)	Baseline (n=30)	Not at all	29 (96,7)
		A little	0
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	29 (96,7)
		A little	1 (3,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	29 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	28 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	25 (92,6)
		A little	1 (3,7)
		Some	1 (3,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 18: Shortness of breath with activity, n (%)	Baseline (n=30)	Not at all	21 (70,0)
		A little	7 (23,3)
		Some	1 (3,3)
		Pretty much	1 (3,3)
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	25 (83,3)
		A little	4 (13,3)
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	23 (79,3)
		A little	6 (20,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	24 (85,7)
		A little	2 (7,1)
		Some	1 (3,6)
		Pretty much	1 (3,6)
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	23 (85,2)
		A little	4 (14,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	17 (89,5)
		A little	1 (5,3)
		Some	0
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 19: Shortness of breath at rest, n (%)	Baseline (n=30)	Not at all	28 (93,3)
		A little	2 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	30 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	29 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	27 (96,4)
		A little	1 (3,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	26 (96,3)
		A little	1 (3,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 20: Swelling in hands/feet, n (%)	Baseline (n=30)	Not at all	30 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	28 (93,3)
		A little	1 (3,3)
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	28 (96,6)
		A little	1 (3,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	25 (89,3)
		A little	3 (10,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	23 (85,2)
		A little	4 (14,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 21: Abdominal pain, n (%)	Baseline (n=30)	Not at all	22 (73,3)
		A little	6 (20,0)
		Some	2 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	16 (53,3)
		A little	6 (20,0)
		Some	6 (20,0)
		Pretty much	1 (3,3)
		A lot	1 (3,3)
	Pre-cycle 5 (n=29)	Not at all	20 (69,0)
		A little	4 (13,8)
		Some	3 (10,3)
		Pretty much	2 (6,9)
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	16 (57,1)
		A little	5 (17,9)
		Some	5 (17,9)
		Pretty much	2 (7,1)
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	21 (77,8)
		A little	2 (7,4)
		Some	3 (11,1)
		Pretty much	1 (3,7)
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	11 (57,9)
		A little	6 (31,6)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 22: Heartburn, n (%)	Baseline (n=30)	Not at all	29 (96,7)
		A little	0
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	27 (90,0)
		A little	3 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	28 (96,6)
		A little	1 (3,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	27 (96,4)
		A little	1 (3,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	26 (96,3)
		A little	0
		Some	1 (3,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 23: Nausea, n (%)	Baseline (n=30)	Not at all	24 (80,0)
		A little	4 (13,3)
		Some	2 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	19 (63,3)
		A little	8 (26,7)
		Some	2 (6,7)
		Pretty much	1 (3,3)
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	18 (62,1)
		A little	8 (27,6)
		Some	2 (6,9)
		Pretty much	1 (3,4)
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	20 (71,4)
		A little	4 (14,3)
		Some	2 (7,1)
		Pretty much	2 (7,1)
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	20 (74,1)
		A little	3 (11,1)
		Some	4 (14,8)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	13 (68,4)
		A little	5 (26,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 24: Vomiting, n (%)	Baseline (n=30)	Not at all	26 (86,7)
		A little	4 (13,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	24 (80,0)
		A little	4 (13,3)
		Some	2 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	21 (72,4)
		A little	7 (24,1)
		Some	1 (3,4)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	23 (82,1)
		A little	2 (7,1)
		Some	3 (10,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	24 (88,9)
		A little	1 (3,7)
		Some	2 (7,4)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 25: Diarrhea, n (%)	Baseline (n=30)	Not at all	24 (80,0)
		A little	3 (10,0)
		Some	2 (6,7)
		Pretty much	0
		A lot	1 (3,3)
	Pre-cycle 3 (n=30)	Not at all	19 (63,3)
		A little	7 (23,3)
		Some	3 (10,0)
		Pretty much	0
		A lot	1 (3,3)
	Pre-cycle 5 (n=29)	Not at all	21 (72,4)
		A little	5 (17,2)
		Some	3 (10,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	17 (60,7)
		A little	7 (25,0)
		Some	4 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	17 (63,0)
		A little	6 (22,2)
		Some	3 (11,1)
		Pretty much	0
		A lot	1 (3,7)
	Pre-cycle 25 (n=19)	Not at all	14 (73,7)
		A little	5 (26,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 26: Constipation, n (%)	Baseline (n=30)	Not at all	25 (83,3)
		A little	2 (6,7)
		Some	3 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	20 (66,7)
		A little	7 (23,3)
		Some	2 (6,7)
		Pretty much	1 (3,3)
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	19 (65,5)
		A little	10 (34,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	23 (82,1)
		A little	5 (17,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	21 (77,8)
		A little	4 (14,8)
		Some	1 (3,7)
		Pretty much	0
		A lot	1 (3,7)
	Pre-cycle 25 (n=19)	Not at all	13 (68,4)
		A little	5 (26,3)
		Some	0
		Pretty much	0
		A lot	1 (5,3)
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 27: Stool incontinence, n (%)	Baseline (n=30)	Not at all	25 (83,3)
		A little	4 (13,3)
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	25 (83,3)
		A little	3 (10,0)
		Some	1 (3,3)
		Pretty much	1 (3,3)
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	25 (86,2)
		A little	4 (13,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	23 (82,1)
		A little	4 (14,3)
		Some	0
		Pretty much	0
		A lot	1 (3,6)
	Pre-cycle 13 (n=27)	Not at all	23 (85,2)
		A little	3 (11,1)
		Some	0
		Pretty much	1 (3,7)
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (5,3)
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 28: Pain with urination, n (%)	Baseline (n=30)	Not at all	29 (96,7)
		A little	1 (3,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	29 (96,7)
		A little	1 (3,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	28 (96,6)
		A little	1 (3,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	28 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	26 (96,3)
		A little	0
		Some	1 (3,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 29: Increased urinary frequency/urgency, n (%)	Baseline (n=30)	Not at all	25 (83,3)
		A little	2 (6,7)
		Some	3 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	28 (93,3)
		A little	2 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	27 (93,1)
		A little	2 (6,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	28 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	26 (96,3)
		A little	1 (3,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 30: Difficulty beginning urination, n (%)	Baseline (n=30)	Not at all	27 (90,0)
		A little	2 (6,7)
		Some	0
		Pretty much	1 (3,3)
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	27 (90,0)
		A little	2 (6,7)
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	27 (93,1)
		A little	2 (6,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	26 (92,9)
		A little	1 (3,6)
		Some	0
		Pretty much	1 (3,6)
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	26 (96,3)
		A little	1 (3,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=18)	Not at all	16 (88,9)
		A little	1 (5,6)
		Some	1 (5,6)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 31: Urinary incontinence, n (%)	Baseline (n=30)	Not at all	25 (83,3)
		A little	1 (3,3)
		Some	2 (6,7)
		Pretty much	1 (3,3)
		A lot	1 (3,3)
	Pre-cycle 3 (n=29)	Not at all	26 (89,7)
		A little	2 (6,9)
		Some	0
		Pretty much	1 (3,4)
		A lot	0
	Pre-cycle 5 (n=28)	Not at all	27 (96,4)
		A little	0
		Some	1 (3,6)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	25 (89,3)
		A little	2 (7,1)
		Some	0
		Pretty much	0
		A lot	1 (3,6)
	Pre-cycle 13 (n=27)	Not at all	24 (88,9)
		A little	2 (7,4)
		Some	0
		Pretty much	1 (3,7)
		A lot	0
	Pre-cycle 25 (n=18)	Not at all	17 (94,4)
		A little	1 (5,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 32: Weakness, n (%)	Baseline (n=30)	Not at all	22 (73,3)
		A little	2 (6,7)
		Some	3 (10,0)
		Pretty much	2 (6,7)
		A lot	1 (3,3)
	Pre-cycle 3 (n=30)	Not at all	24 (80,0)
		A little	3 (10,0)
		Some	1 (3,3)
		Pretty much	2 (6,7)
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	27 (93,1)
		A little	2 (6,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	21 (75,0)
		A little	6 (21,4)
		Some	1 (3,6)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	24 (88,9)
		A little	3 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 33: Muscle pain, n (%)	Baseline (n=30)	Not at all	19 (63,3)
		A little	4 (13,3)
		Some	5 (16,7)
		Pretty much	2 (6,7)
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	21 (70,0)
		A little	6 (20,0)
		Some	1 (3,3)
		Pretty much	2 (6,7)
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	24 (82,8)
		A little	3 (10,3)
		Some	1 (3,4)
		Pretty much	1 (3,4)
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	21 (75,0)
		A little	6 (21,4)
		Some	0
		Pretty much	1 (3,6)
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	22 (81,5)
		A little	2 (7,4)
		Some	2 (7,4)
		Pretty much	1 (3,7)
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 34: Dizziness, n (%)	Baseline (n=30)	Not at all	28 (93,3)
		A little	2 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	25 (83,3)
		A little	4 (13,3)
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	27 (93,1)
		A little	2 (6,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	25 (89,3)
		A little	3 (10,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	25 (92,6)
		A little	1 (3,7)
		Some	1 (3,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 35: Numbness, n (%)	Baseline (n=30)	Not at all	29 (96,7)
		A little	0
		Some	1 (3,3)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=30)	Not at all	29 (96,7)
		A little	1 (3,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	28 (96,6)
		A little	0
		Some	1 (3,4)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	26 (92,9)
		A little	2 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	26 (96,3)
		A little	1 (3,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=30) [a]
Item 36: Tingling, n (%)	Baseline (n=30)	Not at all	26 (86,7)
		A little	1 (3,3)
		Some	1 (3,3)
		Pretty much	1 (3,3)
		A lot	1 (3,3)
	Pre-cycle 3 (n=30)	Not at all	27 (90,0)
		A little	3 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=29)	Not at all	27 (93,1)
		A little	1 (3,4)
		Some	1 (3,4)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=28)	Not at all	27 (96,4)
		A little	1 (3,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=27)	Not at all	26 (96,3)
		A little	1 (3,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 1: Fatigue/feeling tired, n (%)	Baseline (n=20)	Not at all	6 (30,0)
		A little	7 (35,0)
		Some	2 (10,0)
		Pretty much	3 (15,0)
		A lot	2 (10,0)
	Pre-cycle 3 (n=19)	Not at all	7 (36,8)
		A little	5 (26,3)
		Some	4 (21,1)
		Pretty much	0
		A lot	3 (15,8)
	Pre-cycle 5 (n=19)	Not at all	6 (31,6)
		A little	7 (36,8)
		Some	3 (15,8)
		Pretty much	2 (10,5)
		A lot	1 (5,3)
	Pre-cycle 9 (n=19)	Not at all	5 (26,3)
		A little	7 (36,8)
		Some	6 (31,6)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	6 (35,3)
		A little	5 (29,4)
		Some	5 (29,4)
		Pretty much	1 (5,9)
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	5 (33,3)
		A little	7 (46,7)
		Some	2 (13,3)
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	0
		A little	1 (100,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 2: Sleep problems, n (%)	Baseline (n=20)	Not at all	4 (20,0)
		A little	9 (45,0)
		Some	3 (15,0)
		Pretty much	4 (20,0)
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	8 (42,1)
		A little	5 (26,3)
		Some	5 (26,3)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	10 (52,6)
		A little	4 (21,1)
		Some	2 (10,5)
		Pretty much	3 (15,8)
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	9 (47,4)
		A little	7 (36,8)
		Some	3 (15,8)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	10 (58,8)
		A little	3 (17,6)
		Some	3 (17,6)
		Pretty much	0
		A lot	1 (5,9)
	Pre-cycle 25 (n=15)	Not at all	8 (53,3)
		A little	4 (26,7)
		Some	1 (6,7)
		Pretty much	1 (6,7)
		A lot	1 (6,7)
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 3: Less appetite, n (%)	Baseline (n=20)	Not at all	12 (60,0)
		A little	3 (15,0)
		Some	2 (10,0)
		Pretty much	2 (10,0)
		A lot	1 (5,0)
	Pre-cycle 3 (n=19)	Not at all	13 (68,4)
		A little	3 (15,8)
		Some	2 (10,5)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	13 (68,4)
		A little	4 (21,1)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	15 (78,9)
		A little	3 (15,8)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	0
		Some	1 (5,9)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	12 (80,0)
		A little	2 (13,3)
		Some	0
		Pretty much	0
		A lot	1 (6,7)
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 4: More appetite, n (%)	Baseline (n=20)	Not at all	14 (70,0)
		A little	3 (15,0)
		Some	2 (10,0)
		Pretty much	1 (5,0)
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	13 (68,4)
		A little	4 (21,1)
		Some	1 (5,3)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	12 (63,2)
		A little	4 (21,1)
		Some	2 (10,5)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	13 (68,4)
		A little	5 (26,3)
		Some	0
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	1 (5,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	13 (86,7)
		A little	1 (6,7)
		Some	0
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 5: Headaches, n (%)	Baseline (n=20)	Not at all	10 (50,0)
		A little	6 (30,0)
		Some	2 (10,0)
		Pretty much	2 (10,0)
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	11 (57,9)
		A little	5 (26,3)
		Some	3 (15,8)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	9 (47,4)
		A little	7 (36,8)
		Some	3 (15,8)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	13 (68,4)
		A little	5 (26,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	11 (64,7)
		A little	4 (23,5)
		Some	1 (5,9)
		Pretty much	0
		A lot	1 (5,9)
	Pre-cycle 25 (n=15)	Not at all	6 (40,0)
		A little	5 (33,3)
		Some	4 (26,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	0
		A little	0
		Some	1 (100,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 6: Vision changes, n (%)	Baseline (n=20)	Not at all	16 (80,0)
		A little	2 (10,0)
		Some	2 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	16 (84,2)
		A little	1 (5,3)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	14 (73,7)
		A little	5 (26,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	17 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	12 (80,0)
		A little	2 (13,3)
		Some	0
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 7: Decreased hearing, n (%)	Baseline (n=20)	Not at all	19 (95,0)
		A little	0
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	15 (88,2)
		A little	2 (11,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	15 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 8: Mouth sores, n (%)	Baseline (n=20)	Not at all	18 (90,0)
		A little	1 (5,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	16 (84,2)
		A little	2 (10,5)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	15 (78,9)
		A little	3 (15,8)
		Some	0
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	15 (88,2)
		A little	2 (11,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 9: Trouble swallowing, n (%)	Baseline (n=20)	Not at all	17 (85,0)
		A little	2 (10,0)
		Some	0
		Pretty much	0
		A lot	1 (5,0)
	Pre-cycle 3 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	1 (5,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (6,7)
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 10: Choking, n (%)	Baseline (n=20)	Not at all	16 (80,0)
		A little	4 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	17 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (6,7)
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 11: Snoring, n (%)	Baseline (n=20)	Not at all	12 (60,0)
		A little	1 (5,0)
		Some	2 (10,0)
		Pretty much	2 (10,0)
		A lot	3 (15,0)
	Pre-cycle 3 (n=19)	Not at all	12 (63,2)
		A little	2 (10,5)
		Some	4 (21,1)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	12 (63,2)
		A little	3 (15,8)
		Some	3 (15,8)
		Pretty much	0
		A lot	1 (5,3)
	Pre-cycle 9 (n=19)	Not at all	13 (68,4)
		A little	5 (26,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	13 (76,5)
		A little	3 (17,6)
		Some	1 (5,9)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	10 (66,7)
		A little	1 (6,7)
		Some	3 (20,0)
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 12: Frequent awakenings at night, n (%)	Baseline (n=20)	Not at all	9 (45,0)
		A little	5 (25,0)
		Some	3 (15,0)
		Pretty much	2 (10,0)
		A lot	1 (5,0)
	Pre-cycle 3 (n=19)	Not at all	14 (73,7)
		A little	3 (15,8)
		Some	0
		Pretty much	1 (5,3)
		A lot	1 (5,3)
	Pre-cycle 5 (n=19)	Not at all	14 (73,7)
		A little	3 (15,8)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	11 (57,9)
		A little	6 (31,6)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	11 (64,7)
		A little	5 (29,4)
		Some	1 (5,9)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	10 (66,7)
		A little	3 (20,0)
		Some	0
		Pretty much	2 (13,3)
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 13: Cough, n (%)	Baseline (n=20)	Not at all	9 (45,0)
		A little	7 (35,0)
		Some	2 (10,0)
		Pretty much	1 (5,0)
		A lot	1 (5,0)
	Pre-cycle 3 (n=19)	Not at all	10 (52,6)
		A little	3 (15,8)
		Some	4 (21,1)
		Pretty much	2 (10,5)
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	15 (78,9)
		A little	3 (15,8)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	13 (68,4)
		A little	5 (26,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	13 (76,5)
		A little	4 (23,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	8 (53,3)
		A little	6 (40,0)
		Some	0
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	0
		A little	1 (100,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 14: Wheezing, n (%)	Baseline (n=20)	Not at all	17 (85,0)
		A little	1 (5,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	1 (5,0)
	Pre-cycle 3 (n=19)	Not at all	17 (89,5)
		A little	1 (5,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	15 (88,2)
		A little	1 (5,9)
		Some	1 (5,9)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	0
		A little	1 (100,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 15: Difficulty breathing, n (%)	Baseline (n=20)	Not at all	17 (85,0)
		A little	2 (10,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	1 (5,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 16: Chest pain, n (%)	Baseline (n=20)	Not at all	20 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	14 (73,7)
		A little	4 (21,1)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	1 (5,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	0
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 17: Palpitations/fluttering, n (%)	Baseline (n=20)	Not at all	17 (85,0)
		A little	3 (15,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	17 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 18: Shortness of breath with activity, n (%)	Baseline (n=20)	Not at all	15 (75,0)
		A little	1 (5,0)
		Some	4 (20,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	13 (68,4)
		A little	6 (31,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	14 (73,7)
		A little	5 (26,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	13 (76,5)
		A little	3 (17,6)
		Some	0
		Pretty much	1 (5,9)
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	12 (80,0)
		A little	1 (6,7)
		Some	2 (13,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 19: Shortness of breath at rest, n (%)	Baseline (n=20)	Not at all	19 (95,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	17 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	15 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 20: Swelling in hands/feet, n (%)	Baseline (n=20)	Not at all	19 (95,0)
		A little	0
		Some	0
		Pretty much	1 (5,0)
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	16 (84,2)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	2 (10,5)
	Pre-cycle 5 (n=19)	Not at all	14 (73,7)
		A little	2 (10,5)
		Some	2 (10,5)
		Pretty much	0
		A lot	1 (5,3)
	Pre-cycle 9 (n=19)	Not at all	17 (89,5)
		A little	1 (5,3)
		Some	0
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	15 (88,2)
		A little	0
		Some	1 (5,9)
		Pretty much	0
		A lot	1 (5,9)
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	0
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 21: Abdominal pain, n (%)	Baseline (n=20)	Not at all	11 (55,0)
		A little	5 (25,0)
		Some	3 (15,0)
		Pretty much	0
		A lot	1 (5,0)
	Pre-cycle 3 (n=19)	Not at all	14 (73,7)
		A little	4 (21,1)
		Some	0
		Pretty much	0
		A lot	1 (5,3)
	Pre-cycle 5 (n=19)	Not at all	12 (63,2)
		A little	4 (21,1)
		Some	2 (10,5)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	12 (63,2)
		A little	5 (26,3)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	11 (64,7)
		A little	6 (35,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	10 (66,7)
		A little	3 (20,0)
		Some	2 (13,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 22: Heartburn, n (%)	Baseline (n=20)	Not at all	17 (85,0)
		A little	2 (10,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	17 (89,5)
		A little	1 (5,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	17 (89,5)
		A little	1 (5,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	15 (88,2)
		A little	1 (5,9)
		Some	1 (5,9)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	13 (86,7)
		A little	0
		Some	1 (6,7)
		Pretty much	0
		A lot	1 (6,7)
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 23: Nausea, n (%)	Baseline (n=20)	Not at all	14 (70,0)
		A little	4 (20,0)
		Some	2 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	10 (52,6)
		A little	5 (26,3)
		Some	3 (15,8)
		Pretty much	0
		A lot	1 (5,3)
	Pre-cycle 5 (n=19)	Not at all	12 (63,2)
		A little	5 (26,3)
		Some	1 (5,3)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	12 (63,2)
		A little	5 (26,3)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	12 (70,6)
		A little	5 (29,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	10 (66,7)
		A little	3 (20,0)
		Some	2 (13,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 24: Vomiting, n (%)	Baseline (n=20)	Not at all	18 (90,0)
		A little	2 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	12 (63,2)
		A little	4 (21,1)
		Some	3 (15,8)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	15 (78,9)
		A little	3 (15,8)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	15 (88,2)
		A little	2 (11,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	12 (80,0)
		A little	2 (13,3)
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 25: Diarrhea, n (%)	Baseline (n=20)	Not at all	15 (75,0)
		A little	3 (15,0)
		Some	2 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	12 (63,2)
		A little	2 (10,5)
		Some	5 (26,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	13 (68,4)
		A little	4 (21,1)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	13 (68,4)
		A little	3 (15,8)
		Some	3 (15,8)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	13 (76,5)
		A little	3 (17,6)
		Some	1 (5,9)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	13 (86,7)
		A little	2 (13,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	0
		A little	1 (100,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 26: Constipation, n (%)	Baseline (n=20)	Not at all	13 (65,0)
		A little	5 (25,0)
		Some	2 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	15 (78,9)
		A little	2 (10,5)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	11 (64,7)
		A little	6 (35,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	12 (80,0)
		A little	3 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 27: Stool incontinence, n (%)	Baseline (n=20)	Not at all	20 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	1 (5,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	15 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 28: Pain with urination, n (%)	Baseline (n=20)	Not at all	17 (85,0)
		A little	2 (10,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	17 (89,5)
		A little	1 (5,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	16 (84,2)
		A little	2 (10,5)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	15 (88,2)
		A little	2 (11,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	13 (86,7)
		A little	0
		Some	2 (13,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 29: Increased urinary frequency/urgency, n (%)	Baseline (n=20)	Not at all	15 (75,0)
		A little	3 (15,0)
		Some	2 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	13 (68,4)
		A little	5 (26,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	15 (78,9)
		A little	2 (10,5)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	12 (63,2)
		A little	7 (36,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	0
		Some	0
		Pretty much	1 (5,9)
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	0
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 30: Difficulty beginning urination, n (%)	Baseline (n=20)	Not at all	17 (85,0)
		A little	2 (10,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	15 (78,9)
		A little	3 (15,8)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	15 (78,9)
		A little	3 (15,8)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	1 (5,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	13 (86,7)
		A little	2 (13,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 31: Urinary incontinence, n (%)	Baseline (n=20)	Not at all	17 (85,0)
		A little	1 (5,0)
		Some	1 (5,0)
		Pretty much	1 (5,0)
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	0
		Some	1 (5,9)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	15 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 32: Weakness, n (%)	Baseline (n=20)	Not at all	12 (60,0)
		A little	2 (10,0)
		Some	3 (15,0)
		Pretty much	1 (5,0)
		A lot	2 (10,0)
	Pre-cycle 3 (n=19)	Not at all	16 (84,2)
		A little	2 (10,5)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	15 (78,9)
		A little	2 (10,5)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	15 (88,2)
		A little	2 (11,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 33: Muscle pain, n (%)	Baseline (n=20)	Not at all	9 (45,0)
		A little	5 (25,0)
		Some	2 (10,0)
		Pretty much	2 (10,0)
		A lot	2 (10,0)
	Pre-cycle 3 (n=19)	Not at all	14 (73,7)
		A little	4 (21,1)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	14 (73,7)
		A little	5 (26,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	15 (78,9)
		A little	4 (21,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	13 (76,5)
		A little	4 (23,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	10 (66,7)
		A little	4 (26,7)
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	0
		A little	1 (100,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 34: Dizziness, n (%)	Baseline (n=20)	Not at all	16 (80,0)
		A little	3 (15,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	14 (73,7)
		A little	5 (26,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	15 (78,9)
		A little	4 (21,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	15 (78,9)
		A little	3 (15,8)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	13 (76,5)
		A little	4 (23,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	12 (80,0)
		A little	2 (13,3)
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 35: Numbness, n (%)	Baseline (n=20)	Not at all	16 (80,0)
		A little	3 (15,0)
		Some	0
		Pretty much	1 (5,0)
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	1 (5,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a]
Item 36: Tingling, n (%)	Baseline (n=20)	Not at all	15 (75,0)
		A little	4 (20,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=19)	Not at all	17 (89,5)
		A little	1 (5,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=19)	Not at all	15 (78,9)
		A little	4 (21,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=19)	Not at all	16 (84,2)
		A little	2 (10,5)
		Some	0
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 13 (n=17)	Not at all	16 (94,1)
		A little	1 (5,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 1: Fatigue/feeling tired, n (%)	Baseline (n=21)	Not at all	6 (28,6)
		A little	10 (47,6)
		Some	2 (9,5)
		Pretty much	1 (4,8)
		A lot	2 (9,5)
	Pre-cycle 3 (n=21)	Not at all	10 (47,6)
		A little	5 (23,8)
		Some	5 (23,8)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	10 (47,6)
		A little	6 (28,6)
		Some	4 (19,0)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	9 (42,9)
		A little	7 (33,3)
		Some	4 (19,0)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	10 (52,6)
		A little	4 (21,1)
		Some	5 (26,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	6 (50,0)
		A little	4 (33,3)
		Some	2 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	0
		A little	3 (75,0)
		Some	1 (25,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 2: Sleep problems, n (%)	Baseline (n=21)	Not at all	8 (38,1)
		A little	4 (19,0)
		Some	5 (23,8)
		Pretty much	3 (14,3)
		A lot	1 (4,8)
	Pre-cycle 3 (n=21)	Not at all	13 (61,9)
		A little	5 (23,8)
		Some	3 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	16 (76,2)
		A little	2 (9,5)
		Some	2 (9,5)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	13 (61,9)
		A little	3 (14,3)
		Some	3 (14,3)
		Pretty much	1 (4,8)
		A lot	1 (4,8)
	Pre-cycle 13 (n=19)	Not at all	14 (73,7)
		A little	1 (5,3)
		Some	1 (5,3)
		Pretty much	1 (5,3)
		A lot	2 (10,5)
	Pre-cycle 25 (n=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	0
		Some	0
		Pretty much	1 (25,0)
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 3: Less appetite, n (%)	Baseline (n=21)	Not at all	12 (57,1)
		A little	2 (9,5)
		Some	2 (9,5)
		Pretty much	4 (19,0)
		A lot	1 (4,8)
	Pre-cycle 3 (n=21)	Not at all	17 (81,0)
		A little	2 (9,5)
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	14 (66,7)
		A little	6 (28,6)
		Some	0
		Pretty much	0
		A lot	1 (4,8)
	Pre-cycle 9 (n=21)	Not at all	13 (61,9)
		A little	2 (9,5)
		Some	5 (23,8)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	14 (73,7)
		A little	1 (5,3)
		Some	1 (5,3)
		Pretty much	2 (10,5)
		A lot	1 (5,3)
	Pre-cycle 25 (n=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 4: More appetite, n (%)	Baseline (n=21)	Not at all	15 (71,4)
		A little	3 (14,3)
		Some	2 (9,5)
		Pretty much	0
		A lot	1 (4,8)
	Pre-cycle 3 (n=21)	Not at all	9 (42,9)
		A little	8 (38,1)
		Some	3 (14,3)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	12 (57,1)
		A little	6 (28,6)
		Some	2 (9,5)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	15 (71,4)
		A little	5 (23,8)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	14 (73,7)
		A little	1 (5,3)
		Some	3 (15,8)
		Pretty much	0
		A lot	1 (5,3)
	Pre-cycle 25 (n=12)	Not at all	7 (58,3)
		A little	3 (25,0)
		Some	1 (8,3)
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	0
		Some	1 (25,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 5: Headaches, n (%)	Baseline (n=21)	Not at all	13 (61,9)
		A little	4 (19,0)
		Some	4 (19,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	14 (66,7)
		A little	5 (23,8)
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	14 (66,7)
		A little	2 (9,5)
		Some	4 (19,0)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	12 (57,1)
		A little	6 (28,6)
		Some	3 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	13 (68,4)
		A little	5 (26,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	6 (50,0)
		A little	5 (41,7)
		Some	0
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	1 (25,0)
		A little	2 (50,0)
		Some	1 (25,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 6: Vision changes, n (%)	Baseline (n=21)	Not at all	18 (85,7)
		A little	3 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	18 (85,7)
		A little	2 (9,5)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 7: Decreased hearing, n (%)	Baseline (n=21)	Not at all	19 (90,5)
		A little	0
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	20 (95,2)
		A little	0
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	20 (95,2)
		A little	0
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	17 (89,5)
		A little	1 (5,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 8: Mouth sores, n (%)	Baseline (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	20 (95,2)
		A little	0
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	18 (85,7)
		A little	1 (4,8)
		Some	1 (4,8)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	15 (78,9)
		A little	4 (21,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 9: Trouble swallowing, n (%)	Baseline (n=21)	Not at all	18 (85,7)
		A little	1 (4,8)
		Some	1 (4,8)
		Pretty much	0
		A lot	1 (4,8)
	Pre-cycle 3 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	19 (90,5)
		A little	1 (4,8)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 10: Choking, n (%)	Baseline (n=21)	Not at all	17 (81,0)
		A little	2 (9,5)
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	20 (95,2)
		A little	0
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 11: Snoring, n (%)	Baseline (n=21)	Not at all	10 (47,6)
		A little	5 (23,8)
		Some	3 (14,3)
		Pretty much	0
		A lot	3 (14,3)
	Pre-cycle 3 (n=21)	Not at all	13 (61,9)
		A little	6 (28,6)
		Some	0
		Pretty much	2 (9,5)
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	10 (47,6)
		A little	6 (28,6)
		Some	3 (14,3)
		Pretty much	1 (4,8)
		A lot	1 (4,8)
	Pre-cycle 9 (n=21)	Not at all	14 (66,7)
		A little	3 (14,3)
		Some	3 (14,3)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	11 (57,9)
		A little	5 (26,3)
		Some	3 (15,8)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	9 (75,0)
		A little	3 (25,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 12: Frequent awakenings at night, n (%)	Baseline (n=21)	Not at all	9 (42,9)
		A little	5 (23,8)
		Some	4 (19,0)
		Pretty much	2 (9,5)
		A lot	1 (4,8)
	Pre-cycle 3 (n=21)	Not at all	15 (71,4)
		A little	3 (14,3)
		Some	3 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	19 (90,5)
		A little	1 (4,8)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	16 (76,2)
		A little	2 (9,5)
		Some	1 (4,8)
		Pretty much	1 (4,8)
		A lot	1 (4,8)
	Pre-cycle 13 (n=19)	Not at all	12 (63,2)
		A little	4 (21,1)
		Some	0
		Pretty much	1 (5,3)
		A lot	2 (10,5)
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 13: Cough, n (%)	Baseline (n=21)	Not at all	12 (57,1)
		A little	5 (23,8)
		Some	4 (19,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	16 (76,2)
		A little	3 (14,3)
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	13 (61,9)
		A little	6 (28,6)
		Some	1 (4,8)
		Pretty much	0
		A lot	1 (4,8)
	Pre-cycle 9 (n=21)	Not at all	10 (47,6)
		A little	7 (33,3)
		Some	3 (14,3)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	15 (78,9)
		A little	3 (15,8)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	8 (66,7)
		A little	2 (16,7)
		Some	1 (8,3)
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	2 (50,0)
		A little	2 (50,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 14: Wheezing, n (%)	Baseline (n=21)	Not at all	16 (76,2)
		A little	2 (9,5)
		Some	2 (9,5)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	18 (85,7)
		A little	2 (9,5)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	18 (85,7)
		A little	2 (9,5)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	20 (95,2)
		A little	0
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 15: Difficulty breathing, n (%)	Baseline (n=21)	Not at all	18 (85,7)
		A little	3 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	20 (95,2)
		A little	0
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 16: Chest pain, n (%)	Baseline (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 17: Palpitations/fluttering, n (%)	Baseline (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 18: Shortness of breath with activity, n (%)	Baseline (n=21)	Not at all	16 (76,2)
		A little	3 (14,3)
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	18 (85,7)
		A little	3 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	17 (81,0)
		A little	4 (19,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	17 (81,0)
		A little	2 (9,5)
		Some	1 (4,8)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	0
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 19: Shortness of breath at rest, n (%)	Baseline (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 20: Swelling in hands/feet, n (%)	Baseline (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	19 (90,5)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	1 (4,8)
	Pre-cycle 5 (n=21)	Not at all	19 (90,5)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	1 (4,8)
	Pre-cycle 9 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 21: Abdominal pain, n (%)	Baseline (n=21)	Not at all	11 (52,4)
		A little	6 (28,6)
		Some	3 (14,3)
		Pretty much	0
		A lot	1 (4,8)
	Pre-cycle 3 (n=21)	Not at all	8 (38,1)
		A little	6 (28,6)
		Some	4 (19,0)
		Pretty much	1 (4,8)
		A lot	2 (9,5)
	Pre-cycle 5 (n=21)	Not at all	14 (66,7)
		A little	2 (9,5)
		Some	2 (9,5)
		Pretty much	3 (14,3)
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	11 (52,4)
		A little	6 (28,6)
		Some	2 (9,5)
		Pretty much	2 (9,5)
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	16 (84,2)
		A little	1 (5,3)
		Some	1 (5,3)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	8 (66,7)
		A little	3 (25,0)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 22: Heartburn, n (%)	Baseline (n=21)	Not at all	19 (90,5)
		A little	1 (4,8)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 23: Nausea, n (%)	Baseline (n=21)	Not at all	14 (66,7)
		A little	5 (23,8)
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	12 (57,1)
		A little	6 (28,6)
		Some	1 (4,8)
		Pretty much	1 (4,8)
		A lot	1 (4,8)
	Pre-cycle 5 (n=21)	Not at all	14 (66,7)
		A little	4 (19,0)
		Some	1 (4,8)
		Pretty much	2 (9,5)
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	15 (71,4)
		A little	4 (19,0)
		Some	0
		Pretty much	2 (9,5)
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	14 (73,7)
		A little	3 (15,8)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	8 (66,7)
		A little	2 (16,7)
		Some	2 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 24: Vomiting, n (%)	Baseline (n=21)	Not at all	17 (81,0)
		A little	4 (19,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	15 (71,4)
		A little	3 (14,3)
		Some	3 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	16 (76,2)
		A little	3 (14,3)
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	17 (81,0)
		A little	2 (9,5)
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	16 (84,2)
		A little	1 (5,3)
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	9 (75,0)
		A little	2 (16,7)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 25: Diarrhea, n (%)	Baseline (n=21)	Not at all	16 (76,2)
		A little	3 (14,3)
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	14 (66,7)
		A little	4 (19,0)
		Some	3 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	15 (71,4)
		A little	3 (14,3)
		Some	3 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	14 (66,7)
		A little	3 (14,3)
		Some	4 (19,0)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	13 (68,4)
		A little	1 (5,3)
		Some	4 (21,1)
		Pretty much	0
		A lot	1 (5,3)
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	2 (50,0)
		A little	2 (50,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 26: Constipation, n (%)	Baseline (n=21)	Not at all	18 (85,7)
		A little	1 (4,8)
		Some	2 (9,5)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	17 (81,0)
		A little	2 (9,5)
		Some	1 (4,8)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	17 (81,0)
		A little	4 (19,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	18 (85,7)
		A little	3 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	15 (78,9)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	1 (5,3)
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 27: Stool incontinence, n (%)	Baseline (n=21)	Not at all	18 (85,7)
		A little	2 (9,5)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	19 (90,5)
		A little	1 (4,8)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 28: Pain with urination, n (%)	Baseline (n=21)	Not at all	17 (81,0)
		A little	3 (14,3)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	21 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	20 (95,2)
		A little	0
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	0
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 29: Increased urinary frequency/urgency, n (%)	Baseline (n=21)	Not at all	16 (76,2)
		A little	1 (4,8)
		Some	4 (19,0)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	18 (85,7)
		A little	3 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 30: Difficulty beginning urination, n (%)	Baseline (n=21)	Not at all	18 (85,7)
		A little	2 (9,5)
		Some	0
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	18 (85,7)
		A little	2 (9,5)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	18 (85,7)
		A little	2 (9,5)
		Some	0
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	10 (83,3)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 31: Urinary incontinence, n (%)	Baseline (n=21)	Not at all	16 (76,2)
		A little	2 (9,5)
		Some	3 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	19 (90,5)
		A little	1 (4,8)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 32: Weakness, n (%)	Baseline (n=21)	Not at all	13 (61,9)
		A little	2 (9,5)
		Some	3 (14,3)
		Pretty much	1 (4,8)
		A lot	2 (9,5)
	Pre-cycle 3 (n=21)	Not at all	18 (85,7)
		A little	2 (9,5)
		Some	0
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	16 (76,2)
		A little	5 (23,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 33: Muscle pain, n (%)	Baseline (n=21)	Not at all	12 (57,1)
		A little	2 (9,5)
		Some	4 (19,0)
		Pretty much	2 (9,5)
		A lot	1 (4,8)
	Pre-cycle 3 (n=21)	Not at all	15 (71,4)
		A little	4 (19,0)
		Some	1 (4,8)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	17 (81,0)
		A little	3 (14,3)
		Some	0
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	16 (76,2)
		A little	4 (19,0)
		Some	0
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	15 (78,9)
		A little	2 (10,5)
		Some	1 (5,3)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	0
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	3 (75,0)
		A little	1 (25,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 34: Dizziness, n (%)	Baseline (n=21)	Not at all	19 (90,5)
		A little	1 (4,8)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 35: Numbness, n (%)	Baseline (n=21)	Not at all	19 (90,5)
		A little	1 (4,8)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	19 (90,5)
		A little	1 (4,8)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a]
Item 36: Tingling, n (%)	Baseline (n=21)	Not at all	17 (81,0)
		A little	2 (9,5)
		Some	1 (4,8)
		Pretty much	1 (4,8)
		A lot	0
	Pre-cycle 3 (n=21)	Not at all	19 (90,5)
		A little	2 (9,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=21)	Not at all	18 (85,7)
		A little	2 (9,5)
		Some	1 (4,8)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=21)	Not at all	20 (95,2)
		A little	1 (4,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 4)	Not at all	4 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 1: Fatigue/feeling tired, n (%)	Baseline (n=15)	Not at all	4 (26,7)
		A little	8 (53,3)
		Some	2 (13,3)
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	3 (21,4)
		A little	7 (50,0)
		Some	2 (14,3)
		Pretty much	0
		A lot	2 (14,3)
	Pre-cycle 5 (n=14)	Not at all	5 (35,7)
		A little	4 (28,6)
		Some	1 (7,1)
		Pretty much	3 (21,4)
		A lot	1 (7,1)
	Pre-cycle 9 (n=13)	Not at all	4 (30,8)
		A little	5 (38,5)
		Some	3 (23,1)
		Pretty much	1 (7,7)
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	4 (33,3)
		A little	4 (33,3)
		Some	3 (25,0)
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	5 (41,7)
		A little	2 (16,7)
		Some	5 (41,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 2: Sleep problems, n (%)	Baseline (n=15)	Not at all	8 (53,3)
		A little	3 (20,0)
		Some	2 (13,3)
		Pretty much	1 (6,7)
		A lot	1 (6,7)
	Pre-cycle 3 (n=14)	Not at all	10 (71,4)
		A little	1 (7,1)
		Some	3 (21,4)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	9 (64,3)
		A little	1 (7,1)
		Some	2 (14,3)
		Pretty much	2 (14,3)
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	6 (46,2)
		A little	6 (46,2)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	5 (41,7)
		A little	4 (33,3)
		Some	2 (16,7)
		Pretty much	0
		A lot	1 (8,3)
	Pre-cycle 25 (n=12)	Not at all	8 (66,7)
		A little	2 (16,7)
		Some	1 (8,3)
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 3: Less appetite, n (%)	Baseline (n=15)	Not at all	11 (73,3)
		A little	3 (20,0)
		Some	0
		Pretty much	0
		A lot	1 (6,7)
	Pre-cycle 3 (n=14)	Not at all	9 (64,3)
		A little	4 (28,6)
		Some	0
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	11 (78,6)
		A little	2 (14,3)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	8 (66,7)
		A little	3 (25,0)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	9 (75,0)
		A little	3 (25,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 4: More appetite, n (%)	Baseline (n=15)	Not at all	9 (60,0)
		A little	4 (26,7)
		Some	1 (6,7)
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	7 (50,0)
		A little	3 (21,4)
		Some	3 (21,4)
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	4 (28,6)
		A little	4 (28,6)
		Some	5 (35,7)
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	9 (69,2)
		A little	2 (15,4)
		Some	0
		Pretty much	2 (15,4)
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	9 (75,0)
		A little	3 (25,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	7 (58,3)
		A little	4 (33,3)
		Some	0
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 5: Headaches, n (%)	Baseline (n=15)	Not at all	7 (46,7)
		A little	5 (33,3)
		Some	2 (13,3)
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	8 (57,1)
		A little	6 (42,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	7 (50,0)
		A little	7 (50,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	5 (38,5)
		A little	7 (53,8)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	5 (41,7)
		A little	5 (41,7)
		Some	2 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	7 (58,3)
		A little	2 (16,7)
		Some	3 (25,0)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 6: Vision changes, n (%)	Baseline (n=15)	Not at all	13 (86,7)
		A little	1 (6,7)
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 7: Decreased hearing, n (%)	Baseline (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 8: Mouth sores, n (%)	Baseline (n=15)	Not at all	13 (86,7)
		A little	2 (13,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	11 (78,6)
		A little	2 (14,3)
		Some	0
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	11 (78,6)
		A little	2 (14,3)
		Some	0
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	10 (83,3)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 9: Trouble swallowing, n (%)	Baseline (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 10: Choking, n (%)	Baseline (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 11: Snoring, n (%)	Baseline (n=15)	Not at all	12 (80,0)
		A little	1 (6,7)
		Some	0
		Pretty much	1 (6,7)
		A lot	1 (6,7)
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	0
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	13 (92,9)
		A little	0
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	10 (83,3)
		A little	0
		Some	2 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	0
		Some	0
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 12: Frequent awakenings at night, n (%)	Baseline (n=15)	Not at all	10 (66,7)
		A little	2 (13,3)
		Some	2 (13,3)
		Pretty much	0
		A lot	1 (6,7)
	Pre-cycle 3 (n=14)	Not at all	9 (64,3)
		A little	5 (35,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	8 (57,1)
		A little	4 (28,6)
		Some	1 (7,1)
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	7 (53,8)
		A little	5 (38,5)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	8 (66,7)
		A little	2 (16,7)
		Some	2 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	9 (75,0)
		A little	2 (16,7)
		Some	0
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 13: Cough, n (%)	Baseline (n=15)	Not at all	7 (46,7)
		A little	8 (53,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	9 (64,3)
		A little	4 (28,6)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	11 (78,6)
		A little	3 (21,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	6 (46,2)
		A little	7 (53,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	7 (58,3)
		A little	5 (41,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	10 (83,3)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 14: Wheezing, n (%)	Baseline (n=15)	Not at all	15 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 15: Difficulty breathing, n (%)	Baseline (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 16: Chest pain, n (%)	Baseline (n=15)	Not at all	13 (86,7)
		A little	1 (6,7)
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	9 (75,0)
		A little	2 (16,7)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	0
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 17: Palpitations/fluttering, n (%)	Baseline (n=15)	Not at all	14 (93,3)
		A little	0
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 18: Shortness of breath with activity, n (%)	Baseline (n=15)	Not at all	11 (73,3)
		A little	3 (20,0)
		Some	0
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	9 (64,3)
		A little	5 (35,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	10 (83,3)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 19: Shortness of breath at rest, n (%)	Baseline (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 20: Swelling in hands/feet, n (%)	Baseline (n=15)	Not at all	14 (93,3)
		A little	0
		Some	0
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	1 (7,1)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	12 (85,7)
		A little	1 (7,1)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 21: Abdominal pain, n (%)	Baseline (n=15)	Not at all	10 (66,7)
		A little	3 (20,0)
		Some	2 (13,3)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	8 (57,1)
		A little	3 (21,4)
		Some	3 (21,4)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	8 (61,5)
		A little	1 (7,7)
		Some	4 (30,8)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	8 (66,7)
		A little	3 (25,0)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	8 (66,7)
		A little	2 (16,7)
		Some	2 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 22: Heartburn, n (%)	Baseline (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	13 (92,9)
		A little	0
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	10 (83,3)
		A little	0
		Some	2 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	0
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 23: Nausea, n (%)	Baseline (n=15)	Not at all	13 (86,7)
		A little	1 (6,7)
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	10 (71,4)
		A little	3 (21,4)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	7 (50,0)
		A little	6 (42,9)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	7 (53,8)
		A little	4 (30,8)
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	7 (58,3)
		A little	5 (41,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 24: Vomiting, n (%)	Baseline (n=15)	Not at all	13 (86,7)
		A little	2 (13,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	10 (71,4)
		A little	4 (28,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	10 (83,3)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 25: Diarrhea, n (%)	Baseline (n=15)	Not at all	11 (73,3)
		A little	2 (13,3)
		Some	1 (6,7)
		Pretty much	0
		A lot	1 (6,7)
	Pre-cycle 3 (n=14)	Not at all	6 (42,9)
		A little	5 (35,7)
		Some	3 (21,4)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	9 (64,3)
		A little	4 (28,6)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	7 (53,8)
		A little	5 (38,5)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	7 (58,3)
		A little	5 (41,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	9 (75,0)
		A little	3 (25,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 26: Constipation, n (%)	Baseline (n=15)	Not at all	9 (60,0)
		A little	4 (26,7)
		Some	2 (13,3)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	11 (78,6)
		A little	3 (21,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	11 (78,6)
		A little	3 (21,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	9 (69,2)
		A little	3 (23,1)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	8 (66,7)
		A little	3 (25,0)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	7 (58,3)
		A little	4 (33,3)
		Some	0
		Pretty much	0
		A lot	1 (8,3)
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 27: Stool incontinence, n (%)	Baseline (n=15)	Not at all	14 (93,3)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	1 (7,1)
		Some	0
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	10 (76,9)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	1 (7,7)
	Pre-cycle 13 (n=12)	Not at all	11 (91,7)
		A little	0
		Some	0
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (8,3)
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 28: Pain with urination, n (%)	Baseline (n=15)	Not at all	15 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	13 (92,9)
		A little	0
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 29: Increased urinary frequency/urgency, n (%)	Baseline (n=15)	Not at all	10 (66,7)
		A little	4 (26,7)
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	10 (71,4)
		A little	2 (14,3)
		Some	2 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	0
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	0
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 30: Difficulty beginning urination, n (%)	Baseline (n=15)	Not at all	13 (86,7)
		A little	1 (6,7)
		Some	1 (6,7)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	11 (78,6)
		A little	2 (14,3)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=11)	Not at all	10 (90,9)
		A little	1 (9,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 31: Urinary incontinence, n (%)	Baseline (n=15)	Not at all	13 (86,7)
		A little	0
		Some	0
		Pretty much	2 (13,3)
		A lot	0
	Pre-cycle 3 (n=13)	Not at all	12 (92,3)
		A little	0
		Some	0
		Pretty much	1 (7,7)
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	10 (76,9)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	1 (7,7)
	Pre-cycle 13 (n=12)	Not at all	10 (83,3)
		A little	0
		Some	1 (8,3)
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 25 (n=11)	Not at all	11 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 32: Weakness, n (%)	Baseline (n=15)	Not at all	13 (86,7)
		A little	1 (6,7)
		Some	0
		Pretty much	0
		A lot	1 (6,7)
	Pre-cycle 3 (n=14)	Not at all	11 (78,6)
		A little	2 (14,3)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 33: Muscle pain, n (%)	Baseline (n=15)	Not at all	8 (53,3)
		A little	5 (33,3)
		Some	0
		Pretty much	1 (6,7)
		A lot	1 (6,7)
	Pre-cycle 3 (n=14)	Not at all	10 (71,4)
		A little	4 (28,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	12 (85,7)
		A little	1 (7,1)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	7 (58,3)
		A little	5 (41,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 34: Dizziness, n (%)	Baseline (n=15)	Not at all	13 (86,7)
		A little	2 (13,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	7 (50,0)
		A little	6 (42,9)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	11 (78,6)
		A little	3 (21,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	9 (69,2)
		A little	3 (23,1)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	8 (66,7)
		A little	3 (25,0)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	9 (75,0)
		A little	3 (25,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 35: Numbness, n (%)	Baseline (n=15)	Not at all	14 (93,3)
		A little	0
		Some	0
		Pretty much	1 (6,7)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	0
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	0
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.4 Distribution of General PN symptoms item responses over time - PN status at enrollment = Non-progressive (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=15) [a]
Item 36: Tingling, n (%)	Baseline (n=15)	Not at all	12 (80,0)
		A little	1 (6,7)
		Some	1 (6,7)
		Pretty much	0
		A lot	1 (6,7)
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=14)	Not at all	11 (78,6)
		A little	3 (21,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	0
		Pretty much	1 (7,7)
		A lot	0
	Pre-cycle 13 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n= 1)	Not at all	1 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 1: Fatigue/feeling tired, n (%)	Baseline (n=14)	Not at all	7 (50,0)
		A little	3 (21,4)
		Some	1 (7,1)
		Pretty much	2 (14,3)
		A lot	1 (7,1)
	Pre-cycle 3 (n=14)	Not at all	4 (28,6)
		A little	3 (21,4)
		Some	6 (42,9)
		Pretty much	0
		A lot	1 (7,1)
	Pre-cycle 5 (n=13)	Not at all	4 (30,8)
		A little	6 (46,2)
		Some	2 (15,4)
		Pretty much	1 (7,7)
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	5 (38,5)
		A little	5 (38,5)
		Some	3 (23,1)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	5 (38,5)
		A little	6 (46,2)
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	4 (40,0)
		A little	5 (50,0)
		Some	0
		Pretty much	1 (10,0)
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 2: Sleep problems, n (%)	Baseline (n=14)	Not at all	6 (42,9)
		A little	5 (35,7)
		Some	0
		Pretty much	3 (21,4)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	4 (28,6)
		A little	6 (42,9)
		Some	3 (21,4)
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	7 (53,8)
		A little	4 (30,8)
		Some	0
		Pretty much	2 (15,4)
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	6 (46,2)
		A little	4 (30,8)
		Some	3 (23,1)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	11 (84,6)
		A little	0
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	6 (60,0)
		A little	3 (30,0)
		Some	0
		Pretty much	0
		A lot	1 (10,0)

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 3: Less appetite, n (%)	Baseline (n=14)	Not at all	11 (78,6)
		A little	1 (7,1)
		Some	1 (7,1)
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	10 (71,4)
		A little	1 (7,1)
		Some	2 (14,3)
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	10 (76,9)
		A little	1 (7,7)
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	0
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	1 (10,0)

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 4: More appetite, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	10 (71,4)
		A little	1 (7,1)
		Some	0
		Pretty much	2 (14,3)
		A lot	1 (7,1)
	Pre-cycle 5 (n=13)	Not at all	5 (38,5)
		A little	6 (46,2)
		Some	0
		Pretty much	1 (7,7)
		A lot	1 (7,7)
	Pre-cycle 9 (n=13)	Not at all	8 (61,5)
		A little	3 (23,1)
		Some	0
		Pretty much	1 (7,7)
		A lot	1 (7,7)
	Pre-cycle 13 (n=13)	Not at all	11 (84,6)
		A little	0
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	0
		Some	0
		Pretty much	1 (10,0)
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 5: Headaches, n (%)	Baseline (n=14)	Not at all	8 (57,1)
		A little	4 (28,6)
		Some	1 (7,1)
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	8 (57,1)
		A little	2 (14,3)
		Some	4 (28,6)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	8 (61,5)
		A little	4 (30,8)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	10 (76,9)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	1 (7,7)
	Pre-cycle 25 (n=10)	Not at all	6 (60,0)
		A little	2 (20,0)
		Some	2 (20,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 6: Vision changes, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	1 (7,1)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	0
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	9 (69,2)
		A little	4 (30,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	0
		Pretty much	1 (10,0)
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 7: Decreased hearing, n (%)	Baseline (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 8: Mouth sores, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	1 (7,1)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	0
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 9: Trouble swallowing, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	1 (7,1)
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	0
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	12 (92,3)
		A little	0
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (10,0)

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 10: Choking, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (10,0)

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 11: Snoring, n (%)	Baseline (n=14)	Not at all	9 (64,3)
		A little	1 (7,1)
		Some	1 (7,1)
		Pretty much	2 (14,3)
		A lot	1 (7,1)
	Pre-cycle 3 (n=14)	Not at all	8 (57,1)
		A little	3 (21,4)
		Some	3 (21,4)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	8 (61,5)
		A little	2 (15,4)
		Some	3 (23,1)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	8 (61,5)
		A little	5 (38,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	6 (60,0)
		A little	1 (10,0)
		Some	3 (30,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 12: Frequent awakenings at night, n (%)	Baseline (n=14)	Not at all	7 (50,0)
		A little	4 (28,6)
		Some	1 (7,1)
		Pretty much	2 (14,3)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	8 (57,1)
		A little	2 (14,3)
		Some	2 (14,3)
		Pretty much	1 (7,1)
		A lot	1 (7,1)
	Pre-cycle 5 (n=13)	Not at all	7 (53,8)
		A little	4 (30,8)
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	9 (69,2)
		A little	3 (23,1)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	10 (76,9)
		A little	2 (15,4)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	7 (70,0)
		A little	2 (20,0)
		Some	0
		Pretty much	1 (10,0)
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 13: Cough, n (%)	Baseline (n=14)	Not at all	7 (50,0)
		A little	4 (28,6)
		Some	1 (7,1)
		Pretty much	1 (7,1)
		A lot	1 (7,1)
	Pre-cycle 3 (n=14)	Not at all	5 (35,7)
		A little	3 (21,4)
		Some	4 (28,6)
		Pretty much	2 (14,3)
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	8 (61,5)
		A little	4 (30,8)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	8 (61,5)
		A little	5 (38,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	4 (40,0)
		A little	6 (60,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 14: Wheezing, n (%)	Baseline (n=14)	Not at all	13 (92,9)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (7,1)
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	0
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 15: Difficulty breathing, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	1 (7,1)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 16: Chest pain, n (%)	Baseline (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	11 (78,6)
		A little	2 (14,3)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 17: Palpitations/fluttering, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 18: Shortness of breath with activity, n (%)	Baseline (n=14)	Not at all	9 (64,3)
		A little	2 (14,3)
		Some	3 (21,4)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	11 (78,6)
		A little	2 (14,3)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	9 (69,2)
		A little	3 (23,1)
		Some	0
		Pretty much	1 (7,7)
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	7 (70,0)
		A little	1 (10,0)
		Some	2 (20,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 19: Shortness of breath at rest, n (%)	Baseline (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 20: Swelling in hands/feet, n (%)	Baseline (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (7,1)
	Pre-cycle 5 (n=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	0
		Pretty much	1 (7,7)
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	10 (76,9)
		A little	1 (7,7)
		Some	1 (7,7)
		Pretty much	0
		A lot	1 (7,7)
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	0
		Some	1 (10,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 21: Abdominal pain, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	10 (71,4)
		A little	2 (14,3)
		Some	2 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	9 (69,2)
		A little	3 (23,1)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	8 (61,5)
		A little	4 (30,8)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	5 (50,0)
		A little	4 (40,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 22: Heartburn, n (%)	Baseline (n=14)	Not at all	13 (92,9)
		A little	0
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	0
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (10,0)

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 23: Nausea, n (%)	Baseline (n=14)	Not at all	11 (78,6)
		A little	2 (14,3)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	7 (50,0)
		A little	4 (28,6)
		Some	3 (21,4)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	9 (69,2)
		A little	3 (23,1)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	10 (76,9)
		A little	1 (7,7)
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	8 (61,5)
		A little	4 (30,8)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 24: Vomiting, n (%)	Baseline (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	9 (64,3)
		A little	3 (21,4)
		Some	2 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 25: Diarrhea, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	1 (7,1)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	11 (78,6)
		A little	0
		Some	2 (14,3)
		Pretty much	0
		A lot	1 (7,1)
	Pre-cycle 5 (n=13)	Not at all	10 (76,9)
		A little	2 (15,4)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	9 (69,2)
		A little	2 (15,4)
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	7 (70,0)
		A little	3 (30,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 26: Constipation, n (%)	Baseline (n=14)	Not at all	11 (78,6)
		A little	2 (14,3)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	10 (71,4)
		A little	3 (21,4)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	8 (61,5)
		A little	5 (38,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	9 (69,2)
		A little	4 (30,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	7 (70,0)
		A little	3 (30,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 27: Stool incontinence, n (%)	Baseline (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 28: Pain with urination, n (%)	Baseline (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 29: Increased urinary frequency/urgency, n (%)	Baseline (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	11 (78,6)
		A little	2 (14,3)
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 30: Difficulty beginning urination, n (%)	Baseline (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	1 (7,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	0
		Some	1 (10,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 31: Urinary incontinence, n (%)	Baseline (n=14)	Not at all	13 (92,9)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (7,1)
	Pre-cycle 3 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 32: Weakness, n (%)	Baseline (n=14)	Not at all	8 (57,1)
		A little	1 (7,1)
		Some	3 (21,4)
		Pretty much	2 (14,3)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	11 (78,6)
		A little	1 (7,1)
		Some	1 (7,1)
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	9 (69,2)
		A little	2 (15,4)
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 33: Muscle pain, n (%)	Baseline (n=14)	Not at all	8 (57,1)
		A little	2 (14,3)
		Some	3 (21,4)
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	10 (71,4)
		A little	2 (14,3)
		Some	1 (7,1)
		Pretty much	1 (7,1)
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	9 (69,2)
		A little	4 (30,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	9 (69,2)
		A little	4 (30,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	9 (69,2)
		A little	3 (23,1)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	8 (80,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 34: Dizziness, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 35: Numbness, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	14 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.1.3.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, Data cut-off: 29th June 2018

PN symptom checklist	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a]
Item 36: Tingling, n (%)	Baseline (n=14)	Not at all	12 (85,7)
		A little	2 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 3 (n=14)	Not at all	13 (92,9)
		A little	0
		Some	1 (7,1)
		Pretty much	0
		A lot	0
	Pre-cycle 5 (n=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 9 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 13 (n=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 25 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0

[a] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.2.1 NRS-11 score categories of change over time - percentage of patients with Improvement by >=2 points (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Response category	Selumetinib 25 mg/m² BID (N=34) [a] n	% [b]	95% CI [c]
Self-selected tumour pain score	Overall (N=31)	Categories of change [d]			
		Improvement	20	64,5	45,4, 80,8
		No improvement	11	35,5	19,2, 54,6
Physician-selected target tumour [e]	Overall (N=25)	Categories of change [d]			
		Improvement	14	56,0	34,9, 75,6
		No improvement	11	44,0	24,4, 65,1
Overall tumour pain	Overall (N=26)	Categories of change [d]			
		Improvement	14	53,8	33,4, 73,4
		No improvement	12	46,2	26,6, 66,6
Other pain	Overall (N=26)	Categories of change [d]			
		Improvement	15	57,7	36,9, 76,6
		No improvement	11	42,3	23,4, 63,1

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the NRS-11.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 2.
[e] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same. NC - not calculated.

Table 2.2.2.1 NRS-11 score categories of change over time and Improvement by >=2 points - Gender = Male (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a] n	% [b]	95% CI [c]
Self-selected tumour pain score	Overall (N=19)	Categories of change [d]			
		Improvement	12	63,2	38,4, 83,7
		No improvement	7	36,8	16,3, 61,6
Physician-selected target tumour [e]	Overall (N=14)	Categories of change [d]			
		Improvement	8	57,1	28,9, 82,3
		No improvement	6	42,9	17,7, 71,1
Overall tumour pain	Overall (N=14)	Categories of change [d]			
		Improvement	7	50,0	23,0, 77,0
		No improvement	7	50,0	23,0, 77,0
Other pain	Overall (N=16)	Categories of change [d]			
		Improvement	8	50,0	24,7, 75,3
		No improvement	8	50,0	24,7, 75,3

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the NRS-11.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 2.
[e] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same. NC - not calculated.

Table 2.2.2.2 NRS-11 score categories of change over time and Improvement by >=2 points - Gender = Female (Full analysis set)

Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Response category	Selumetinib 25 mg/m² BID (N=13) [a] n	% [b]	95% CI [c]
Self-selected tumour pain score	Overall (N=12)	Categories of change [d]			
		Improvement	8	66,7	34,9, 90,1
		No improvement	4	33,3	9,9, 65,1
Physician-selected target tumour [e]	Overall (N=11)	Categories of change [d]			
		Improvement	6	54,5	23,4, 83,3
		No improvement	5	45,5	16,7, 76,6
Overall tumour pain	Overall (N=12)	Categories of change [d]			
		Improvement	7	58,3	27,7, 84,8
		No improvement	5	41,7	15,2, 72,3
Other pain	Overall (N=10)	Categories of change [d]			
		Improvement	7	70,0	34,8, 93,3
		No improvement	3	30,0	6,7, 65,2

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the NRS-11.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 2.
[e] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same. NC - not calculated.

Table 2.2.2.3 NRS-11 score categories of change over time and Improvement by >=2 points - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a] n	% [b]	95% CI [c]
Self-selected tumour pain score	Overall (N=11)	Categories of change [d]			
		Improvement	7	63,6	30,8, 89,1
		No improvement	4	36,4	10,9, 69,2
Physician-selected target tumour [e]	Overall (N=7)	Categories of change [d]			
		Improvement	4	57,1	18,4, 90,1
		No improvement	3	42,9	9,9, 81,6
Overall tumour pain	Overall (N=8)	Categories of change [d]			
		Improvement	5	62,5	24,5, 91,5
		No improvement	3	37,5	8,5, 75,5
Other pain	Overall (N=10)	Categories of change [d]			
		Improvement	8	80,0	44,4, 97,5
		No improvement	2	20,0	2,5, 55,6

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the NRS-11.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 2.
[e] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same. NC - not calculated.

Table 2.2.2.4 NRS-11 score categories of change over time and Improvement by >=2 points - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a] n	% [b]	95% CI [c]
Self-selected tumour pain score	Overall (N=10)	Categories of change [d]			
		Improvement	7	70,0	34,8, 93,3
		No improvement	3	30,0	6,7, 65,2
Physician-selected target tumour [e]	Overall (N=9)	Categories of change [d]			
		Improvement	6	66,7	29,9, 92,5
		No improvement	3	33,3	7,5, 70,1
Overall tumour pain	Overall (N=8)	Categories of change [d]			
		Improvement	4	50,0	15,7, 84,3
		No improvement	4	50,0	15,7, 84,3
Other pain	Overall (N=8)	Categories of change [d]			
		Improvement	4	50,0	15,7, 84,3
		No improvement	4	50,0	15,7, 84,3

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the NRS-11.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 2.
[e] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same. NC - not calculated.

Table 2.2.2.5 NRS-11 score categories of change over time and Improvement by >=2 points - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=12) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Overall (N=10)	Categories of change [d]			
		Improvement	6	60,0	26,2, 87,8
		No improvement	4	40,0	12,2, 73,8
Physician-selected target tumour [e]	Overall (N=9)	Categories of change [d]			
		Improvement	4	44,4	13,7, 78,8
		No improvement	5	55,6	21,2, 86,3
Overall tumour pain	Overall (N=10)	Categories of change [d]			
		Improvement	5	50,0	18,7, 81,3
		No improvement	5	50,0	18,7, 81,3
Other pain	Overall (N=8)	Categories of change [d]			
		Improvement	3	37,5	8,5, 75,5
		No improvement	5	62,5	24,5, 91,5

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the NRS-11.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 2.
[e] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same. NC - not calculated.

Table 2.2.3.1 NRS-11 pain intensity scores over time and change from baseline over time - Gender = Male
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]											
		Absolute values						Change from baseline					
NRS-11 Pain intensity score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Self-selected tumour pain	Baseline (n=20)	3,05	2,982	2,50	0,0	9,0	4,8							
	Pre-cycle 3 (n=19)	1,26	1,996	0,00	0,0	8,0	9,5	19	-1,84	2,734	-1,00	-9,0	1,0	9,5
	Pre-cycle 5 (n=19)	0,89	1,696	0,00	0,0	7,0	9,5	19	-2,21	2,740	-2,00	-8,0	3,0	9,5
	Pre-cycle 9 (n=19)	0,74	1,851	0,00	0,0	8,0	9,5	19	-2,37	2,432	-2,00	-8,0	0,0	9,5
	Pre-cycle 13 (n=18)	0,50	1,150	0,00	0,0	4,0	14,3	18	-2,28	2,782	-2,00	-9,0	1,0	14,3
	Pre-cycle 25 (n=13)	0,23	0,832	0,00	0,0	3,0	38,1	13	-1,62	1,895	-2,00	-5,0	1,0	38,1
	Pre-cycle 37 (n=4)	0,00	0,000	0,00	0,0	0,0	81,0	4	-1,50	1,732	-1,50	-3,0	0,0	81,0
Physician-selected target tumour pain [c]	Baseline (n=15)	2,73	2,738	2,00	0,0	9,0	28,6							
	Pre-cycle 3 (n=14)	1,64	2,061	1,00	0,0	8,0	33,3	14	-1,14	1,748	-1,00	-6,0	1,0	33,3
	Pre-cycle 5 (n=14)	1,50	2,312	0,00	0,0	7,0	33,3	14	-1,29	2,701	-0,50	-8,0	3,0	33,3
	Pre-cycle 9 (n=14)	1,00	2,148	0,00	0,0	8,0	33,3	14	-1,79	1,762	-1,50	-6,0	0,0	33,3
	Pre-cycle 13 (n=13)	0,46	0,967	0,00	0,0	3,0	38,1	13	-2,31	3,250	-2,00	-9,0	1,0	38,1
	Pre-cycle 25 (n=9)	0,44	1,014	0,00	0,0	3,0	57,1	9	-1,33	1,871	0,00	-4,0	1,0	57,1
	Pre-cycle 37 (n=1)	NC	NC	NC	0,0	0,0	95,2	1	NC	NC	NC	0,0	0,0	95,2

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
[c] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.2.3.1 NRS-11 pain intensity scores over time and change from baseline over time - Gender = Male
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]												
		Absolute values						Change from baseline						
NRS-11 Pain intensity score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Overall tumour pain	Baseline (n=15)	2,40	2,586	2,00	0,0	7,0	28,6							
	Pre-cycle 3 (n=16)	1,63	1,586	1,00	0,0	4,0	23,8	13	-0,92	2,597	0,00	-5,0	3,0	38,1
	Pre-cycle 5 (n=16)	1,00	1,932	0,00	0,0	6,0	23,8	13	-1,46	3,688	0,00	-7,0	4,0	38,1
	Pre-cycle 9 (n=17)	0,71	1,160	0,00	0,0	4,0	19,0	14	-1,64	2,341	-0,50	-6,0	1,0	33,3
	Pre-cycle 13 (n=14)	0,86	1,791	0,00	0,0	5,0	33,3	13	-1,23	2,587	0,00	-6,0	3,0	38,1
	Pre-cycle 25 (n=11)	0,00	0,000	0,00	0,0	0,0	47,6	9	-1,33	2,062	0,00	-5,0	0,0	57,1
	Pre-cycle 37 (n=4)	0,00	0,000	0,00	0,0	0,0	81,0	4	-1,00	2,000	0,00	-4,0	0,0	81,0
Other pain	Baseline (n=17)	3,53	2,809	4,00	0,0	8,0	19,0							
	Pre-cycle 3 (n=18)	3,44	2,975	3,50	0,0	10,0	14,3	15	-0,13	2,503	0,00	-6,0	4,0	28,6
	Pre-cycle 5 (n=15)	2,07	1,710	2,00	0,0	6,0	28,6	13	-1,00	2,799	0,00	-6,0	3,0	38,1
	Pre-cycle 9 (n=15)	2,93	2,658	3,00	0,0	9,0	28,6	14	-0,64	3,500	-0,50	-5,0	6,0	33,3
	Pre-cycle 13 (n=11)	2,27	2,573	2,00	0,0	7,0	47,6	9	-0,89	2,261	0,00	-6,0	1,0	57,1
	Pre-cycle 25 (n=6)	1,50	1,975	0,50	0,0	4,0	71,4	6	-1,17	2,563	0,00	-6,0	1,0	71,4
	Pre-cycle 37 (n=3)	1,00	1,732	0,00	0,0	3,0	85,7	3	-3,00	3,000	-3,00	-6,0	0,0	85,7

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
[c] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.2.3.2 NRS-11 pain intensity scores over time and change from baseline over time - Gender = Female
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]											
		Absolute values						Change from baseline					
NRS-11 Pain intensity score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Self-selected tumour pain	Baseline (n=13)	3,92	3,523	5,00	0,0	10,0	0,0							
	Pre-cycle 3 (n=12)	2,42	2,021	3,00	0,0	6,0	7,7	12	-1,83	2,980	-2,00	-7,0	3,0	7,7
	Pre-cycle 5 (n=12)	2,25	2,179	2,00	0,0	6,0	7,7	12	-2,00	1,907	-2,50	-4,0	2,0	7,7
	Pre-cycle 9 (n=12)	2,00	2,523	1,00	0,0	8,0	7,7	12	-2,25	2,006	-2,00	-6,0	0,0	7,7
	Pre-cycle 13 (n=11)	2,09	2,508	1,00	0,0	7,0	15,4	11	-2,45	2,659	-2,00	-8,0	0,0	15,4
	Pre-cycle 25 (n=9)	1,78	2,438	0,00	0,0	5,0	30,8	9	-2,00	3,536	-3,00	-6,0	5,0	30,8
Physician-selected target tumour pain [c]	Baseline (n=11)	3,73	3,690	3,00	0,0	10,0	15,4							
	Pre-cycle 3 (n=11)	2,09	1,758	3,00	0,0	5,0	15,4	11	-1,64	2,873	-1,00	-7,0	3,0	15,4
	Pre-cycle 5 (n=11)	2,00	2,366	2,00	0,0	6,0	15,4	11	-1,73	1,902	-2,00	-4,0	2,0	15,4
	Pre-cycle 9 (n=11)	1,73	2,573	0,00	0,0	8,0	15,4	11	-2,00	2,098	-2,00	-6,0	0,0	15,4
	Pre-cycle 13 (n=11)	1,64	2,541	0,00	0,0	7,0	15,4	11	-2,09	2,548	-1,00	-8,0	0,0	15,4
	Pre-cycle 25 (n=9)	1,11	2,205	0,00	0,0	5,0	30,8	9	-1,67	3,317	-1,00	-6,0	5,0	30,8

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
[c] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.2.3.2 NRS-11 pain intensity scores over time and change from baseline over time - Gender = Female
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]											
		Absolute values						Change from baseline					
NRS-11 Pain intensity score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Overall tumour pain	Baseline (n=13)	3,69	3,637	5,00	0,0	10,0	0,0							
	Pre-cycle 3 (n=12)	2,08	2,109	1,50	0,0	6,0	7,7	12	-1,92	2,778	-0,50	-7,0	1,0	7,7
	Pre-cycle 5 (n=11)	1,45	1,968	0,00	0,0	6,0	15,4	11	-2,00	2,236	-2,00	-7,0	0,0	15,4
	Pre-cycle 9 (n=12)	1,17	1,528	0,00	0,0	4,0	7,7	12	-2,83	3,040	-2,00	-8,0	0,0	7,7
	Pre-cycle 13 (n=10)	1,60	1,838	1,00	0,0	5,0	23,1	10	-3,10	3,071	-4,00	-7,0	1,0	23,1
	Pre-cycle 25 (n=6)	1,83	2,401	1,00	0,0	6,0	53,8	6	-2,17	2,041	-2,00	-5,0	0,0	53,8
Other pain	Baseline (n=12)	4,50	2,680	5,50	0,0	8,0	7,7							
	Pre-cycle 3 (n=7)	3,57	2,440	4,00	0,0	7,0	46,2	7	-1,29	2,430	-2,00	-5,0	3,0	46,2
	Pre-cycle 5 (n=6)	3,50	1,378	3,50	2,0	5,0	53,8	6	-1,67	3,559	-2,50	-5,0	5,0	53,8
	Pre-cycle 9 (n=8)	3,50	2,330	3,50	0,0	7,0	38,5	7	-1,43	2,936	-3,00	-4,0	4,0	46,2
	Pre-cycle 13 (n=9)	3,22	2,224	3,00	0,0	7,0	30,8	9	-1,78	2,728	-2,00	-6,0	3,0	30,8
	Pre-cycle 25 (n=7)	2,71	2,498	2,00	0,0	7,0	46,2	6	-2,50	3,507	-2,50	-6,0	1,0	53,8

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
[c] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.2.3.3 NRS-11 pain intensity scores over time and change from baseline over time - PN status at enrollment = Progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
NRS-11 Pain intensity score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Self-selected tumour pain	Baseline (n=11)	4,00	3,742	3,00	0,0	10,0	0,0							
	Pre-cycle 3 (n=11)	2,09	2,386	2,00	0,0	8,0	0,0	11	-1,91	2,914	-1,00	-7,0	1,0	0,0
	Pre-cycle 5 (n=11)	1,82	2,523	1,00	0,0	7,0	0,0	11	-2,18	2,857	-2,00	-8,0	3,0	0,0
	Pre-cycle 9 (n=11)	1,73	3,165	0,00	0,0	8,0	0,0	11	-2,27	2,240	-2,00	-6,0	0,0	0,0
	Pre-cycle 13 (n=10)	0,70	1,337	0,00	0,0	4,0	9,1	10	-3,60	3,534	-2,50	-9,0	0,0	9,1
	Pre-cycle 25 (n=6)	0,00	0,000	0,00	0,0	0,0	45,5	6	-1,67	1,862	-1,50	-4,0	0,0	45,5
	Pre-cycle 37 (n=3)	0,00	0,000	0,00	0,0	0,0	72,7	3	-2,00	1,732	-3,00	-3,0	0,0	72,7
Physician-selected target tumour pain [c]	Baseline (n=7)	4,43	4,541	4,00	0,0	10,0	36,4							
	Pre-cycle 3 (n=7)	2,43	2,760	2,00	0,0	8,0	36,4	7	-2,00	3,162	-1,00	-7,0	1,0	36,4
	Pre-cycle 5 (n=7)	2,29	3,094	0,00	0,0	7,0	36,4	7	-2,14	3,579	-2,00	-8,0	3,0	36,4
	Pre-cycle 9 (n=7)	2,57	3,780	0,00	0,0	8,0	36,4	7	-1,86	2,340	-1,00	-6,0	0,0	36,4
	Pre-cycle 13 (n=7)	0,29	0,756	0,00	0,0	2,0	36,4	7	-4,14	4,180	-4,00	-9,0	0,0	36,4
	Pre-cycle 25 (n=4)	0,00	0,000	0,00	0,0	0,0	63,6	4	-1,00	2,000	0,00	-4,0	0,0	63,6
	Pre-cycle 37 (n=1)	NC	NC	NC	0,0	0,0	90,9	1	NC	NC	NC	0,0	0,0	90,9

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.2.3.3 NRS-11 pain intensity scores over time and change from baseline over time - PN status at enrollment = Progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
NRS-11 Pain intensity score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Overall tumour pain	Baseline (n=8)	3,75	3,655	3,00	0,0	10,0	27,3							
	Pre-cycle 3 (n=9)	1,78	1,716	1,00	0,0	4,0	18,2	8	-1,75	3,412	-2,00	-7,0	3,0	27,3
	Pre-cycle 5 (n=9)	1,00	2,121	0,00	0,0	6,0	18,2	7	-1,57	4,276	-1,00	-7,0	4,0	36,4
	Pre-cycle 9 (n=10)	0,80	1,317	0,00	0,0	4,0	9,1	8	-2,88	3,044	-2,50	-8,0	1,0	27,3
	Pre-cycle 13 (n=8)	1,88	2,357	0,50	0,0	5,0	27,3	7	-2,00	3,512	-2,00	-6,0	3,0	36,4
	Pre-cycle 25 (n=4)	0,00	0,000	0,00	0,0	0,0	63,6	3	-1,33	2,309	0,00	-4,0	0,0	72,7
	Pre-cycle 37 (n=3)	0,00	0,000	0,00	0,0	0,0	72,7	3	-1,33	2,309	0,00	-4,0	0,0	72,7
Other pain	Baseline (n=10)	4,80	2,201	5,50	0,0	7,0	9,1							
	Pre-cycle 3 (n=10)	4,70	3,268	5,00	0,0	10,0	9,1	9	-0,11	2,147	0,00	-2,0	4,0	18,2
	Pre-cycle 5 (n=8)	2,25	1,909	2,00	0,0	6,0	27,3	8	-2,38	2,134	-2,00	-5,0	0,0	27,3
	Pre-cycle 9 (n=9)	3,22	3,420	4,00	0,0	9,0	18,2	9	-1,44	3,358	-2,00	-5,0	6,0	18,2
	Pre-cycle 13 (n=6)	3,83	3,312	4,50	0,0	7,0	45,5	6	-1,17	2,787	0,00	-6,0	1,0	45,5
	Pre-cycle 25 (n=3)	1,33	2,309	0,00	0,0	4,0	72,7	3	-2,67	3,055	-2,00	-6,0	0,0	72,7
	Pre-cycle 37 (n=2)	NC	NC	NC	0,0	3,0	81,8	2	NC	NC	NC	-6,0	-3,0	81,8

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.2.3.4 NRS-11 pain intensity scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
NRS-11 Pain intensity score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Self-selected tumour pain	Baseline (n=11)	3,27	2,936	3,00	0,0	9,0	0,0							
	Pre-cycle 3 (n=10)	0,80	1,033	0,50	0,0	3,0	9,1	10	-2,80	2,898	-2,50	-9,0	0,0	9,1
	Pre-cycle 5 (n=10)	0,80	1,317	0,00	0,0	4,0	9,1	10	-2,80	2,440	-2,50	-8,0	0,0	9,1
	Pre-cycle 9 (n=10)	0,70	1,059	0,00	0,0	3,0	9,1	10	-2,90	2,424	-3,00	-8,0	0,0	9,1
	Pre-cycle 13 (n=9)	0,67	1,000	0,00	0,0	3,0	18,2	9	-2,33	2,345	-2,00	-5,0	1,0	18,2
	Pre-cycle 25 (n=9)	0,44	1,014	0,00	0,0	3,0	18,2	9	-2,56	2,506	-3,00	-6,0	1,0	18,2
	Pre-cycle 37 (n=1)	NC	NC	NC	0,0	0,0	90,9	1	NC	NC	NC	0,0	0,0	90,9
Physician-selected target tumour pain [c]	Baseline (n=9)	2,56	1,667	3,00	0,0	6,0	18,2							
	Pre-cycle 3 (n=9)	1,00	1,118	1,00	0,0	3,0	18,2	9	-1,56	1,236	-1,00	-3,0	0,0	18,2
	Pre-cycle 5 (n=9)	1,00	1,732	0,00	0,0	4,0	18,2	9	-1,56	1,424	-2,00	-3,0	1,0	18,2
	Pre-cycle 9 (n=9)	0,67	1,000	0,00	0,0	3,0	18,2	9	-1,89	1,269	-2,00	-3,0	0,0	18,2
	Pre-cycle 13 (n=8)	0,63	1,061	0,00	0,0	3,0	27,3	8	-1,88	1,885	-2,00	-5,0	1,0	27,3
	Pre-cycle 25 (n=7)	0,43	1,134	0,00	0,0	3,0	36,4	7	-2,14	2,340	-3,00	-6,0	1,0	36,4

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
[c] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.2.3.4 NRS-11 pain intensity scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
NRS-11 Pain intensity score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Overall tumour pain	Baseline (n=9)	2,67	3,202	0,00	0,0	7,0	18,2							
	Pre-cycle 3 (n=9)	1,33	1,323	1,00	0,0	3,0	18,2	7	-2,29	2,690	-3,00	-6,0	1,0	36,4
	Pre-cycle 5 (n=8)	0,38	0,744	0,00	0,0	2,0	27,3	7	-3,14	3,078	-4,00	-7,0	0,0	36,4
	Pre-cycle 9 (n=9)	0,78	1,202	0,00	0,0	3,0	18,2	8	-2,13	2,357	-1,50	-5,0	0,0	27,3
	Pre-cycle 13 (n=7)	0,14	0,378	0,00	0,0	1,0	36,4	7	-2,43	3,101	0,00	-7,0	0,0	36,4
	Pre-cycle 25 (n=7)	0,29	0,756	0,00	0,0	2,0	36,4	6	-1,50	2,345	0,00	-5,0	0,0	45,5
	Pre-cycle 37 (n=1)	NC	NC	NC	0,0	0,0	90,9	1	NC	NC	NC	0,0	0,0	90,9
Other pain	Baseline (n=9)	4,33	3,082	5,00	0,0	8,0	18,2							
	Pre-cycle 3 (n=9)	2,44	1,509	3,00	0,0	4,0	18,2	8	-2,00	2,390	-1,50	-6,0	1,0	27,3
	Pre-cycle 5 (n=8)	2,50	0,926	2,50	1,0	4,0	27,3	7	-1,43	3,101	-1,00	-6,0	3,0	36,4
	Pre-cycle 9 (n=8)	3,13	1,885	3,50	0,0	6,0	27,3	7	-1,14	3,579	-3,00	-4,0	6,0	36,4
	Pre-cycle 13 (n=6)	1,33	1,506	1,00	0,0	3,0	45,5	5	-2,40	2,881	-1,00	-6,0	0,0	54,5
	Pre-cycle 25 (n=5)	2,20	1,304	2,00	1,0	4,0	54,5	4	-2,50	3,512	-2,50	-6,0	1,0	63,6
	Pre-cycle 37 (n=1)	NC	NC	NC	0,0	0,0	90,9	1	NC	NC	NC	0,0	0,0	90,9

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
[c] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.2.3.5 NRS-11 pain intensity scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]											
		Absolute values						Change from baseline					
NRS-11 Pain intensity score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Self-selected tumour pain	Baseline (n=11)	2,91	3,015	2,00	0,0	9,0	8,3							
	Pre-cycle 3 (n=10)	2,20	2,300	2,00	0,0	6,0	16,7	10	-0,80	2,394	0,00	-5,0	3,0	16,7
	Pre-cycle 5 (n=10)	1,60	1,897	1,50	0,0	6,0	16,7	10	-1,40	1,838	-2,00	-4,0	2,0	16,7
	Pre-cycle 9 (n=10)	1,20	1,751	0,00	0,0	4,0	16,7	10	-1,80	2,150	-1,50	-6,0	0,0	16,7
	Pre-cycle 13 (n=10)	1,90	2,767	0,00	0,0	7,0	16,7	10	-1,10	1,287	-0,50	-3,0	0,0	16,7
	Pre-cycle 25 (n=7)	2,14	2,673	0,00	0,0	5,0	41,7	7	-0,86	3,288	0,00	-5,0	5,0	41,7
Physician-selected target tumour pain [c]	Baseline (n=10)	2,80	3,084	1,50	0,0	9,0	16,7							
	Pre-cycle 3 (n=9)	2,22	1,641	2,00	0,0	5,0	25,0	9	-0,67	2,345	0,00	-5,0	3,0	25,0
	Pre-cycle 5 (n=9)	2,00	2,179	2,00	0,0	6,0	25,0	9	-0,89	2,028	0,00	-4,0	2,0	25,0
	Pre-cycle 9 (n=9)	1,00	1,581	0,00	0,0	4,0	25,0	9	-1,89	2,205	-1,00	-6,0	0,0	25,0
	Pre-cycle 13 (n=9)	1,89	2,759	0,00	0,0	7,0	25,0	9	-1,00	1,658	0,00	-4,0	1,0	25,0
	Pre-cycle 25 (n=7)	1,57	2,370	0,00	0,0	5,0	41,7	7	-1,14	3,338	-1,00	-5,0	5,0	41,7

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
[c] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

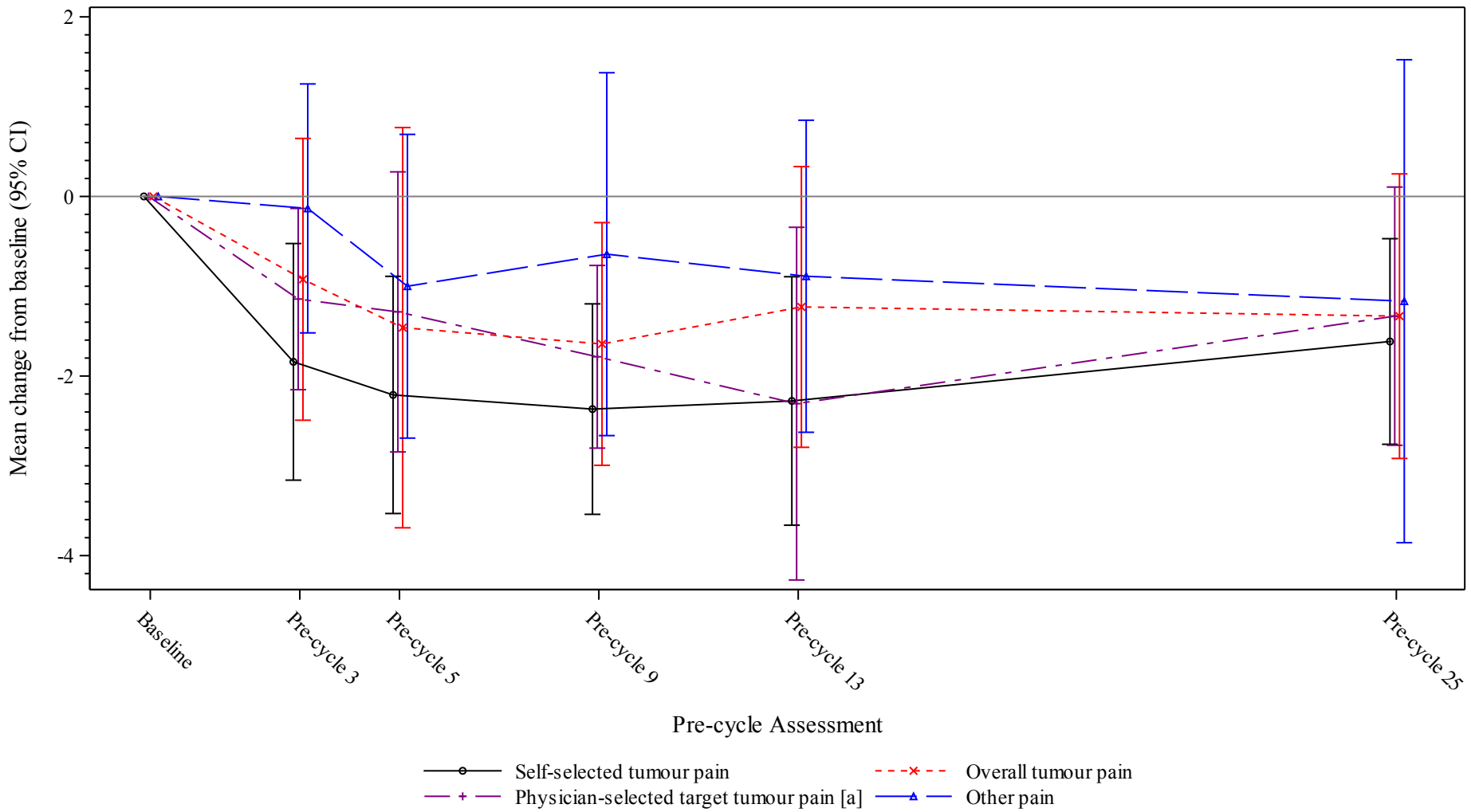
Table 2.2.3.5 NRS-11 pain intensity scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]											
		Absolute values						Change from baseline					
NRS-11 Pain intensity score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Overall tumour pain	Baseline (n=11)	2,73	2,867	2,00	0,0	8,0	8,3							
	Pre-cycle 3 (n=10)	2,30	2,263	1,50	0,0	6,0	16,7	10	-0,50	1,900	0,00	-4,0	1,0	16,7
	Pre-cycle 5 (n=10)	2,00	2,211	1,50	0,0	6,0	16,7	10	-0,80	1,687	0,00	-4,0	2,0	16,7
	Pre-cycle 9 (n=10)	1,10	1,524	0,00	0,0	4,0	16,7	10	-1,70	2,830	-0,50	-8,0	1,0	16,7
	Pre-cycle 13 (n=9)	1,33	1,732	1,00	0,0	5,0	25,0	9	-1,78	2,539	0,00	-6,0	1,0	25,0
	Pre-cycle 25 (n=6)	1,50	2,510	0,00	0,0	6,0	50,0	6	-2,00	1,897	-2,00	-5,0	0,0	50,0
Other pain	Baseline (n=10)	2,70	2,751	1,00	0,0	7,0	16,7							
	Pre-cycle 3 (n=6)	3,00	3,033	3,00	0,0	7,0	50,0	5	1,20	2,168	0,00	-1,0	4,0	58,3
	Pre-cycle 5 (n=5)	2,80	2,588	4,00	0,0	5,0	58,3	4	1,50	3,109	1,50	-2,0	5,0	66,7
	Pre-cycle 9 (n=6)	3,00	2,000	3,00	0,0	6,0	50,0	5	0,40	2,966	0,00	-4,0	4,0	58,3
	Pre-cycle 13 (n=8)	2,88	1,885	3,50	0,0	5,0	33,3	7	-0,71	1,976	-1,00	-3,0	3,0	41,7
	Pre-cycle 25 (n=5)	2,60	3,209	1,00	0,0	7,0	58,3	5	-0,80	2,950	0,00	-6,0	1,0	58,3

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
[c] Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Figure 2.2.4.1 Mean change from baseline of NRS-11 pain intensity scores - Gender = Male (Full analysis set)
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

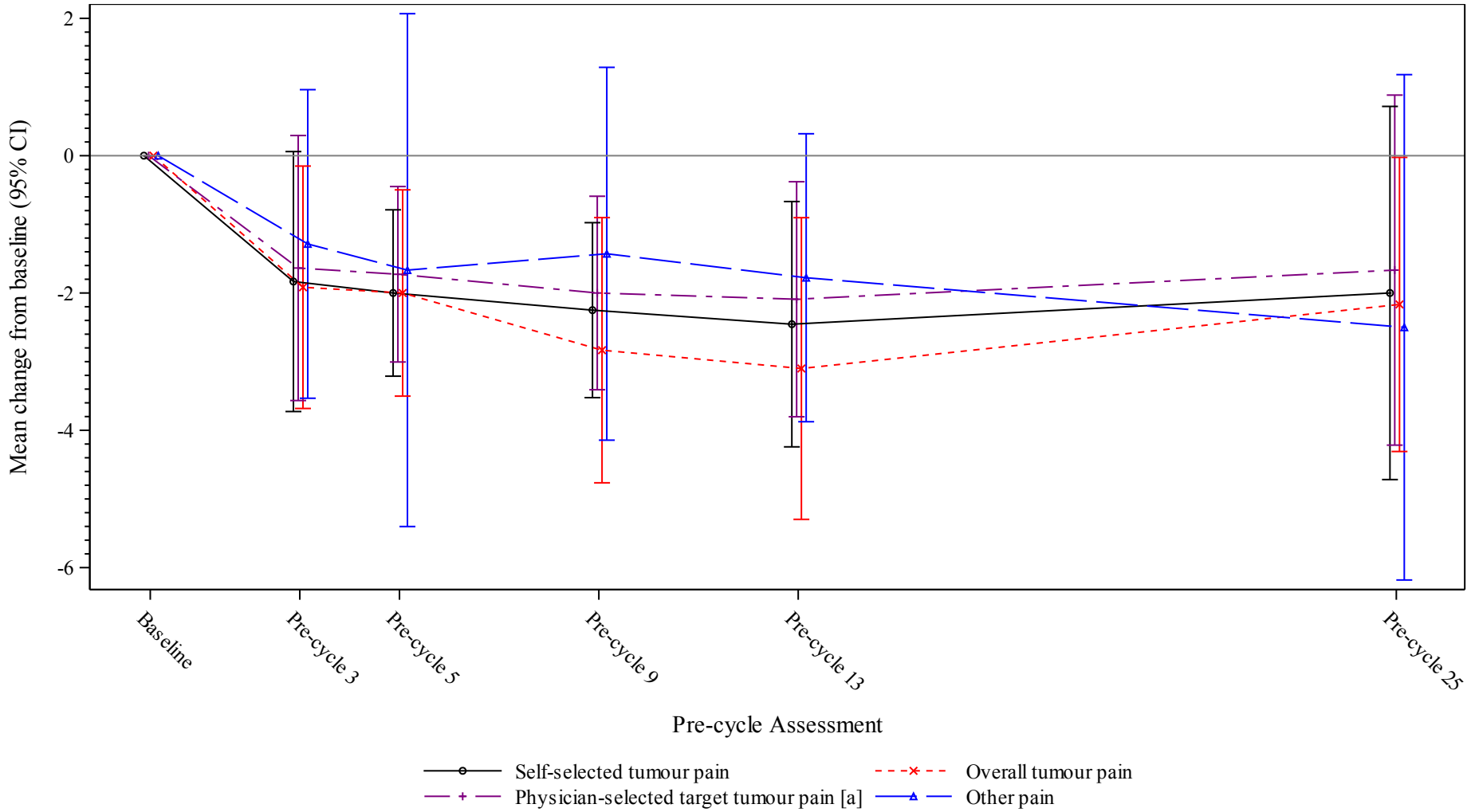
N = 21



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[a]Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
CI = Confidence interval.

Figure 2.2.4.2 Mean change from baseline of NRS-11 pain intensity scores - Gender = Female (Full analysis set)
SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

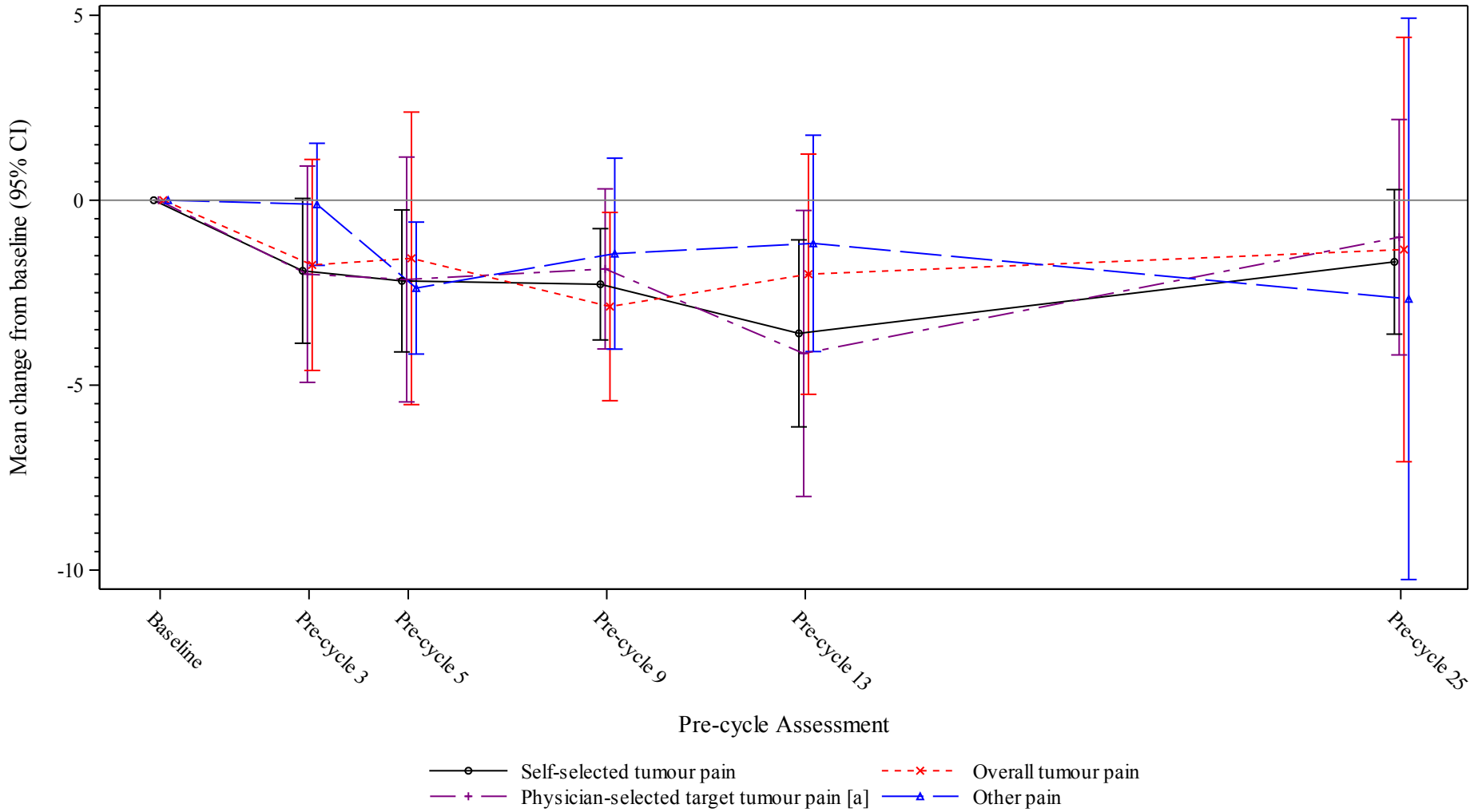
N = 13



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[a]Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
CI = Confidence interval.

Figure 2.2.4.3 Mean change from baseline of NRS-11 pain intensity scores - PN status at enrollment = Progressive
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

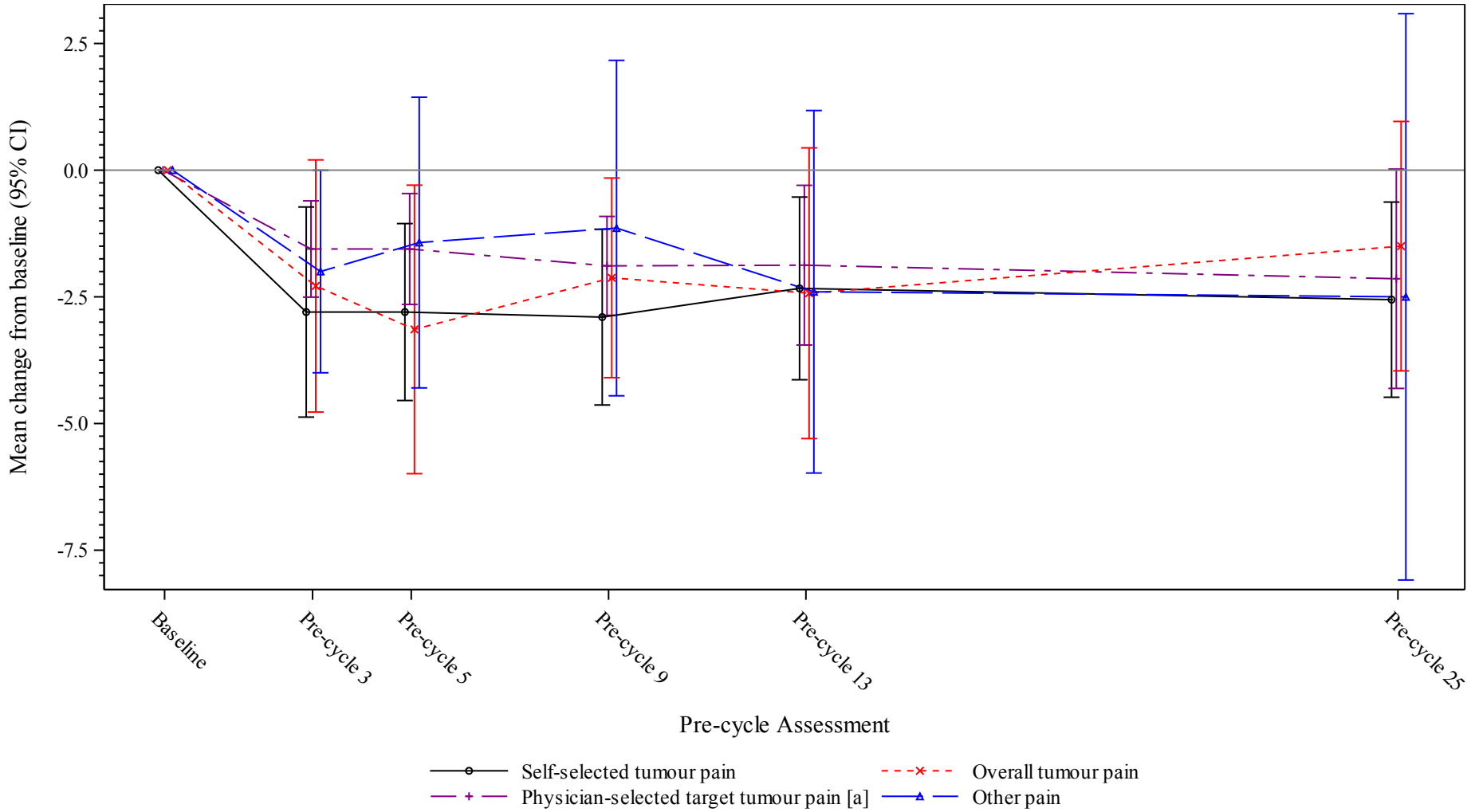
N = 11



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[a]Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
CI = Confidence interval.

Figure 2.2.4.4 Mean change from baseline of NRS-11 pain intensity scores - PN status at enrollment = Non-progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

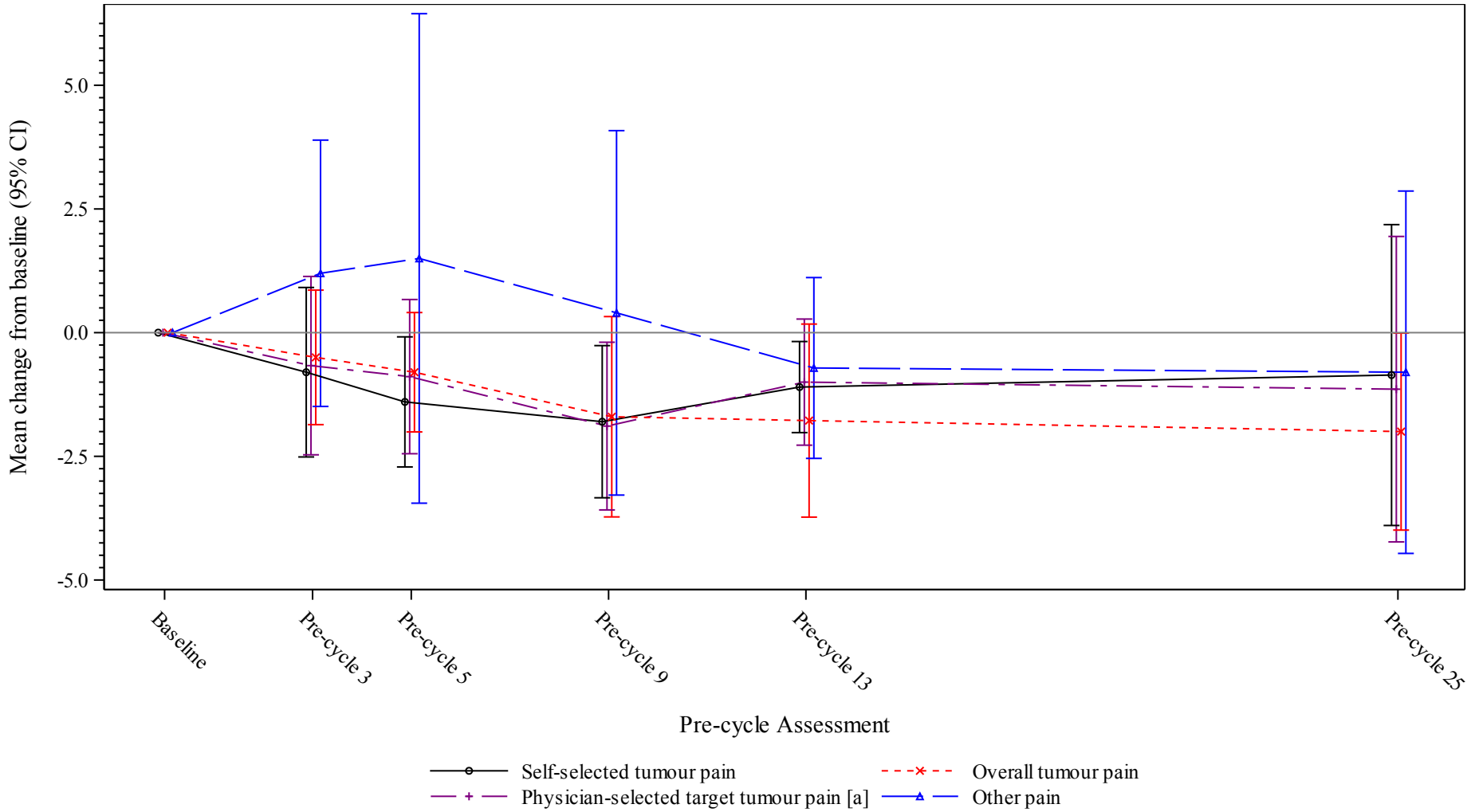
N = 11



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[a]Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
CI = Confidence interval.

Figure 2.2.4.5 Mean change from baseline of NRS-11 pain intensity scores - PN status at enrollment = Unknown
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

N = 12



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.
[a]Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
CI = Confidence interval.

Table 2.3.1 PII self-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=34) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=31)	Categories of change [d]			
		Improvement	7	22,6	9,6, 41,1
		No improvement	24	77,4	58,9, 90,4
	Pre-cycle 5 (N=31)	Categories of change [d]			
		Improvement	9	29,0	14,2, 48,0
		No improvement	22	71,0	52,0, 85,8
	Pre-cycle 9 (N=31)	Categories of change [d]			
		Improvement	9	29,0	14,2, 48,0
		No improvement	22	71,0	52,0, 85,8
	Pre-cycle 13 (N=29)	Categories of change [d]			
		Improvement	9	31,0	15,3, 50,8
		No improvement	20	69,0	49,2, 84,7
	Pre-cycle 25 (N=23)	Categories of change [d]			
		Improvement	6	26,1	10,2, 48,4
		No improvement	17	73,9	51,6, 89,8
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Overall (N=31)	Categories of change [d]			
		Improvement	12	38,7	21,8, 57,8
		No improvement	19	61,3	42,2, 78,2

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the Pain Interference Index (PII).
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.1.1.1 PII self-report pain interference scores and change from baseline over time - Gender = Male
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]											
		Absolute values						Change from baseline					
PII self-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=20)	0,94	1,212	0,50	0,0	3,8	4,8							
	Pre-cycle 3 (n=19)	1,08	1,123	0,50	0,0	3,8	9,5	19	0,09	1,574	0,00	-3,0	3,8	9,5
	Pre-cycle 5 (n=19)	0,78	0,986	0,40	0,0	3,3	9,5	19	-0,22	1,473	0,00	-3,5	3,3	9,5
	Pre-cycle 9 (n=19)	0,56	0,917	0,17	0,0	3,6	9,5	19	-0,43	1,559	-0,17	-3,7	3,6	9,5
	Pre-cycle 13 (n=18)	0,43	0,747	0,00	0,0	2,8	14,3	18	-0,40	0,982	0,00	-3,5	0,8	14,3
	Pre-cycle 25 (n=14)	0,14	0,291	0,00	0,0	0,8	33,3	14	-0,57	0,984	-0,08	-3,0	0,7	33,3
	Pre-cycle 37 (n=4)	0,00	0,000	0,00	0,0	0,0	81,0	4	-0,54	0,975	-0,08	-2,0	0,0	81,0

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the PII.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.3.1.1.2 PII self-report pain interference scores and change from baseline over time - Gender = Female
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]											
		Absolute values						Change from baseline					
PII self-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=13)	1,65	1,827	0,83	0,0	5,5	0,0							
	Pre-cycle 3 (n=12)	0,40	0,459	0,21	0,0	1,2	7,7	12	-1,24	1,845	-0,50	-5,0	0,7	7,7
	Pre-cycle 5 (n=12)	0,71	0,954	0,33	0,0	2,8	7,7	12	-0,93	1,140	-0,50	-3,2	0,2	7,7
	Pre-cycle 9 (n=12)	0,76	1,217	0,17	0,0	4,2	7,7	12	-0,88	1,380	-0,42	-3,8	0,3	7,7
	Pre-cycle 13 (n=11)	0,76	1,042	0,33	0,0	3,2	15,4	11	-0,97	1,140	-0,50	-3,3	0,0	15,4
	Pre-cycle 25 (n=9)	0,83	1,656	0,33	0,0	5,2	30,8	9	-0,61	1,467	-0,50	-4,0	0,7	30,8

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the PII.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.3.1.1.3 PII self-report pain interference scores and change from baseline over time - PN status at enrollment = Progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
PII self-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=11)	1,21	1,706	0,50	0,0	5,5	0,0							
	Pre-cycle 3 (n=11)	1,23	1,081	0,83	0,0	3,0	0,0	11	0,02	1,895	0,50	-5,0	2,2	0,0
	Pre-cycle 5 (n=11)	1,02	0,960	0,67	0,0	2,3	0,0	11	-0,19	1,243	0,00	-3,2	2,0	0,0
	Pre-cycle 9 (n=11)	0,70	0,732	0,33	0,0	2,0	0,0	11	-0,51	1,206	-0,17	-3,5	0,7	0,0
	Pre-cycle 13 (n=10)	0,85	0,951	0,58	0,0	2,8	9,1	10	-0,42	1,155	0,00	-3,3	0,6	9,1
	Pre-cycle 25 (n=6)	0,14	0,340	0,00	0,0	0,8	45,5	6	-0,33	0,901	-0,08	-2,0	0,7	45,5
	Pre-cycle 37 (n=3)	0,00	0,000	0,00	0,0	0,0	72,7	3	-0,72	1,110	-0,17	-2,0	0,0	72,7

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the PII.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.3.1.1.4 PII self-report pain interference scores and change from baseline over time
- PN status at enrollment = Non-progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
PII self-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=11)	1,01	1,112	0,83	0,0	3,8	0,0							
	Pre-cycle 3 (n=10)	0,83	1,114	0,58	0,0	3,8	9,1	10	-0,10	1,700	-0,17	-3,0	3,8	9,1
	Pre-cycle 5 (n=10)	0,45	1,037	0,00	0,0	3,3	9,1	10	-0,48	1,702	-0,67	-3,5	3,3	9,1
	Pre-cycle 9 (n=10)	0,53	1,123	0,00	0,0	3,6	9,1	10	-0,41	1,794	-0,58	-3,7	3,6	9,1
	Pre-cycle 13 (n=9)	0,07	0,169	0,00	0,0	0,5	18,2	9	-0,54	0,551	-0,50	-1,2	0,0	18,2
	Pre-cycle 25 (n=9)	0,20	0,309	0,00	0,0	0,7	18,2	9	-0,41	0,646	-0,50	-1,2	0,7	18,2
	Pre-cycle 37 (n=1)	NC	NC	NC	0,0	0,0	90,9	1	NC	NC	NC	0,0	0,0	90,9

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the PII.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

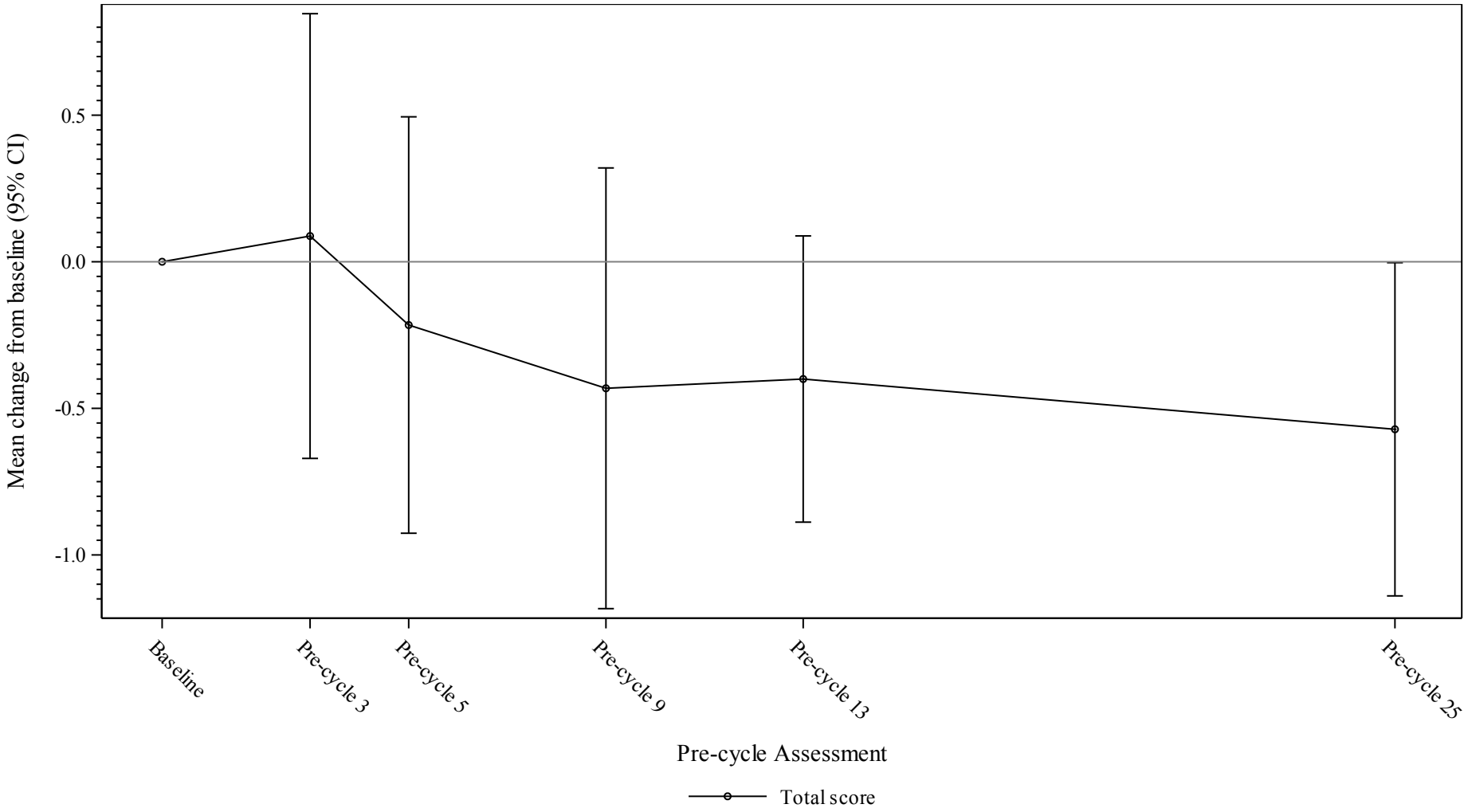
Table 2.3.1.1.5 PII self-report pain interference scores and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]											
		Absolute values						Change from baseline					
PII self-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=11)	1,44	1,716	0,67	0,0	4,5	8,3							
	Pre-cycle 3 (n=10)	0,34	0,405	0,21	0,0	1,2	16,7	10	-1,24	1,607	-0,33	-4,0	0,3	16,7
	Pre-cycle 5 (n=10)	0,75	0,879	0,58	0,0	2,8	16,7	10	-0,83	1,222	-0,33	-2,8	0,7	16,7
	Pre-cycle 9 (n=10)	0,68	1,285	0,17	0,0	4,2	16,7	10	-0,90	1,538	-0,25	-3,8	0,5	16,7
	Pre-cycle 13 (n=10)	0,70	1,030	0,17	0,0	3,2	16,7	10	-0,88	1,333	-0,50	-3,5	0,8	16,7
	Pre-cycle 25 (n=8)	0,85	1,769	0,17	0,0	5,2	33,3	8	-0,98	1,712	-0,25	-4,0	0,7	33,3

[a] Children, ages 8 to 18 years at enrolment, completed self-report measures of the PII.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Figure 2.3.1.2.1 Mean change from baseline of PII self-report pain interference scores - Gender = Male
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

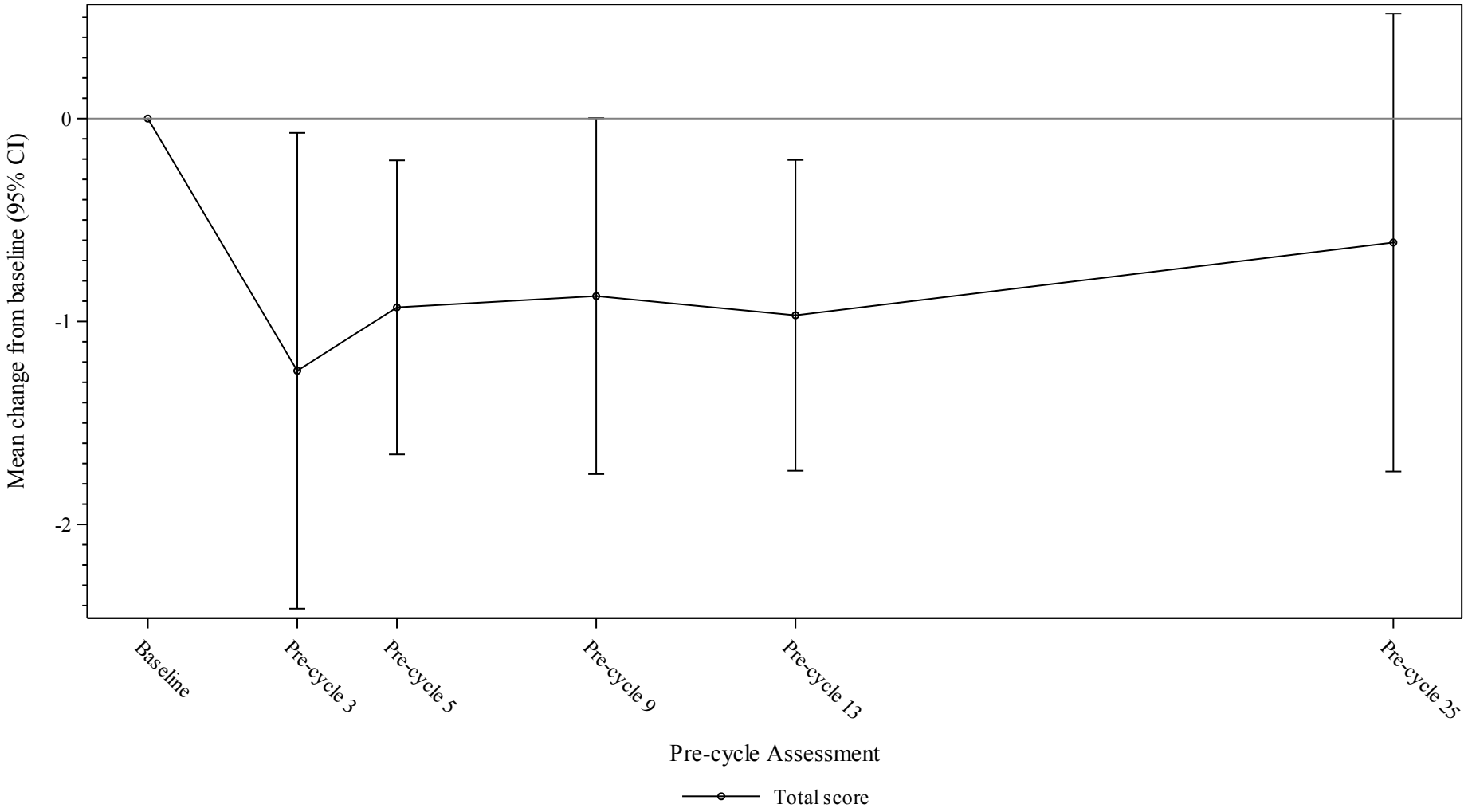
N = 21



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PII.
CI = Confidence interval.

Figure 2.3.1.2.2 Mean change from baseline of PII self-report pain interference scores - Gender = Female
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

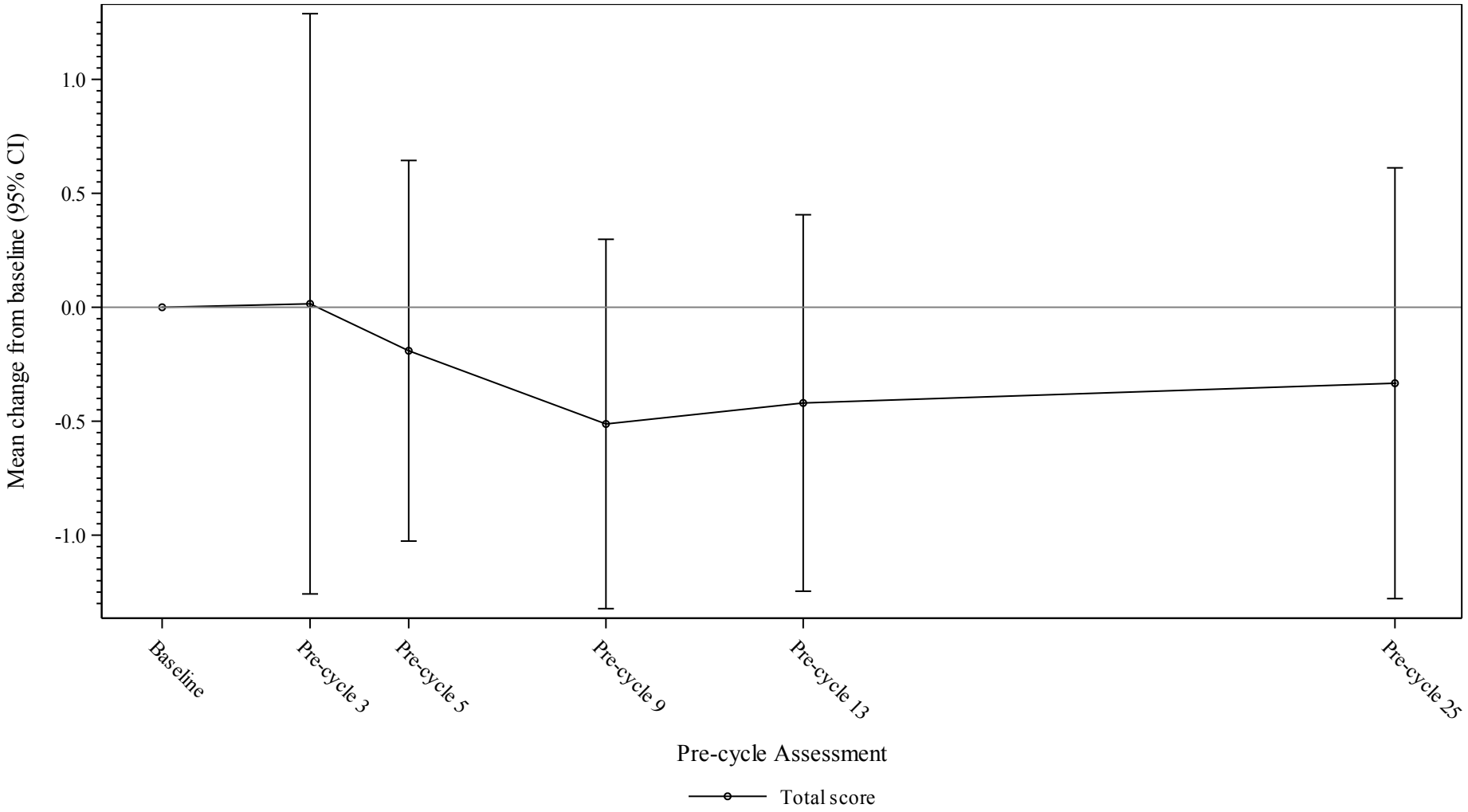
N = 13



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PII.
CI = Confidence interval.

Figure 2.3.1.2.3 Mean change from baseline of PII self-report pain interference scores - PN status at enrollment = Progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

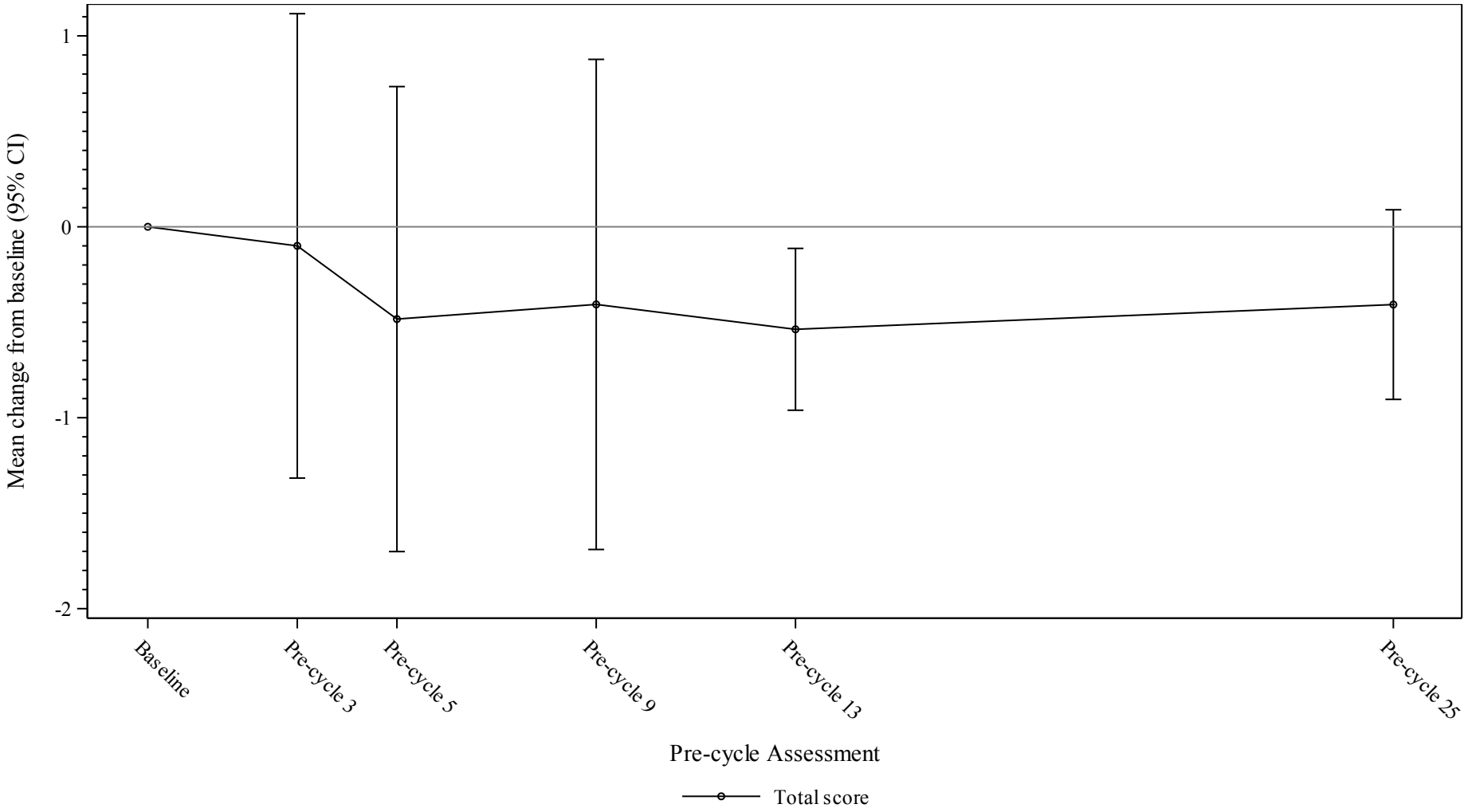
N = 11



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PII.
CI = Confidence interval.

Figure 2.3.1.2.4 Mean change from baseline of PII self-report pain interference scores - PN status at enrollment = Non-progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

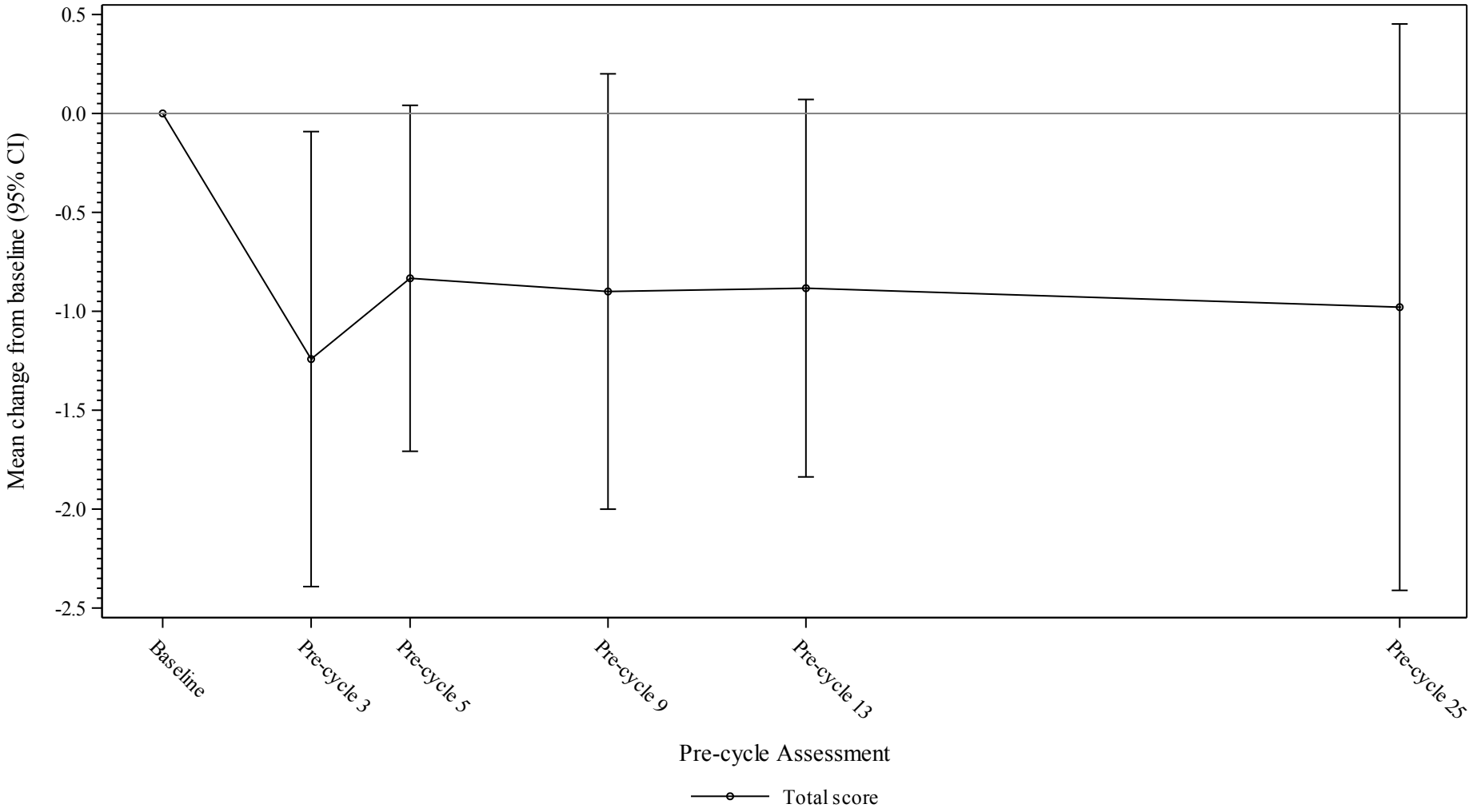
N = 11



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PII.
CI = Confidence interval.

Figure 2.3.1.2.5 Mean change from baseline of PII self-report pain interference scores - PN status at enrollment = Unknown (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

N = 12



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PII.
CI = Confidence interval.

Table 2.3.2 PII parent-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=48) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=45)	Categories of change [d]			
		Improvement	19	42,2	27,7, 57,8
		No improvement	26	57,8	42,2, 72,3
	Pre-cycle 5 (N=43)	Categories of change [d]			
		Improvement	19	44,2	29,1, 60,1
		No improvement	24	55,8	39,9, 70,9
	Pre-cycle 9 (N=45)	Categories of change [d]			
		Improvement	22	48,9	33,7, 64,2
		No improvement	23	51,1	35,8, 66,3
	Pre-cycle 13 (N=42)	Categories of change [d]			
		Improvement	21	50,0	34,2, 65,8
		No improvement	21	50,0	34,2, 65,8
	Pre-cycle 25 (N=33)	Categories of change [d]			
		Improvement	13	39,4	22,9, 57,9
		No improvement	20	60,6	42,1, 77,1
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	2	40,0	5,3, 85,3
		No improvement	3	60,0	14,7, 94,7
	Overall (N=45)	Categories of change [d]			
		Improvement	25	55,6	40,0, 70,4
		No improvement	20	44,4	29,6, 60,0

[a] Parents or legal guardians of children 5-18 years of age at enrolment completed the parent proxy measures of the Pain Interferen
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.2.1.1 PII parent-report pain interference scores and change from baseline over time - Gender = Male
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=28) [a]											
		Absolute values						Change from baseline					
PII parent-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=27)	1,46	1,381	1,67	0,0	4,0	3,6							
	Pre-cycle 3 (n=27)	0,55	0,670	0,17	0,0	2,2	3,6	26	-0,98	1,368	-1,17	-3,8	2,2	7,1
	Pre-cycle 5 (n=26)	0,83	1,193	0,17	0,0	4,0	7,1	25	-0,70	1,826	-0,50	-3,5	4,0	10,7
	Pre-cycle 9 (n=27)	0,75	1,058	0,00	0,0	3,5	3,6	26	-0,74	1,652	-1,00	-3,3	3,5	7,1
	Pre-cycle 13 (n=26)	0,64	1,304	0,00	0,0	6,0	7,1	25	-0,80	1,792	-0,50	-3,7	4,3	10,7
	Pre-cycle 25 (n=19)	0,30	0,620	0,00	0,0	2,3	32,1	18	-0,94	1,068	-0,33	-3,0	0,0	35,7
	Pre-cycle 37 (n=4)	0,08	0,167	0,00	0,0	0,3	85,7	4	-1,42	1,450	-1,17	-3,3	0,0	85,7

[a] Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PII.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.3.2.1.2 PII parent-report pain interference scores and change from baseline over time - Gender = Female
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]											
		Absolute values						Change from baseline					
PII parent-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=20)	1,57	1,634	1,25	0,0	4,8	0,0							
	Pre-cycle 3 (n=19)	1,26	1,235	1,00	0,0	3,7	5,0	19	-0,32	1,255	0,00	-2,3	1,7	5,0
	Pre-cycle 5 (n=18)	0,86	1,044	0,33	0,0	3,2	10,0	18	-0,81	1,164	-0,50	-2,7	0,8	10,0
	Pre-cycle 9 (n=19)	1,01	1,300	0,33	0,0	3,7	5,0	19	-0,57	1,607	-0,33	-4,0	3,7	5,0
	Pre-cycle 13 (n=17)	0,72	0,901	0,33	0,0	3,0	15,0	17	-0,83	1,378	-1,00	-3,3	2,2	15,0
	Pre-cycle 25 (n=15)	0,87	1,259	0,17	0,0	3,8	25,0	15	-0,40	1,348	-0,33	-3,3	2,2	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	0,0	0,0	95,0	1	NC	NC	NC	0,0	0,0	95,0

[a] Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PII.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.3.2.1.3 PII parent-report pain interference scores and change from baseline over time
- PN status at enrollment = Progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]											
		Absolute values						Change from baseline					
PII parent-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=19)	1,66	1,559	1,67	0,0	4,8	5,0							
	Pre-cycle 3 (n=20)	0,73	1,016	0,25	0,0	3,7	0,0	19	-0,95	1,257	-1,17	-3,3	1,7	5,0
	Pre-cycle 5 (n=19)	0,96	1,199	0,33	0,0	3,7	5,0	18	-0,82	1,519	-0,50	-3,5	3,0	10,0
	Pre-cycle 9 (n=20)	0,70	1,075	0,08	0,0	3,7	0,0	19	-0,92	1,682	-1,50	-3,3	3,7	5,0
	Pre-cycle 13 (n=19)	0,81	1,455	0,17	0,0	6,0	5,0	18	-0,89	1,997	-1,08	-3,7	4,3	10,0
	Pre-cycle 25 (n=13)	0,72	0,987	0,33	0,0	3,0	35,0	12	-0,63	1,223	-0,08	-3,0	1,2	40,0
	Pre-cycle 37 (n=4)	0,08	0,167	0,00	0,0	0,3	80,0	4	-1,42	1,450	-1,17	-3,3	0,0	80,0

[a] Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PII.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.3.2.1.4 PII self-report pain interference scores and change from baseline over time
- PN status at enrollment = Non-progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]											
		Absolute values						Change from baseline					
PII parent-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=14)	1,31	1,463	0,75	0,0	4,2	0,0							
	Pre-cycle 3 (n=13)	0,86	1,047	0,33	0,0	3,3	7,1	13	-0,45	1,048	0,00	-2,3	1,2	7,1
	Pre-cycle 5 (n=13)	0,64	0,938	0,17	0,0	2,7	7,1	13	-0,67	1,424	-0,33	-2,7	2,7	7,1
	Pre-cycle 9 (n=13)	0,87	1,147	0,33	0,0	3,3	7,1	13	-0,44	1,641	-0,33	-4,0	2,5	7,1
	Pre-cycle 13 (n=11)	0,35	0,896	0,00	0,0	3,0	21,4	11	-0,61	0,828	-0,17	-2,5	0,0	21,4
	Pre-cycle 25 (n=11)	0,23	0,754	0,00	0,0	2,5	21,4	11	-0,73	0,905	-0,33	-2,5	0,0	21,4
	Pre-cycle 37 (n=1)	NC	NC	NC	0,0	0,0	92,9	1	NC	NC	NC	0,0	0,0	92,9

[a] Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PII.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

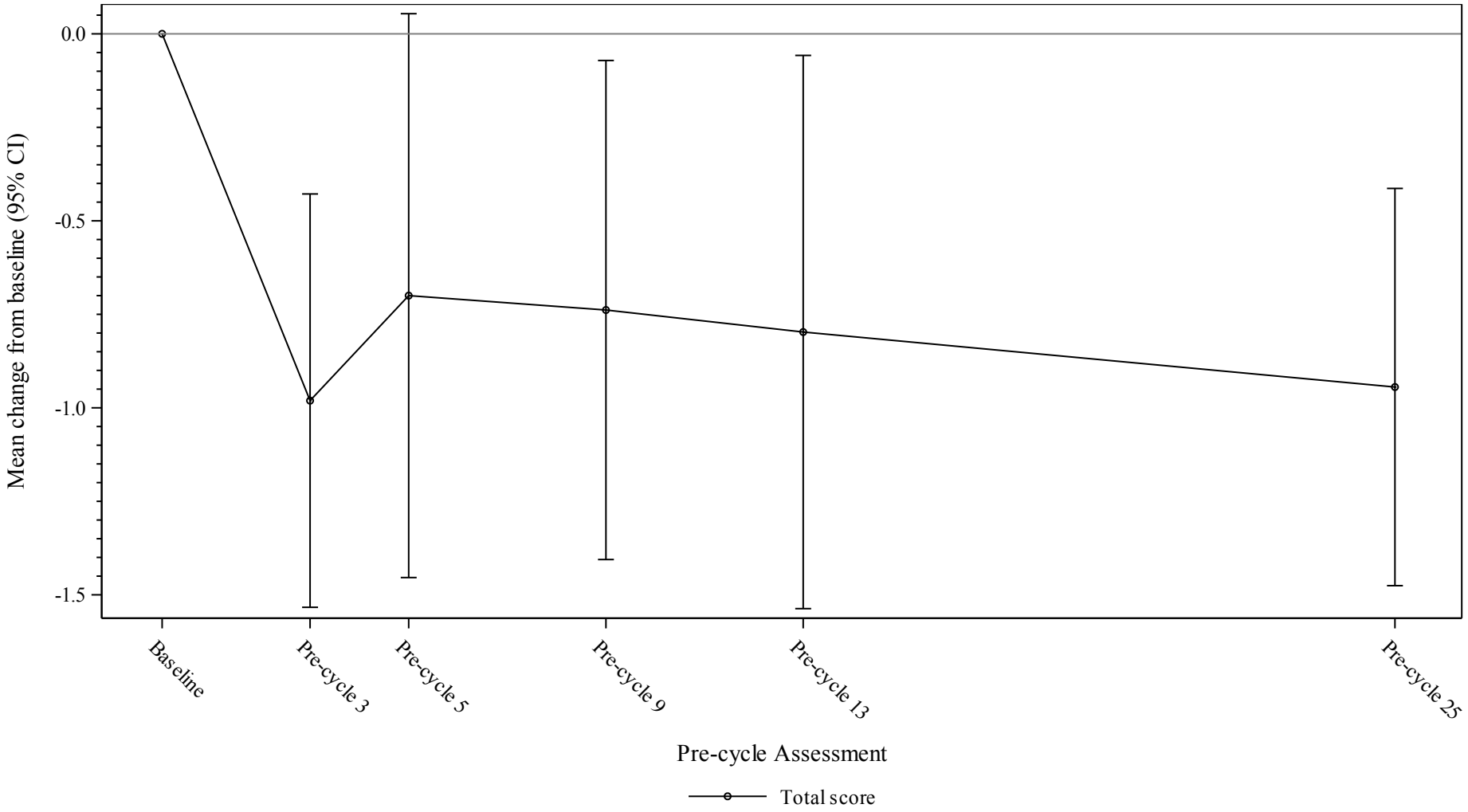
Table 2.3.2.1.5 PII self-report pain interference scores and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]											
		Absolute values						Change from baseline					
PII parent-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=14)	1,49	1,465	1,50	0,0	4,3	0,0							
	Pre-cycle 3 (n=13)	1,01	0,973	0,67	0,0	2,8	7,1	13	-0,59	1,737	-0,67	-3,8	2,2	7,1
	Pre-cycle 5 (n=12)	0,88	1,239	0,33	0,0	4,0	14,3	12	-0,71	1,892	-0,92	-2,8	4,0	14,3
	Pre-cycle 9 (n=13)	1,08	1,336	0,33	0,0	3,5	7,1	13	-0,53	1,569	-1,17	-2,3	3,5	7,1
	Pre-cycle 13 (n=13)	0,73	0,809	0,50	0,0	2,2	7,1	13	-0,87	1,637	-1,17	-3,3	2,2	7,1
	Pre-cycle 25 (n=10)	0,68	1,190	0,08	0,0	3,8	28,6	10	-0,75	1,582	-1,17	-3,3	2,2	28,6

[a] Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PII.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Figure 2.3.2.2.1 Mean change from baseline of PII parent-report pain interference scores - Gender = Male
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

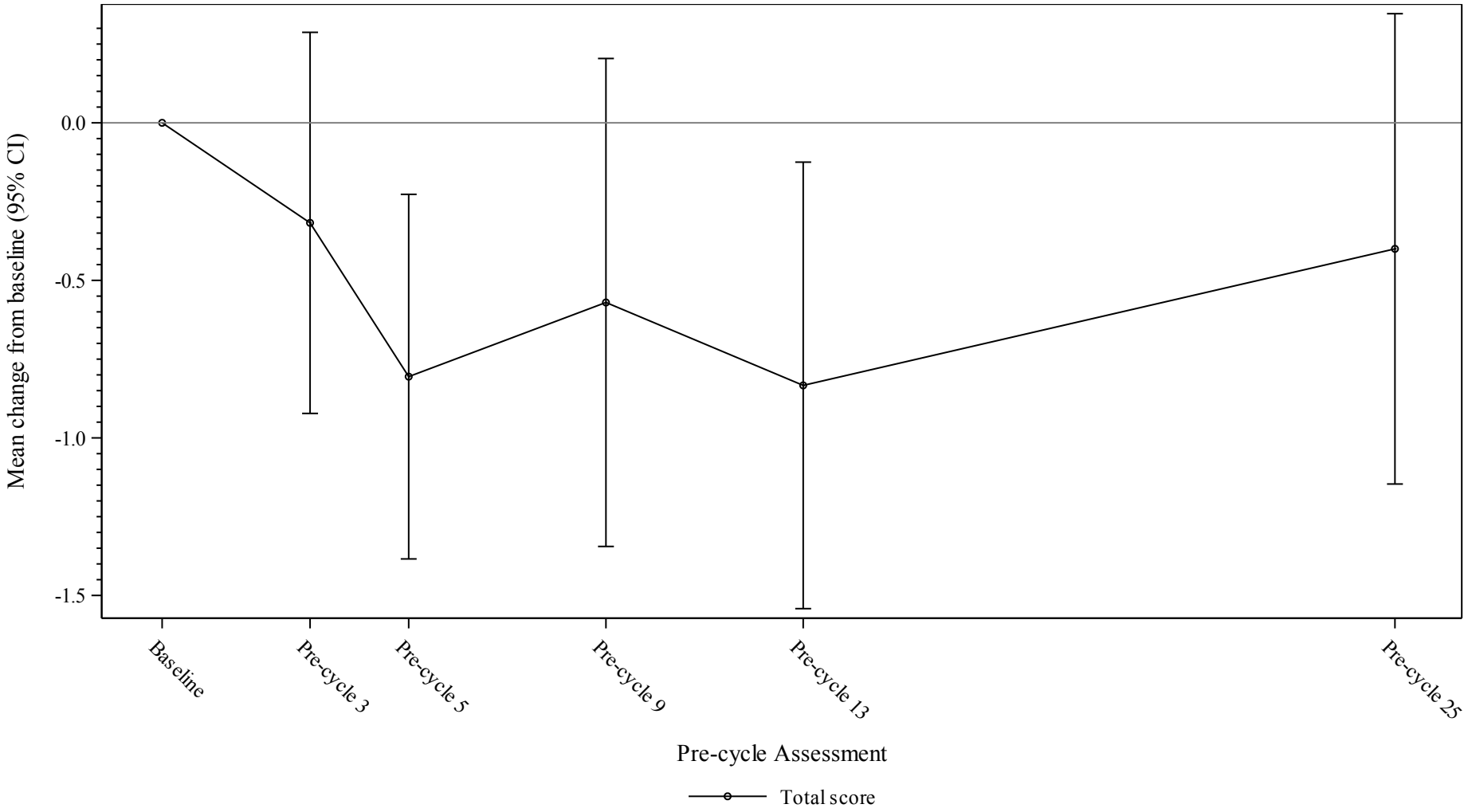
N = 28



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PII.
CI = Confidence interval.

Figure 2.3.2.2.2 Mean change from baseline of PII parent-report pain interference scores - Gender = Female
(Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

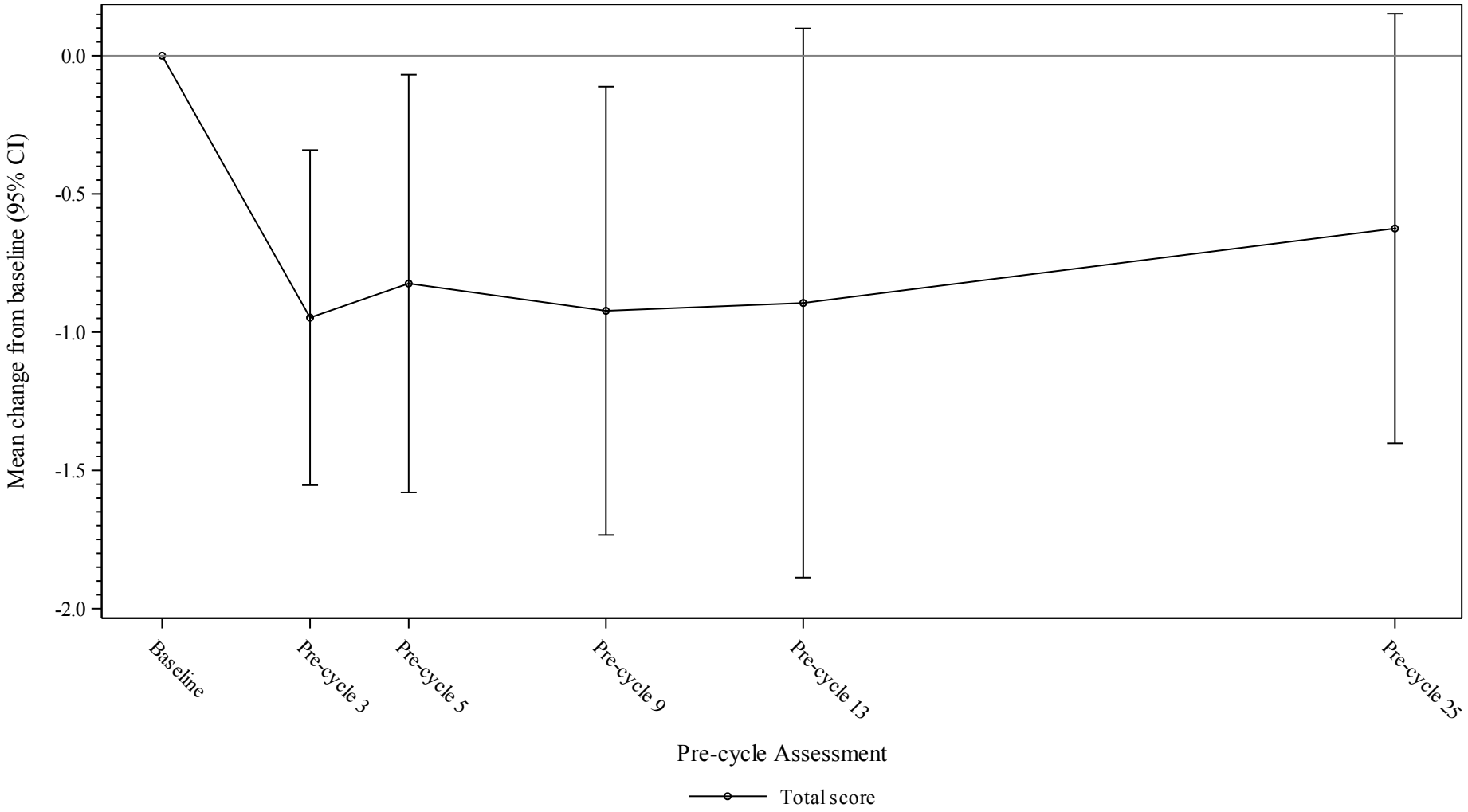
N = 20



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PII.
CI = Confidence interval.

Figure 2.3.2.2.3 Mean change from baseline of PII parent-report pain interference scores - PN status at enrollment = Progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

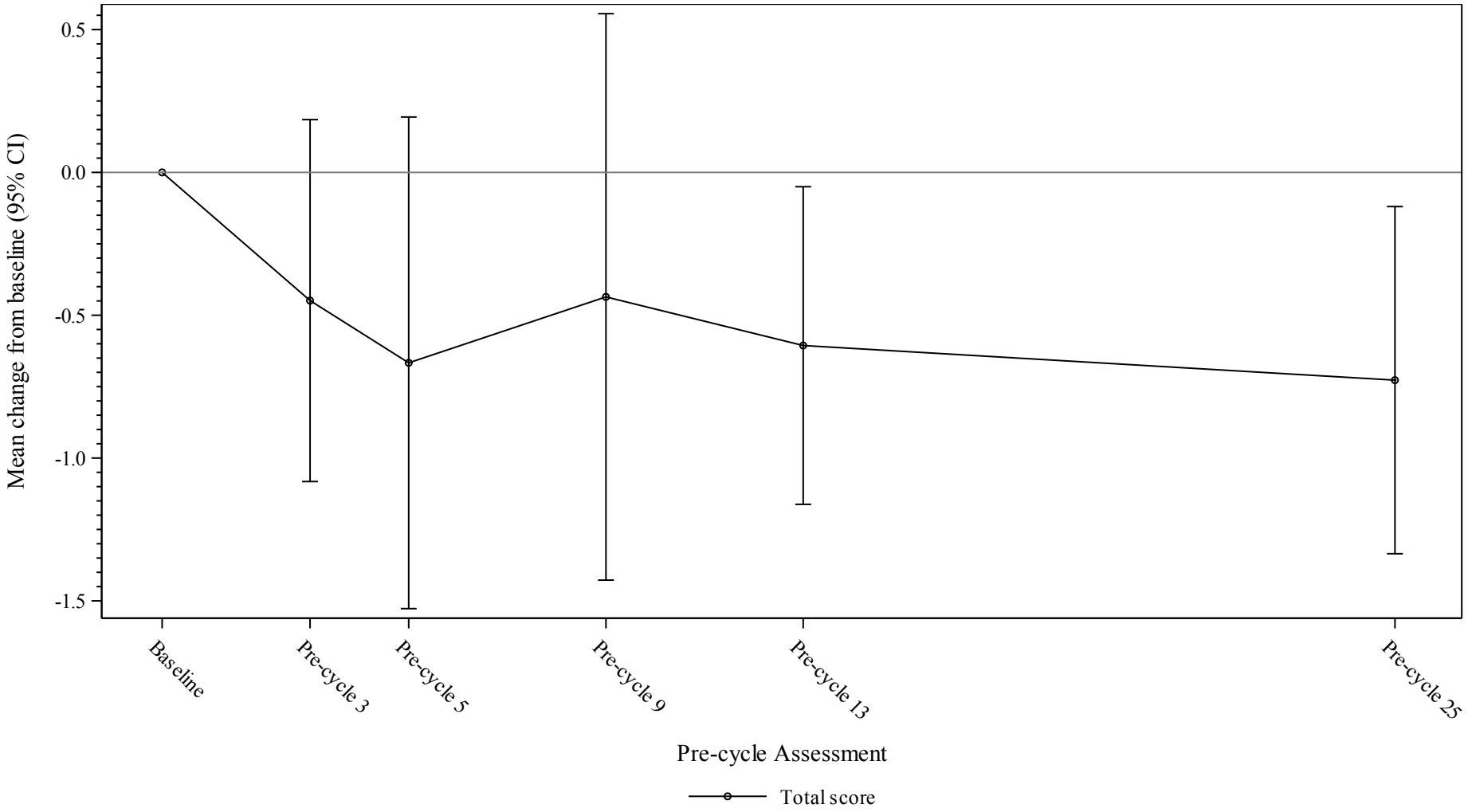
N = 20



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PII.
CI = Confidence interval.

Figure 2.3.2.2.4 Mean change from baseline of PII parent-report pain interference scores - PN status at enrollment = Non-progressive (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

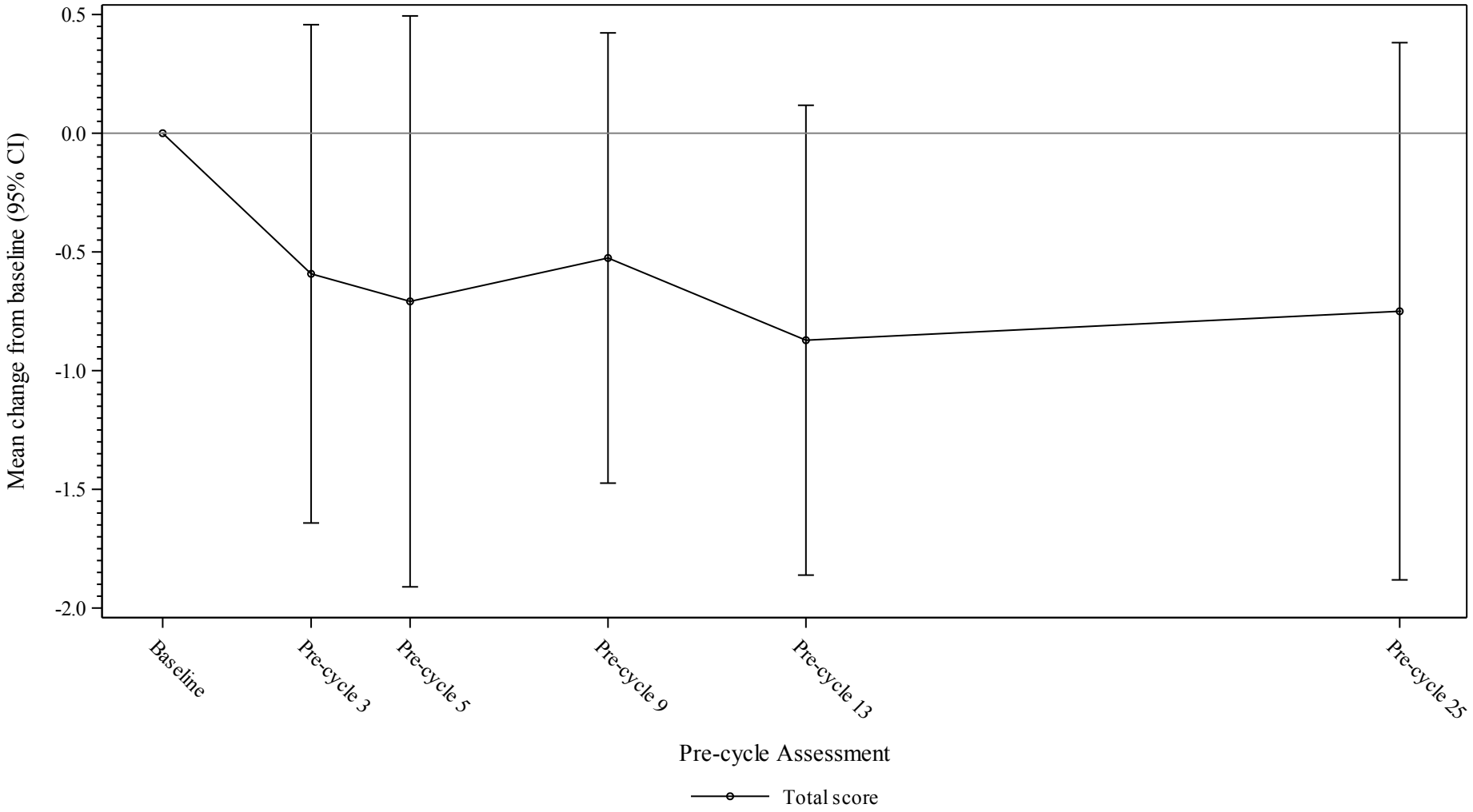
N = 14



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PII.
CI = Confidence interval.

Figure 2.3.2.2.5 Mean change from baseline of PII parent-report pain interference scores - PN status at enrollment = Unknown (Full analysis set) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

N = 14



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PII.
CI = Confidence interval.

Table 2.3.3.1 PII self-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points - Gender = Male (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=21) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=19)	Categories of change [d]			
		Improvement	3	15,8	3,4, 39,6
		No improvement	16	84,2	60,4, 96,6
	Pre-cycle 5 (N=19)	Categories of change [d]			
		Improvement	4	21,1	6,1, 45,6
		No improvement	15	78,9	54,4, 93,9
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	6	31,6	12,6, 56,6
		No improvement	13	68,4	43,4, 87,4
	Pre-cycle 13 (N=18)	Categories of change [d]			
		Improvement	5	27,8	9,7, 53,5
		No improvement	13	72,2	46,5, 90,3
	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	4	28,6	8,4, 58,1
		No improvement	10	71,4	41,9, 91,6
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Overall (N=19)	Categories of change [d]			
		Improvement	7	36,8	16,3, 61,6
		No improvement	12	63,2	38,4, 83,7

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the Pain Interference Index (PII).
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.3.2 PII self-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points - Gender = Female (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=13) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	3	25,0	5,5, 57,2
		No improvement	9	75,0	42,8, 94,5
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22,2	2,8, 60,0
		No improvement	7	77,8	40,0, 97,2
	Overall (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the Pain Interference Index (PII).
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.3.3 PII self-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points - PN status at enrollment = Progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	2	18,2	2,3, 51,8
		No improvement	9	81,8	48,2, 97,7
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	1	9,1	0,2, 41,3
		No improvement	10	90,9	58,7, 99,8
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
	Overall (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the Pain Interference Index (PII).
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.3.4 PII self-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points - PN status at enrollment = Non-progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33,3	7,5, 70,1
		No improvement	6	66,7	29,9, 92,5
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22,2	2,8, 60,0
		No improvement	7	77,8	40,0, 97,2
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the Pain Interference Index (PII).
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.3.5 PII self-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points - PN status at enrollment = Unknown (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=12) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	3	37,5	8,5, 75,5
		No improvement	5	62,5	24,5, 91,5
	Overall (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the Pain Interference Index (PII).
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.4.1 PII parent-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points - Gender = Male (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=28) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=26)	Categories of change [d]			
		Improvement	14	53,8	33,4, 73,4
		No improvement	12	46,2	26,6, 66,6
	Pre-cycle 5 (N=25)	Categories of change [d]			
		Improvement	12	48,0	27,8, 68,7
		No improvement	13	52,0	31,3, 72,2
	Pre-cycle 9 (N=26)	Categories of change [d]			
		Improvement	14	53,8	33,4, 73,4
		No improvement	12	46,2	26,6, 66,6
	Pre-cycle 13 (N=25)	Categories of change [d]			
		Improvement	12	48,0	27,8, 68,7
		No improvement	13	52,0	31,3, 72,2
	Pre-cycle 25 (N=18)	Categories of change [d]			
		Improvement	8	44,4	21,5, 69,2
		No improvement	10	55,6	30,8, 78,5
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	2	50,0	6,8, 93,2
		No improvement	2	50,0	6,8, 93,2
	Overall (N=26)	Categories of change [d]			
		Improvement	15	57,7	36,9, 76,6
		No improvement	11	42,3	23,4, 63,1

[a] Parents or legal guardians of children 5-18 years of age at enrolment completed the parent proxy measures of the Pain Interferen
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.4.2 PII parent-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points - Gender = Female (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=20) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=19)	Categories of change [d]			
		Improvement	5	26,3	9,1, 51,2
		No improvement	14	73,7	48,8, 90,9
	Pre-cycle 5 (N=18)	Categories of change [d]			
		Improvement	7	38,9	17,3, 64,3
		No improvement	11	61,1	35,7, 82,7
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	8	42,1	20,3, 66,5
		No improvement	11	57,9	33,5, 79,7
	Pre-cycle 13 (N=17)	Categories of change [d]			
		Improvement	9	52,9	27,8, 77,0
		No improvement	8	47,1	23,0, 72,2
	Pre-cycle 25 (N=15)	Categories of change [d]			
		Improvement	5	33,3	11,8, 61,6
		No improvement	10	66,7	38,4, 88,2
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=19)	Categories of change [d]			
		Improvement	10	52,6	28,9, 75,6
		No improvement	9	47,4	24,4, 71,1

[a] Parents or legal guardians of children 5-18 years of age at enrolment completed the parent proxy measures of the Pain Interferen
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.4.3 PII parent-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points - PN status at enrollment = Progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=20) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=19)	Categories of change [d]			
		Improvement	10	52,6	28,9, 75,6
		No improvement	9	47,4	24,4, 71,1
	Pre-cycle 5 (N=18)	Categories of change [d]			
		Improvement	8	44,4	21,5, 69,2
		No improvement	10	55,6	30,8, 78,5
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	10	52,6	28,9, 75,6
		No improvement	9	47,4	24,4, 71,1
	Pre-cycle 13 (N=18)	Categories of change [d]			
		Improvement	9	50,0	26,0, 74,0
		No improvement	9	50,0	26,0, 74,0
	Pre-cycle 25 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	2	50,0	6,8, 93,2
		No improvement	2	50,0	6,8, 93,2
	Overall (N=19)	Categories of change [d]			
		Improvement	11	57,9	33,5, 79,7
		No improvement	8	42,1	20,3, 66,5

[a] Parents or legal guardians of children 5-18 years of age at enrolment completed the parent proxy measures of the Pain Interferen
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.4.4 PII parent-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points - PN status at enrollment = Non-progressive (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=14) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=13)	Categories of change [d]			
		Improvement	3	23,1	5,0, 53,8
		No improvement	10	76,9	46,2, 95,0
	Pre-cycle 5 (N=13)	Categories of change [d]			
		Improvement	5	38,5	13,9, 68,4
		No improvement	8	61,5	31,6, 86,1
	Pre-cycle 9 (N=13)	Categories of change [d]			
		Improvement	4	30,8	9,1, 61,4
		No improvement	9	69,2	38,6, 90,9
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1
	Pre-cycle 25 (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=13)	Categories of change [d]			
		Improvement	6	46,2	19,2, 74,9
		No improvement	7	53,8	25,1, 80,8

[a] Parents or legal guardians of children 5-18 years of age at enrolment completed the parent proxy measures of the Pain Interferen
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.4.5 PII parent-reported pain interference score categories of change over time - percentage of patients with Improvement by >= 0.9 points - PN status at enrollment = Unknown (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=14) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=13)	Categories of change [d]			
		Improvement	6	46,2	19,2, 74,9
		No improvement	7	53,8	25,1, 80,8
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	6	50,0	21,1, 78,9
		No improvement	6	50,0	21,1, 78,9
	Pre-cycle 9 (N=13)	Categories of change [d]			
		Improvement	8	61,5	31,6, 86,1
		No improvement	5	38,5	13,9, 68,4
	Pre-cycle 13 (N=13)	Categories of change [d]			
		Improvement	8	61,5	31,6, 86,1
		No improvement	5	38,5	13,9, 68,4
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	5	50,0	18,7, 81,3
		No improvement	5	50,0	18,7, 81,3
	Overall (N=13)	Categories of change [d]			
		Improvement	8	61,5	31,6, 86,1
		No improvement	5	38,5	13,9, 68,4

[a] Parents or legal guardians of children 5-18 years of age at enrolment completed the parent proxy measures of the Pain Interferen
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.9 for Total score. NC - not calculated.

Table 2.3.5.1.1 Analysis of time to pain palliation (months) of NRS-11 pain items - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Statistic	Selumetinib 25 mg/m² BID (N=21)
Target tumour pain		
Definition 1: Including only symptomatic patients		
Using threshold of 2 points	Total events, n(%)	8 (38.1)
	Censored patients, n(%)	7 (33.3)
	Median time to pain palliation (months) [a]	3.25
	95% CI for median time to pain palliation [a]	1.74, 7.33
Definition 2: Including both symptomatic and asymptomatic patients		
Using threshold of 2 points	Total events, n(%)	9 (42.9)
	Censored patients, n(%)	6 (28.6)
	Median time to pain palliation (months) [a]	3.73
	95% CI for median time to pain palliation [a]	1.84, NC

[a] Calculated using Kaplan-Meier technique.
Definition 1: Events include only symptomatic patients with a pain score >=2 points at baseline;
the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use.
All other patients censored. Definition 2: For asymptomatic patients with a pain score <2 points at baseline AND an analgesic score >=2 points at baseline, pain palliation is defined as stable (or reduced) pain intensity score AND decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without analgesic use. All other patients censored.
Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.

Table 2.3.5.1.2 Analysis of time to pain palliation (months) of NRS-11 pain items - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Statistic	Selumetinib 25 mg/m² BID (N=13)
Target tumour pain		
Definition 1: Including only symptomatic patients		
Using threshold of 2 points	Total events, n(%)	6 (46.2)
	Censored patients, n(%)	5 (38.5)
	Median time to pain palliation (months) [a]	1.87
	95% CI for median time to pain palliation [a]	1.71, 3.71
Definition 2: Including both symptomatic and asymptomatic patients		
Using threshold of 2 points	Total events, n(%)	6 (46.2)
	Censored patients, n(%)	5 (38.5)
	Median time to pain palliation (months) [a]	3.71
	95% CI for median time to pain palliation [a]	1.81, NC

[a] Calculated using Kaplan-Meier technique.
Definition 1: Events include only symptomatic patients with a pain score >=2 points at baseline;
the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use.
All other patients censored. Definition 2: For asymptomatic patients with a pain score <2 points at baseline AND an analgesic score >=2 points at baseline, pain palliation is defined as stable (or reduced) pain intensity score AND decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without analgesic use. All other patients censored.
Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.

Table 2.3.5.1.3 Analysis of time to pain palliation (months) of NRS-11 pain items - PN statuts at enrollment = Progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Statistic	Selumetinib 25 mg/m² BID (N=11)
Target tumour pain		
Definition 1: Including only symptomatic patients		
Using threshold of 2 points	Total events, n(%)	4 (36.4)
	Censored patients, n(%)	3 (27.3)
	Median time to pain palliation (months) [a]	2.56
	95% CI for median time to pain palliation [a]	1.87, 3.91
Definition 2: Including both symptomatic and asymptomatic patients		
Using threshold of 2 points	Total events, n(%)	4 (36.4)
	Censored patients, n(%)	3 (27.3)
	Median time to pain palliation (months) [a]	3.91
	95% CI for median time to pain palliation [a]	1.87, NC

[a] Calculated using Kaplan-Meier technique.
Definition 1: Events include only symptomatic patients with a pain score >=2 points at baseline;
the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use.
All other patients censored. Definition 2: For asymptomatic patients with a pain score <2 points at baseline AND an analgesic score >=2 points at baseline, pain palliation is defined as stable (or reduced) pain intensity score AND decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without analgesic use. All other patients censored.
Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.

Table 2.3.5.1.4 Analysis of time to pain palliation (months) of NRS-11 pain items - PN statuts at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Statistic	Selumetinib 25 mg/m² BID (N=11)
Target tumour pain		
Definition 1: Including only symptomatic patients		
Using threshold of 2 points	Total events, n(%)	6 (54.5)
	Censored patients, n(%)	3 (27.3)
	Median time to pain palliation (months) [a]	1.87
	95% CI for median time to pain palliation [a]	1.74, 7.33
Definition 2: Including both symptomatic and asymptomatic patients		
Using threshold of 2 points	Total events, n(%)	6 (54.5)
	Censored patients, n(%)	3 (27.3)
	Median time to pain palliation (months) [a]	3.55
	95% CI for median time to pain palliation [a]	1.74, NC

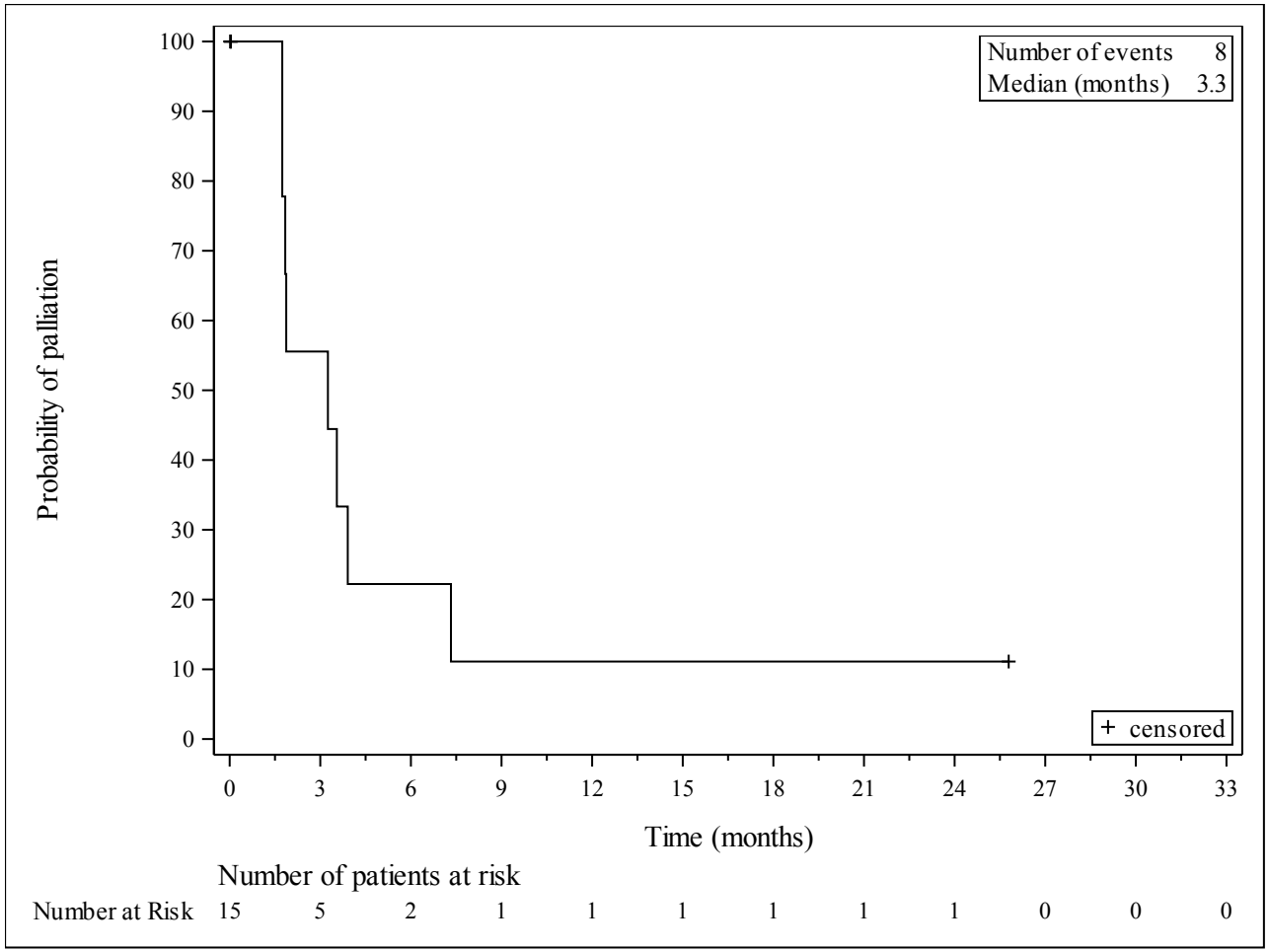
[a] Calculated using Kaplan-Meier technique.
Definition 1: Events include only symptomatic patients with a pain score >=2 points at baseline;
the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use.
All other patients censored. Definition 2: For asymptomatic patients with a pain score <2 points at baseline AND an analgesic score >=2 points at baseline, pain palliation is defined as stable (or reduced) pain intensity score AND decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without analgesic use. All other patients censored.
Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.

Table 2.3.5.1.5 Analysis of time to pain palliation (months) of NRS-11 pain items - PN statuts at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Statistic	Selumetinib 25 mg/m² BID (N=12)
Target tumour pain		
Definition 1: Including only symptomatic patients		
Using threshold of 2 points	Total events, n(%)	4 (33.3)
	Censored patients, n(%)	6 (50.0)
	Median time to pain palliation (months) [a]	1.86
	95% CI for median time to pain palliation [a]	1.71, 3.71
Definition 2: Including both symptomatic and asymptomatic patients		
Using threshold of 2 points	Total events, n(%)	5 (41.7)
	Censored patients, n(%)	5 (41.7)
	Median time to pain palliation (months) [a]	3.71
	95% CI for median time to pain palliation [a]	1.71, NC

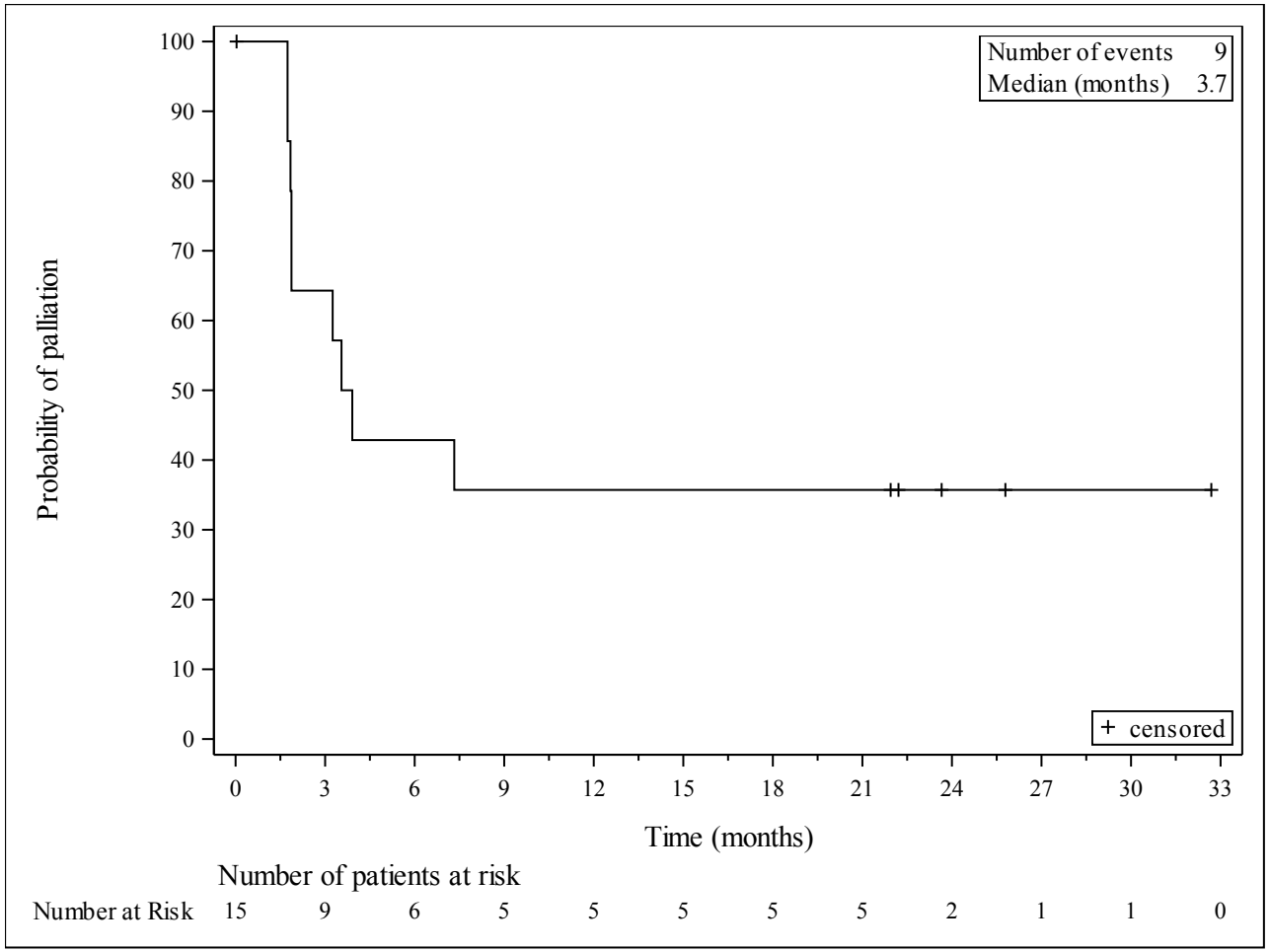
[a] Calculated using Kaplan-Meier technique.
Definition 1: Events include only symptomatic patients with a pain score >=2 points at baseline;
the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use.
All other patients censored. Definition 2: For asymptomatic patients with a pain score <2 points at baseline AND an analgesic score >=2 points at baseline, pain palliation is defined as stable (or reduced) pain intensity score AND decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without analgesic use. All other patients censored.
Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the NRS-11.

Figure 2.3.5.2.1 Kaplan-Meier plot for time to pain palliation - NRS-11 target tumour pain - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018
Including only symptomatic patients - Using threshold of 2 points [a]
N = 21



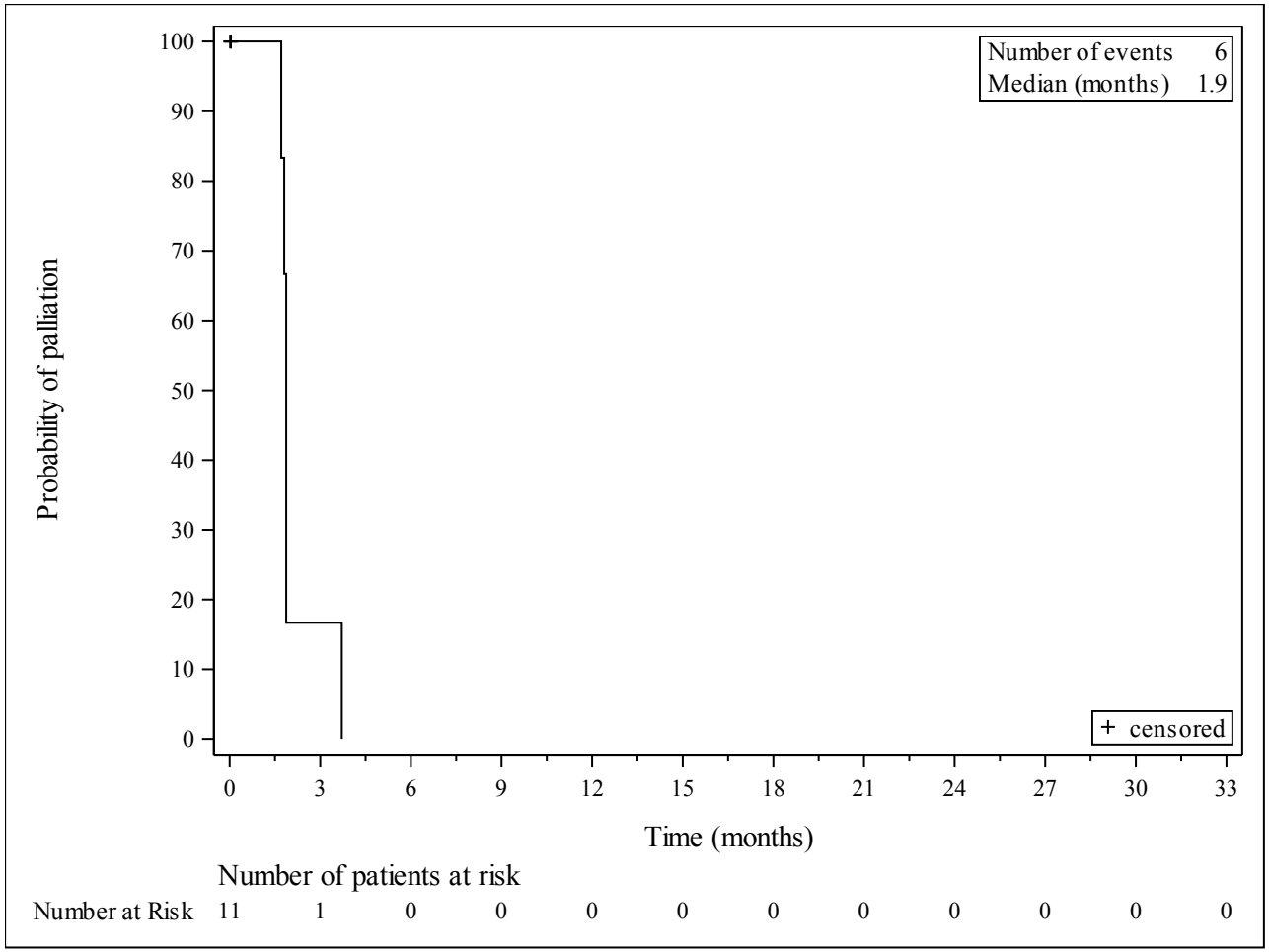
Time to pain palliation was defined as the time from the first dose of study drug until the date of the first observed pain palliation. Patients with no pain palliation were censored at the date of the last available PRO assessment.
[a] For asymptomatic patients with a pain intensity score < 2 pts AND an analgesic score >=2 pts at baseline, pain palliation is defined as a stable (or reduced) pain intensity score AND a decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. For symptomatic patients with a pain score >=2 points at baseline; the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. Note: Children, ages 8 to 18 years at enrolment completed self-report measures of NRS-11. Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpainplsub.sas smpainplsuba.rtf 20MAY2021:16:32 icesas184PD

Figure 2.3.5.2.1 Kaplan-Meier plot for time to pain palliation - NRS-11 target tumour pain - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018
Including symptomatic and asymptomatic patients - Using threshold of 2 points [a]
N = 21



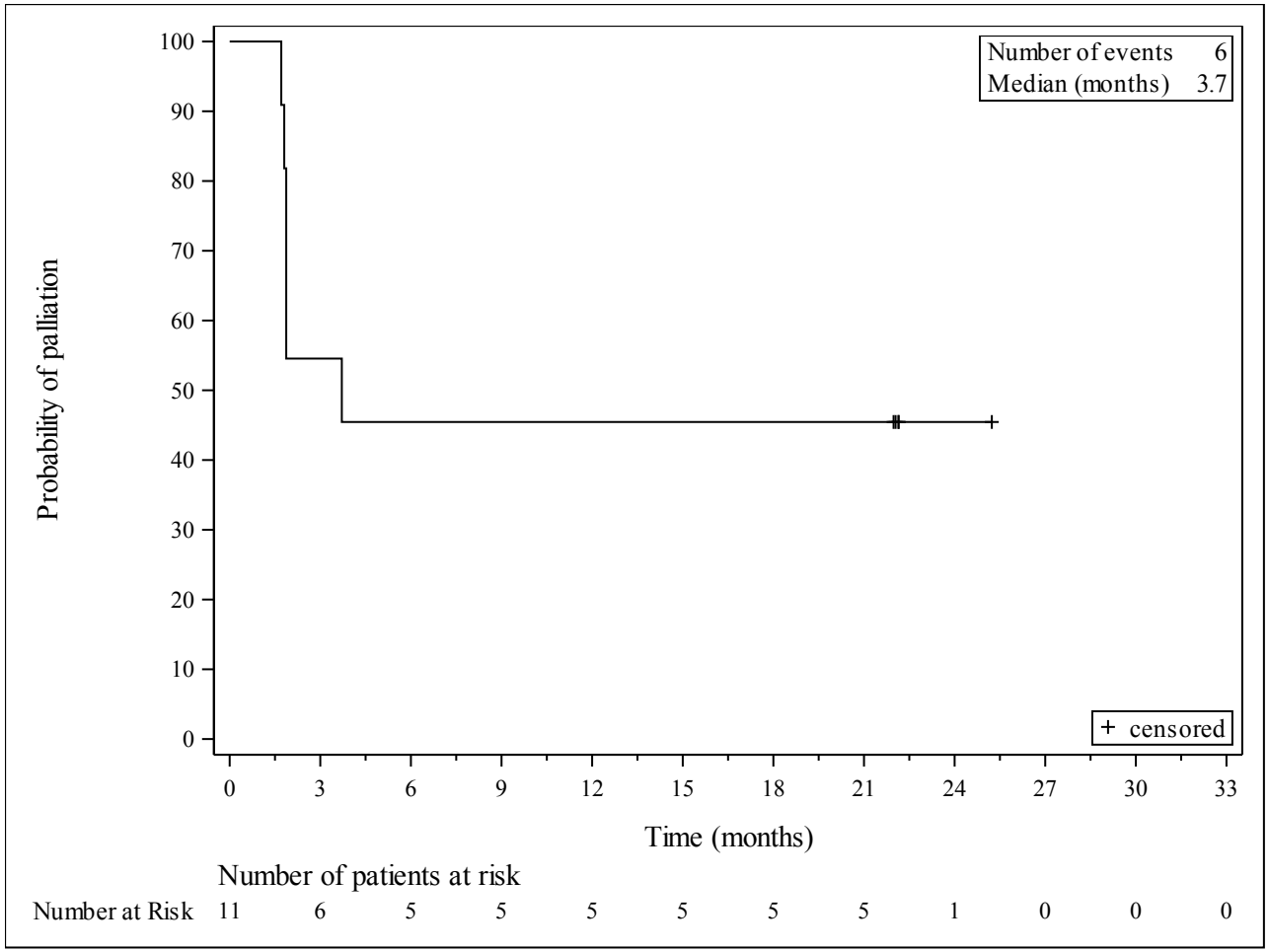
Time to pain palliation was defined as the time from the first dose of study drug until the date of the first observed pain palliation. Patients with no pain palliation were censored at the date of the last available PRO assessment.
[a] For asymptomatic patients with a pain intensity score < 2 pts AND an analgesic score >=2 pts at baseline, pain palliation is defined as a stable (or reduced) pain intensity score AND a decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. For symptomatic patients with a pain score >=2 points at baseline; the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. Note: Children, ages 8 to 18 years at enrolment completed self-report measures of NRS-11. Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpainplsub.sas smpainplsuba.rtf 20MAY2021:16:32 icesas184PD

Figure 2.3.5.2.2 Kaplan-Meier plot for time to pain palliation - NRS-11 target tumour pain - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018
Including only symptomatic patients - Using threshold of 2 points [a]
N = 13



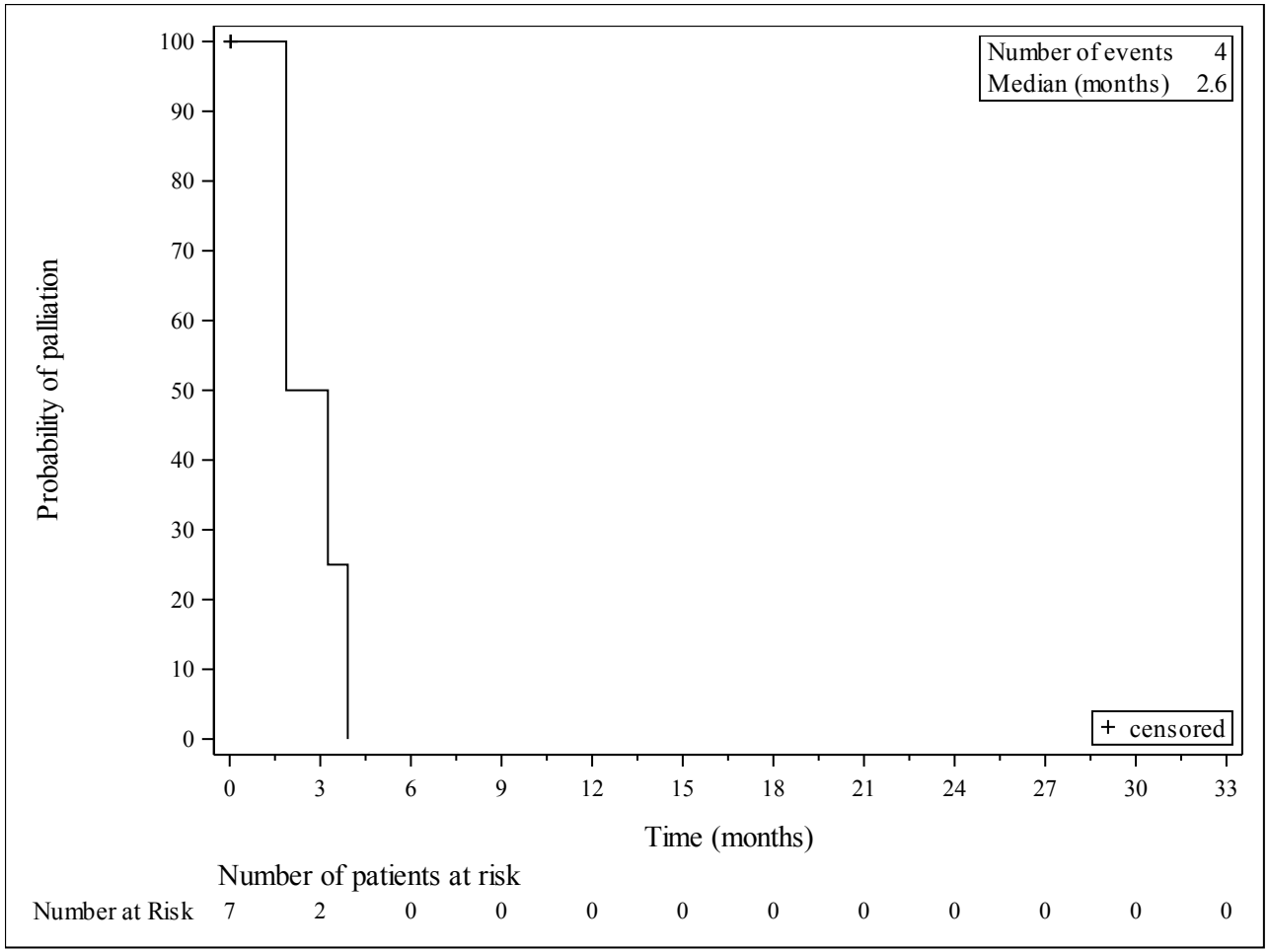
Time to pain palliation was defined as the time from the first dose of study drug until the date of the first observed pain palliation. Patients with no pain palliation were censored at the date of the last available PRO assessment.
[a] For asymptomatic patients with a pain intensity score < 2 pts AND an analgesic score >=2 pts at baseline, pain palliation is defined as a stable (or reduced) pain intensity score AND a decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. For symptomatic patients with a pain score >=2 points at baseline; the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. Note: Children, ages 8 to 18 years at enrolment completed self-report measures of NRS-11. Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpainplsub.sas smpainplsubb.rtf 20MAY2021:16:32 icesas184PD

Figure 2.3.5.2.2 Kaplan-Meier plot for time to pain palliation - NRS-11 target tumour pain - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018
Including symptomatic and asymptomatic patients - Using threshold of 2 points [a]
N = 13



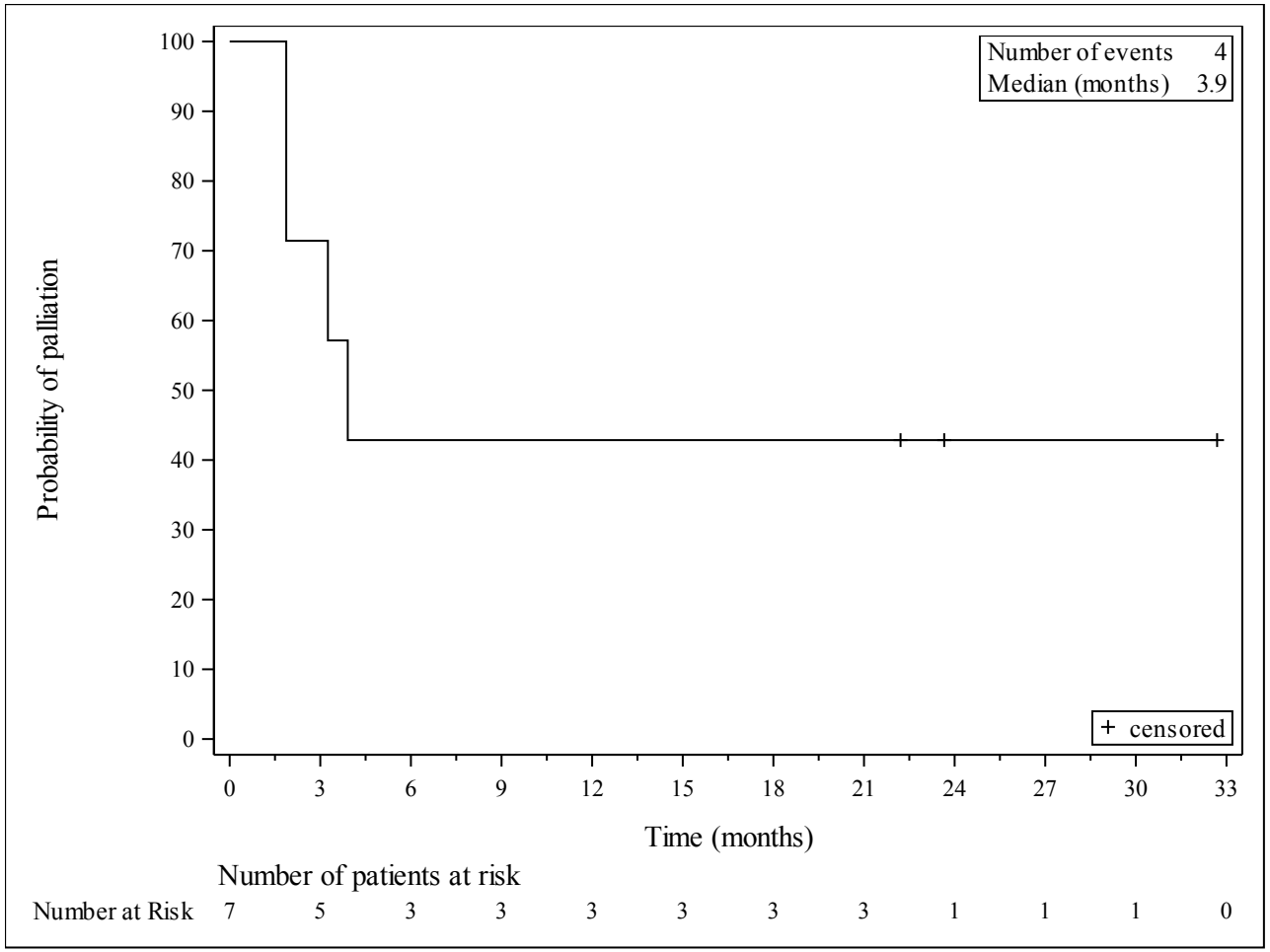
Time to pain palliation was defined as the time from the first dose of study drug until the date of the first observed pain palliation. Patients with no pain palliation were censored at the date of the last available PRO assessment.
[a] For asymptomatic patients with a pain intensity score < 2 pts AND an analgesic score >=2 pts at baseline, pain palliation is defined as a stable (or reduced) pain intensity score AND a decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. For symptomatic patients with a pain score >=2 points at baseline; the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. Note: Children, ages 8 to 18 years at enrolment completed self-report measures of NRS-11. Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpainplsub.sas smpainplsubb.rtf 20MAY2021:16:32 icesas184PD

Figure 2.3.5.2.3 Kaplan-Meier plot for time to pain palliation - NRS-11 target tumour pain - PN statuts at enrol. = Progressive
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018
Including only symptomatic patients - Using threshold of 2 points [a]
N = 11



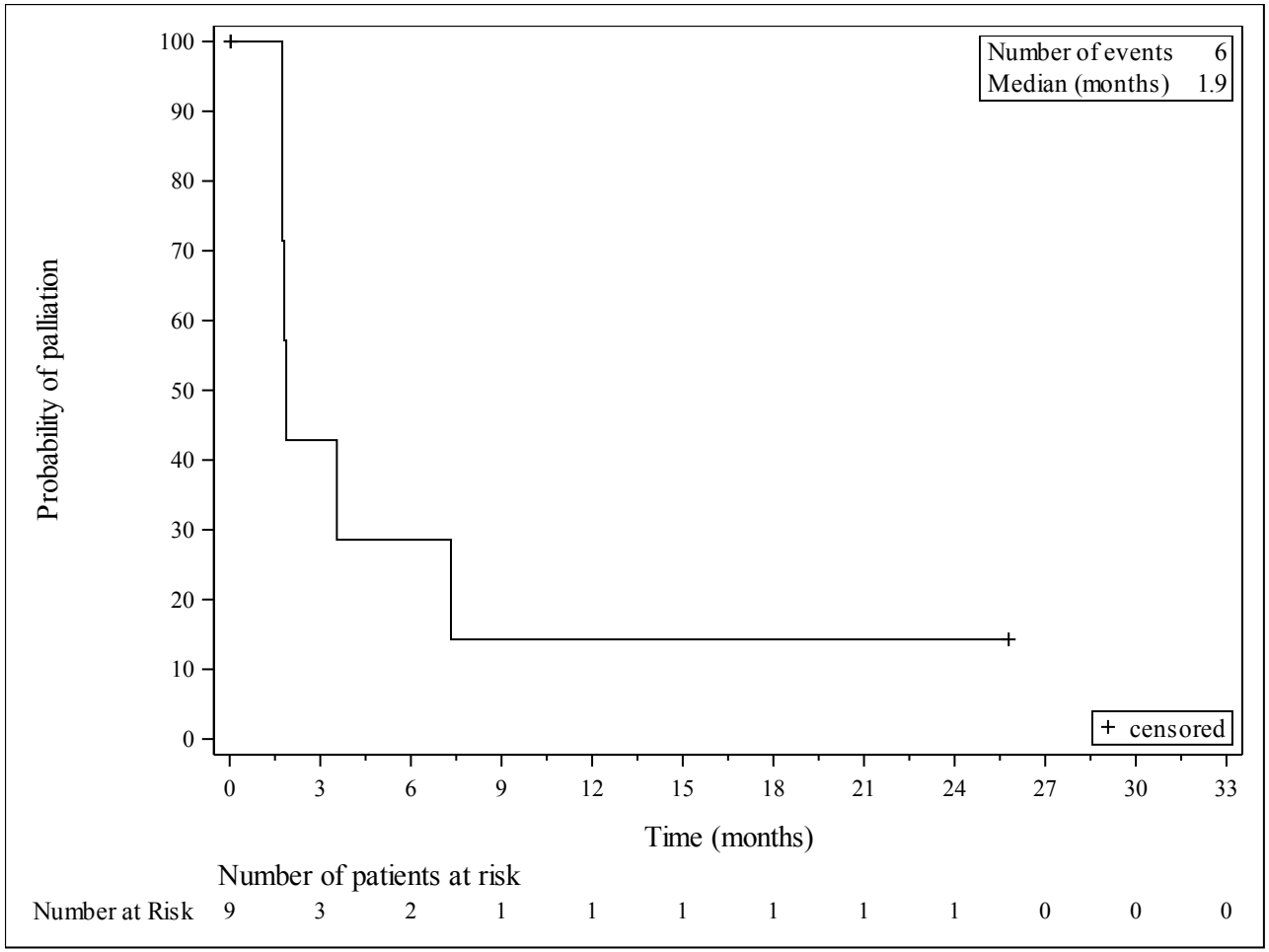
Time to pain palliation was defined as the time from the first dose of study drug until the date of the first observed pain palliation. Patients with no pain palliation were censored at the date of the last available PRO assessment.
[a] For asymptomatic patients with a pain intensity score < 2 pts AND an analgesic score >=2 pts at baseline, pain palliation is defined as a stable (or reduced) pain intensity score AND a decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. For symptomatic patients with a pain score >=2 points at baseline; the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. Note: Children, ages 8 to 18 years at enrolment completed self-report measures of NRS-11. Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpainplsub.sas smpainplsubc.rtf 20MAY2021:16:32 icesas184PD

Figure 2.3.5.2.3 Kaplan-Meier plot for time to pain palliation - NRS-11 target tumour pain - PN statuts at enrol. = Progressive
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018
Including symptomatic and asymptomatic patients - Using threshold of 2 points [a]
N = 11



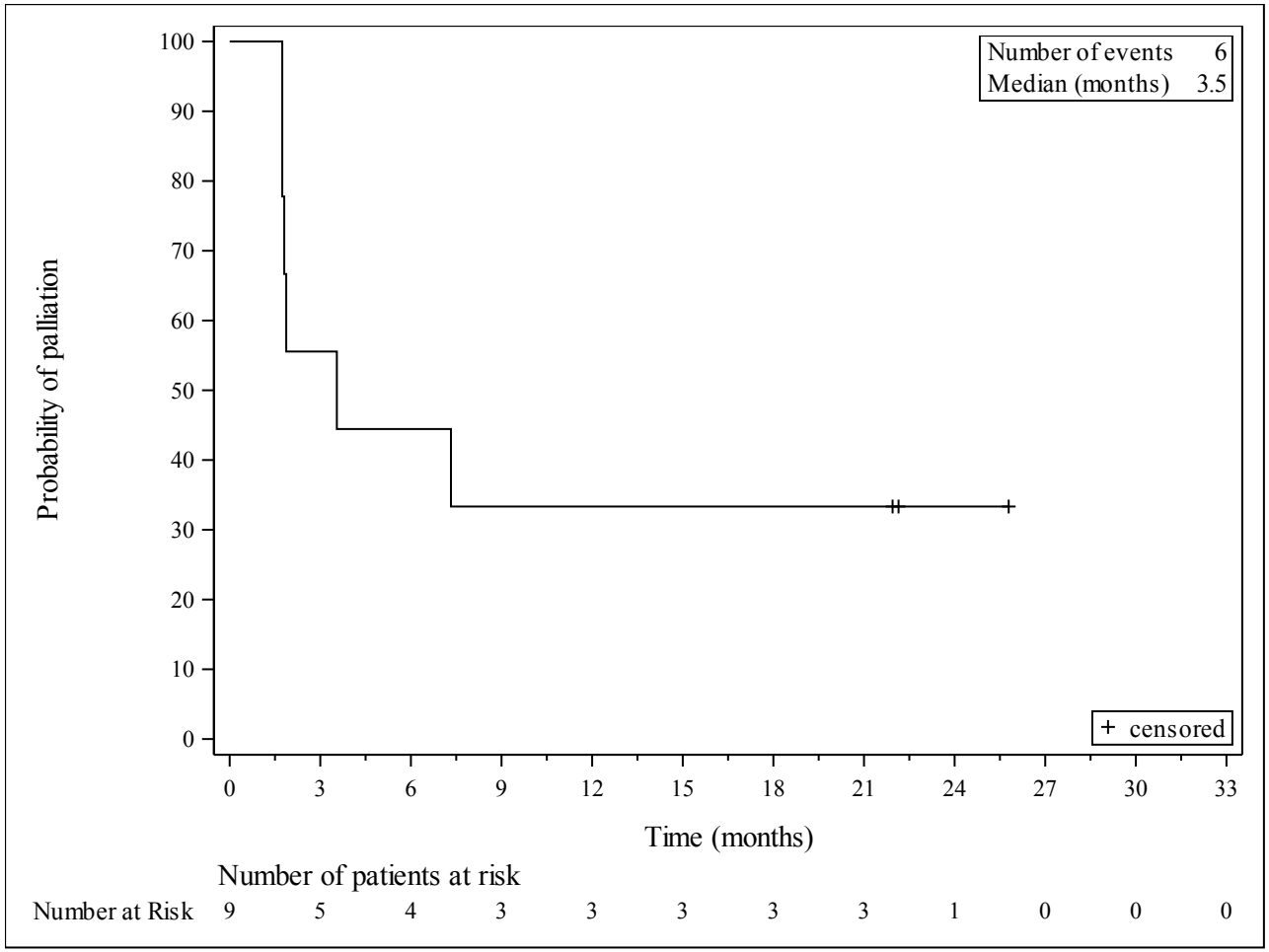
Time to pain palliation was defined as the time from the first dose of study drug until the date of the first observed pain palliation. Patients with no pain palliation were censored at the date of the last available PRO assessment.
[a] For asymptomatic patients with a pain intensity score < 2 pts AND an analgesic score >=2 pts at baseline, pain palliation is defined as a stable (or reduced) pain intensity score AND a decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. For symptomatic patients with a pain score >=2 points at baseline; the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. Note: Children, ages 8 to 18 years at enrolment completed self-report measures of NRS-11. Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpainplsub.sas smpainplsubc.rtf 20MAY2021:16:32 icesas184PD

Figure 2.3.5.2.4 Kaplan-Meier plot for time to pain palliation - NRS-11 target tumour pain - PN statuts at enrol. = Non-progressive
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018
Including only symptomatic patients - Using threshold of 2 points [a]
N = 11



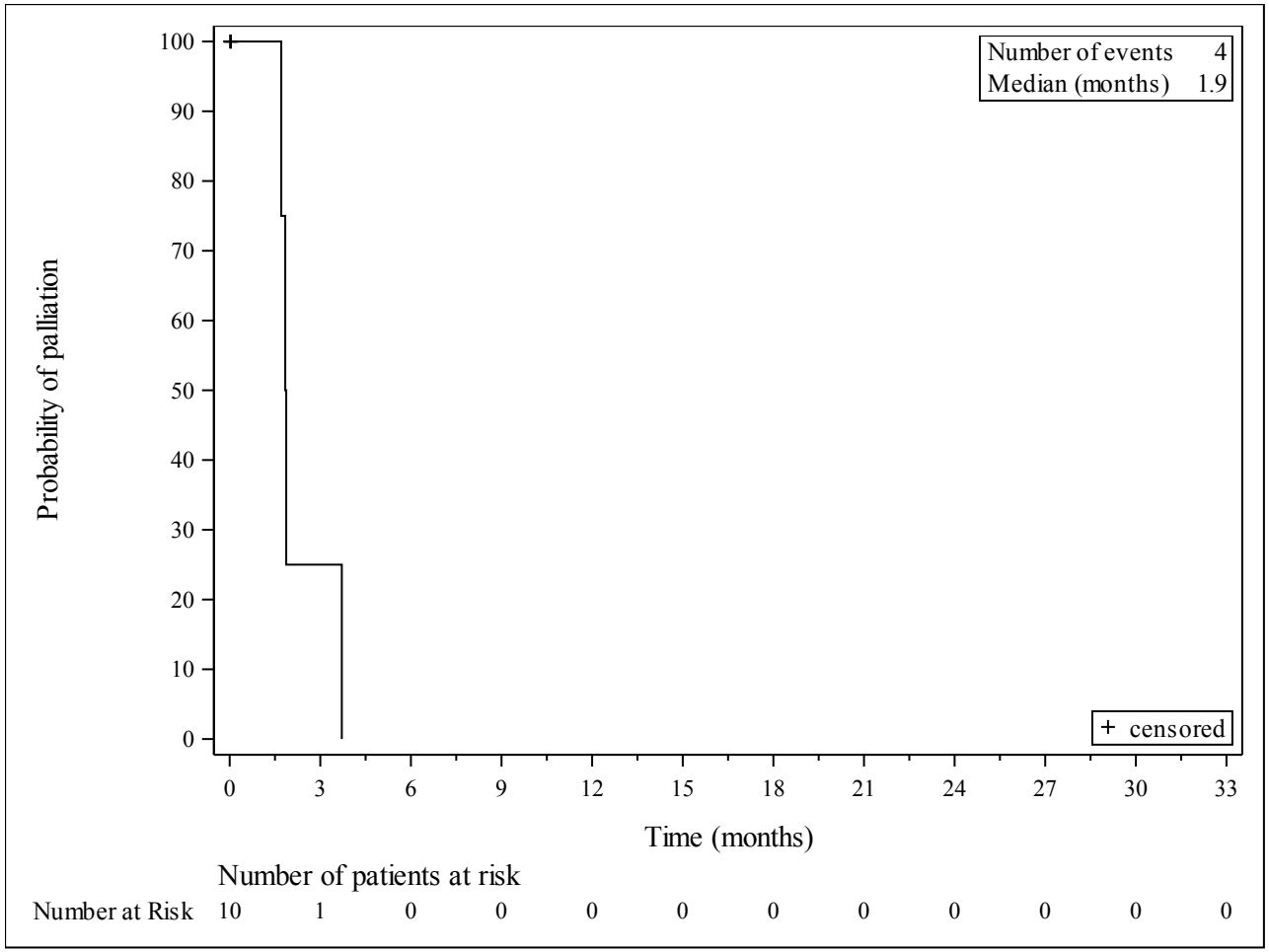
Time to pain palliation was defined as the time from the first dose of study drug until the date of the first observed pain palliation. Patients with no pain palliation were censored at the date of the last available PRO assessment.
[a] For asymptomatic patients with a pain intensity score < 2 pts AND an analgesic score >=2 pts at baseline, pain palliation is defined as a stable (or reduced) pain intensity score AND a decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. For symptomatic patients with a pain score >=2 points at baseline; the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. Note: Children, ages 8 to 18 years at enrolment completed self-report measures of NRS-11. Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpainplsub.sas smpainplsubd.rtf 20MAY2021:16:32 icesas184PD

Figure 2.3.5.2.4 Kaplan-Meier plot for time to pain palliation - NRS-11 target tumour pain - PN statuts at enrol. = Non-progressive
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018
Including symptomatic and asymptomatic patients - Using threshold of 2 points [a]
N = 11



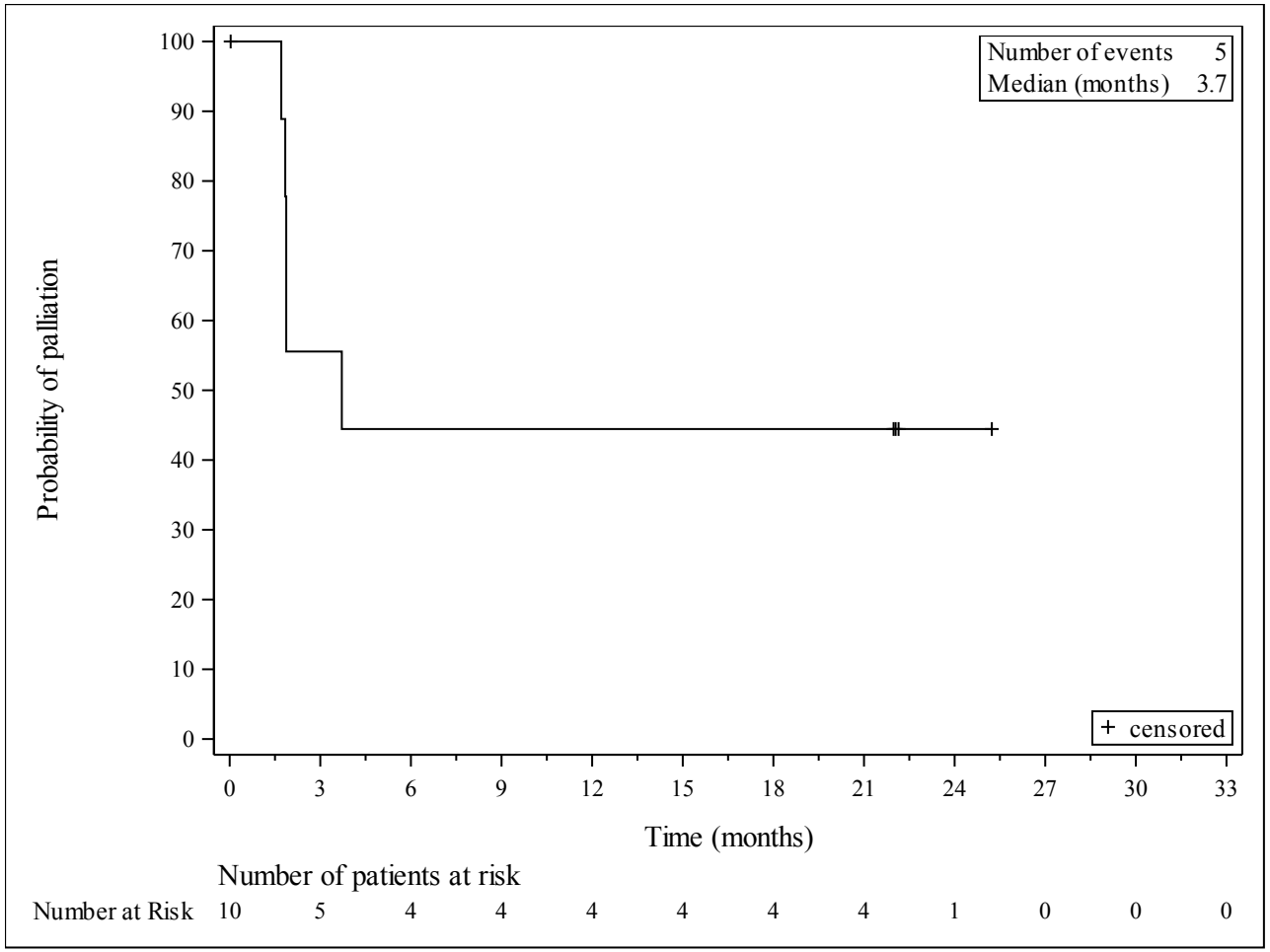
Time to pain palliation was defined as the time from the first dose of study drug until the date of the first observed pain palliation. Patients with no pain palliation were censored at the date of the last available PRO assessment.
[a] For asymptomatic patients with a pain intensity score < 2 pts AND an analgesic score >=2 pts at baseline, pain palliation is defined as a stable (or reduced) pain intensity score AND a decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. For symptomatic patients with a pain score >=2 points at baseline; the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. Note: Children, ages 8 to 18 years at enrolment completed self-report measures of NRS-11. Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpainplsub.sas smpainplsubd.rtf 20MAY2021:16:32 icesas184PD

Figure 2.3.5.2.5 Kaplan-Meier plot for time to pain palliation - NRS-11 target tumour pain - PN statuts at enrol. = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018
Including only symptomatic patients - Using threshold of 2 points [a]
N = 12



Time to pain palliation was defined as the time from the first dose of study drug until the date of the first observed pain palliation. Patients with no pain palliation were censored at the date of the last available PRO assessment.
[a] For asymptomatic patients with a pain intensity score < 2 pts AND an analgesic score >=2 pts at baseline, pain palliation is defined as a stable (or reduced) pain intensity score AND a decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. For symptomatic patients with a pain score >=2 points at baseline; the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. Note: Children, ages 8 to 18 years at enrolment completed self-report measures of NRS-11. Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpainplsub.sas smpainplsube.rtf 20MAY2021:16:33 icesas184PD

Figure 2.3.5.2.5 Kaplan-Meier plot for time to pain palliation - NRS-11 target tumour pain - PN statuts at enrol. = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018
Including symptomatic and asymptomatic patients - Using threshold of 2 points [a]
N = 12



Time to pain palliation was defined as the time from the first dose of study drug until the date of the first observed pain palliation. Patients with no pain palliation were censored at the date of the last available PRO assessment.
[a] For asymptomatic patients with a pain intensity score < 2 pts AND an analgesic score >=2 pts at baseline, pain palliation is defined as a stable (or reduced) pain intensity score AND a decrease of at least 1 level in the analgesic score category. For symptomatic patients with a pain score >=2 points at baseline, the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. For symptomatic patients with a pain score >=2 points at baseline; the definition of pain palliation is a decrease of >=2 points NRS-11 scale without increased analgesic use. Note: Children, ages 8 to 18 years at enrolment completed self-report measures of NRS-11. Patients having their baseline evaluation using an earlier version of the NRS-11, which did not yet include the target tumour item, were considered only if self-selected and target PN were the same.
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpainplsub.sas smpainplsube.rtf 20MAY2021:16:33 icesas184PD

Table 2.4.1 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=33) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 5 (N=30)	Categories of change [d]			
		Improvement	1	3,3	0,1, 17,2
		No improvement	29	96,7	82,8, 99,9
	Pre-cycle 9 (N=29)	Categories of change [d]			
		Improvement	1	3,4	0,1, 17,8
		No improvement	28	96,6	82,2, 99,9
	Pre-cycle 13 (N=27)	Categories of change [d]			
		Improvement	1	3,7	0,1, 19,0
		No improvement	26	96,3	81,0, 99,9
	Pre-cycle 25 (N=20)	Categories of change [d]			
		Improvement	1	5,0	0,1, 24,9
		No improvement	19	95,0	75,1, 99,9
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=30)	Categories of change [d]			
		Improvement	1	3,3	0,1, 17,2
		No improvement	29	96,7	82,8, 99,9

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.1 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=33) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Lower	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	1	8,3	0,2, 38,5
		No improvement	11	91,7	61,5, 99,8
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	1	8,3	0,2, 38,5
		No improvement	11	91,7	61,5, 99,8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Overall (N=12)	Categories of change [d]			
		Improvement	1	8,3	0,2, 38,5
		No improvement	11	91,7	61,5, 99,8

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.1 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=33) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Upper	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	0	0	0, 28,5
		No improvement	11	100	71,5, 100
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	0	0	0, 28,5
		No improvement	11	100	71,5, 100
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	0	0	0, 28,5
		No improvement	11	100	71,5, 100
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	0	0	0, 33,6
		No improvement	9	100	66,4, 100
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=11)	Categories of change [d]			
		Improvement	0	0	0, 28,5
		No improvement	11	100	71,5, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.1 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=33) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral Lower	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.1 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=33) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral Upper	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100
	Pre-cycle 9 (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100
	Pre-cycle 13 (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100
	Pre-cycle 25 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Overall (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.2.1.1 Motor function primary outcome scores and change from baseline over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=19) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Strength MMT - Total	Baseline (n=17)	4,18	0,777	4,16	1,8	5,0	10,5							
	Pre-cycle 5 (n=16)	4,30	0,788	4,54	2,0	5,0	15,8	16	0,17	0,403	0,06	-0,3	1,4	15,8
	Pre-cycle 9 (n=15)	4,20	0,753	4,52	2,2	5,0	21,1	15	0,05	0,578	0,12	-1,7	1,0	21,1
	Pre-cycle 13 (n=15)	4,39	0,768	4,61	2,1	5,0	21,1	15	0,25	0,309	0,25	-0,3	0,9	21,1
	Pre-cycle 25 (n=10)	4,40	0,880	4,67	2,1	5,0	47,4	10	0,26	0,387	0,25	-0,3	1,1	47,4
	Pre-cycle 37 (n=1)	NC	NC	NC	5,0	5,0	94,7	1	NC	NC	NC	0,3	0,3	94,7
Strength MMT - Unilateral Lower	Baseline (n=4)	3,79	0,256	3,72	3,6	4,2	78,9							
	Pre-cycle 5 (n=4)	4,27	0,672	4,33	3,4	5,0	78,9	4	0,48	0,713	0,38	-0,3	1,4	78,9
	Pre-cycle 9 (n=4)	4,18	0,432	4,19	3,8	4,6	78,9	4	0,39	0,441	0,24	0,1	1,0	78,9
	Pre-cycle 13 (n=4)	4,37	0,409	4,31	4,0	4,9	78,9	4	0,59	0,314	0,57	0,3	0,9	78,9
	Pre-cycle 25 (n=2)	NC	NC	NC	4,4	4,6	89,5	2	NC	NC	NC	0,7	1,1	89,5
Strength MMT - Unilateral Upper	Baseline (n=6)	4,11	1,132	4,60	1,8	4,8	68,4							
	Pre-cycle 5 (n=6)	4,19	1,105	4,56	2,0	4,9	68,4	6	0,08	0,244	0,04	-0,2	0,5	68,4
	Pre-cycle 9 (n=6)	4,24	1,006	4,62	2,2	4,9	68,4	6	0,13	0,254	0,11	-0,2	0,5	68,4
	Pre-cycle 13 (n=6)	4,31	1,093	4,64	2,1	5,0	68,4	6	0,21	0,200	0,27	-0,1	0,5	68,4
	Pre-cycle 25 (n=5)	4,22	1,209	4,71	2,1	5,0	73,7	5	0,12	0,256	0,25	-0,3	0,3	73,7
	Pre-cycle 37 (n=1)	NC	NC	NC	5,0	5,0	94,7	1	NC	NC	NC	0,3	0,3	94,7
Strength MMT - Bilateral Lower	Baseline (n=1)	NC	NC	NC	4,7	4,7	94,7							
	Pre-cycle 5 (n=1)	NC	NC	NC	4,9	4,9	94,7	1	NC	NC	NC	0,2	0,2	94,7
	Pre-cycle 9 (n=1)	NC	NC	NC	4,9	4,9	94,7	1	NC	NC	NC	0,2	0,2	94,7
	Pre-cycle 13 (n=1)	NC	NC	NC	4,9	4,9	94,7	1	NC	NC	NC	0,2	0,2	94,7
Strength MMT - Bilateral Upper	Baseline (n=6)	4,41	0,599	4,41	3,7	5,0	68,4							
	Pre-cycle 5 (n=5)	4,35	0,596	3,96	3,9	5,0	73,7	5	0,02	0,146	0,00	-0,1	0,3	73,7
	Pre-cycle 9 (n=4)	3,97	0,733	3,81	3,3	5,0	78,9	4	-0,44	0,872	-0,08	-1,7	0,1	78,9
	Pre-cycle 13 (n=4)	4,40	0,699	4,43	3,7	5,0	78,9	4	-0,01	0,183	0,00	-0,3	0,2	78,9
	Pre-cycle 25 (n=3)	4,62	0,615	4,96	3,9	5,0	84,2	3	0,07	0,155	0,00	0,0	0,2	84,2

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
MMT - Manual muscle test. NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.4.2.1.1 Motor function primary outcome scores and change from baseline over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=19) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Range of motion (degrees) - Total	Baseline (n=19)	980,53	473,646	886,00	345,0	1853,0	0,0							
	Pre-cycle 5 (n=15)	1001,73	483,907	958,00	416,0	1920,0	21,1	15	98,33	121,596	57,00	-40,0	384,0	21,1
	Pre-cycle 9 (n=15)	1051,73	497,875	985,00	393,0	1892,0	21,1	15	103,73	123,500	61,00	-25,0	401,0	21,1
	Pre-cycle 13 (n=15)	1000,27	487,621	968,00	355,0	1895,0	21,1	15	101,93	111,696	78,00	-15,0	351,0	21,1
	Pre-cycle 25 (n=10)	1124,70	538,096	1000,00	356,0	1916,0	47,4	10	112,70	124,889	51,00	-4,0	351,0	47,4
	Pre-cycle 37 (n=1)	NC	NC	NC	969,0	969,0	94,7	1	NC	NC	NC	320,0	320,0	94,7
Range of motion (degrees) - Unilateral Lower	Baseline (n=4)	407,75	64,422	407,50	345,0	471,0	78,9							
	Pre-cycle 5 (n=4)	450,75	36,207	446,00	416,0	495,0	78,9	4	43,00	79,708	25,00	-28,0	150,0	78,9
	Pre-cycle 9 (n=4)	437,75	35,743	440,00	393,0	478,0	78,9	4	30,00	55,341	20,00	-25,0	105,0	78,9
	Pre-cycle 13 (n=4)	444,75	60,196	470,00	355,0	484,0	78,9	4	37,00	59,352	14,00	-5,0	125,0	78,9
	Pre-cycle 25 (n=2)	NC	NC	NC	356,0	502,0	89,5	2	NC	NC	NC	-4,0	31,0	89,5
Range of motion (degrees) - Unilateral Upper	Baseline (n=6)	784,33	81,419	785,00	649,0	890,0	68,4							
	Pre-cycle 5 (n=5)	905,00	89,591	941,00	760,0	985,0	73,7	5	117,80	129,324	120,00	-40,0	309,0	73,7
	Pre-cycle 9 (n=4)	955,00	48,194	960,00	897,0	1003,0	78,9	4	171,00	121,576	151,50	45,0	336,0	78,9
	Pre-cycle 13 (n=5)	926,80	88,638	968,00	785,0	1006,0	73,7	5	139,60	126,611	137,00	-15,0	328,0	73,7
	Pre-cycle 25 (n=4)	931,25	94,373	962,50	800,0	1000,0	78,9	4	137,50	158,847	99,50	0,0	351,0	78,9
	Pre-cycle 37 (n=1)	NC	NC	NC	969,0	969,0	94,7	1	NC	NC	NC	320,0	320,0	94,7
Range of motion (degrees) - Bilateral Lower	Baseline (n=1)	NC	NC	NC	908,0	908,0	94,7							
	Pre-cycle 5 (n=1)	NC	NC	NC	965,0	965,0	94,7	1	NC	NC	NC	57,0	57,0	94,7
	Pre-cycle 9 (n=1)	NC	NC	NC	969,0	969,0	94,7	1	NC	NC	NC	61,0	61,0	94,7
	Pre-cycle 13 (n=1)	NC	NC	NC	921,0	921,0	94,7	1	NC	NC	NC	13,0	13,0	94,7
Range of motion (degrees) - Bilateral Upper	Baseline (n=8)	1423,13	353,934	1464,50	886,0	1853,0	57,9							
	Pre-cycle 5 (n=5)	1546,60	351,930	1558,00	1070,0	1920,0	73,7	5	131,40	157,893	67,00	9,0	384,0	73,7
	Pre-cycle 9 (n=6)	1539,33	310,102	1546,50	1054,0	1892,0	68,4	6	115,17	153,328	60,00	-2,0	401,0	68,4
	Pre-cycle 13 (n=5)	1534,00	385,525	1580,00	998,0	1895,0	73,7	5	134,00	125,465	111,00	42,0	351,0	73,7
	Pre-cycle 25 (n=4)	1666,00	304,873	1748,50	1251,0	1916,0	78,9	4	137,50	114,695	109,50	39,0	292,0	78,9

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
MMT - Manual muscle test. NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.4.2.1.2 Motor function primary outcome scores and change from baseline over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Strength MMT - Total	Baseline (n=14)	4,54	0,427	4,65	3,6	5,0	0,0							
	Pre-cycle 5 (n=14)	4,59	0,376	4,60	3,6	5,0	0,0	14	0,05	0,196	0,00	-0,3	0,4	0,0
	Pre-cycle 9 (n=14)	4,72	0,378	4,91	3,7	5,0	0,0	14	0,18	0,221	0,18	-0,2	0,6	0,0
	Pre-cycle 13 (n=12)	4,76	0,254	4,81	4,1	5,0	14,3	12	0,18	0,195	0,19	-0,3	0,4	14,3
	Pre-cycle 25 (n=10)	4,74	0,304	4,82	4,1	5,0	28,6	10	0,20	0,272	0,28	-0,4	0,6	28,6
Strength MMT - Unilateral Lower	Baseline (n=8)	4,56	0,470	4,68	3,6	5,0	42,9							
	Pre-cycle 5 (n=8)	4,58	0,450	4,67	3,6	5,0	42,9	8	0,03	0,217	0,00	-0,3	0,4	42,9
	Pre-cycle 9 (n=8)	4,70	0,423	4,82	3,7	5,0	42,9	8	0,14	0,281	0,09	-0,2	0,6	42,9
	Pre-cycle 13 (n=6)	4,76	0,183	4,76	4,6	5,0	57,1	6	0,10	0,222	0,13	-0,3	0,3	57,1
	Pre-cycle 25 (n=5)	4,75	0,258	4,77	4,4	5,0	64,3	5	0,15	0,370	0,22	-0,4	0,6	64,3
Strength MMT - Unilateral Upper	Baseline (n=5)	4,46	0,420	4,59	3,7	4,8	64,3							
	Pre-cycle 5 (n=5)	4,53	0,265	4,59	4,1	4,8	64,3	5	0,07	0,201	0,00	-0,1	0,4	64,3
	Pre-cycle 9 (n=5)	4,72	0,370	4,91	4,1	5,0	64,3	5	0,26	0,096	0,21	0,2	0,4	64,3
	Pre-cycle 13 (n=5)	4,73	0,354	4,84	4,1	5,0	64,3	5	0,28	0,148	0,34	0,1	0,4	64,3
	Pre-cycle 25 (n=4)	4,68	0,411	4,82	4,1	5,0	71,4	4	0,30	0,143	0,34	0,1	0,4	71,4
Strength MMT - Bilateral Upper	Baseline (n=1)	NC	NC	NC	4,8	4,8	92,9							
	Pre-cycle 5 (n=1)	NC	NC	NC	4,9	4,9	92,9	1	NC	NC	NC	0,1	0,1	92,9
	Pre-cycle 9 (n=1)	NC	NC	NC	5,0	5,0	92,9	1	NC	NC	NC	0,1	0,1	92,9
	Pre-cycle 13 (n=1)	NC	NC	NC	5,0	5,0	92,9	1	NC	NC	NC	0,1	0,1	92,9
	Pre-cycle 25 (n=1)	NC	NC	NC	5,0	5,0	92,9	1	NC	NC	NC	0,1	0,1	92,9

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
MMT - Manual muscle test. NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.4.2.1.2 Motor function primary outcome scores and change from baseline over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Range of motion (degrees) - Total	Baseline (n=14)	669,86	279,643	520,00	455,0	1445,0	0,0							
	Pre-cycle 5 (n=13)	701,85	329,096	528,00	445,0	1616,0	7,1	13	23,92	48,188	9,00	-11,0	171,0	7,1
	Pre-cycle 9 (n=14)	700,29	311,742	517,00	475,0	1608,0	0,0	14	30,43	75,320	17,50	-54,0	229,0	0,0
	Pre-cycle 13 (n=11)	721,09	335,042	529,00	470,0	1584,0	21,4	11	39,27	84,281	23,00	-73,0	241,0	21,4
	Pre-cycle 25 (n=10)	752,70	341,334	666,00	465,0	1580,0	28,6	10	48,40	78,056	22,50	-10,0	237,0	28,6
Range of motion (degrees) - Unilateral Lower	Baseline (n=8)	491,50	25,674	497,00	455,0	530,0	42,9							
	Pre-cycle 5 (n=8)	499,88	30,116	501,00	445,0	542,0	42,9	8	8,38	18,134	4,50	-10,0	44,0	42,9
	Pre-cycle 9 (n=8)	498,63	17,079	505,00	475,0	519,0	42,9	8	7,13	18,856	12,50	-26,0	32,0	42,9
	Pre-cycle 13 (n=6)	497,83	23,181	496,50	470,0	529,0	57,1	6	10,50	23,158	17,50	-36,0	26,0	57,1
	Pre-cycle 25 (n=5)	504,60	26,931	519,00	465,0	530,0	64,3	5	11,20	15,975	10,00	-10,0	34,0	64,3
Range of motion (degrees) - Unilateral Upper	Baseline (n=5)	800,20	133,887	869,00	565,0	881,0	64,3							
	Pre-cycle 5 (n=4)	877,25	52,347	887,50	805,0	929,0	71,4	4	18,25	24,958	18,00	-11,0	48,0	71,4
	Pre-cycle 9 (n=5)	841,40	55,873	816,00	794,0	914,0	64,3	5	41,20	110,409	19,00	-54,0	229,0	64,3
	Pre-cycle 13 (n=4)	840,25	80,363	852,50	743,0	913,0	71,4	4	57,50	131,794	31,00	-73,0	241,0	71,4
	Pre-cycle 25 (n=4)	856,00	60,006	852,50	802,0	917,0	71,4	4	73,25	110,943	32,50	-9,0	237,0	71,4
Range of motion (degrees) - Bilateral Upper	Baseline (n=1)	NC	NC	NC	1445,0	1445,0	92,9							
	Pre-cycle 5 (n=1)	NC	NC	NC	1616,0	1616,0	92,9	1	NC	NC	NC	171,0	171,0	92,9
	Pre-cycle 9 (n=1)	NC	NC	NC	1608,0	1608,0	92,9	1	NC	NC	NC	163,0	163,0	92,9
	Pre-cycle 13 (n=1)	NC	NC	NC	1584,0	1584,0	92,9	1	NC	NC	NC	139,0	139,0	92,9
	Pre-cycle 25 (n=1)	NC	NC	NC	1580,0	1580,0	92,9	1	NC	NC	NC	135,0	135,0	92,9

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
MMT - Manual muscle test. NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.4.2.1.3 Motor function primary outcome scores and change from baseline over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Strength MMT - Total	Baseline (n=11)	4,41	0,472	4,63	3,6	4,9	0,0							
	Pre-cycle 5 (n=11)	4,67	0,251	4,66	4,1	5,0	0,0	11	0,26	0,463	0,18	-0,3	1,4	0,0
	Pre-cycle 9 (n=11)	4,62	0,293	4,63	3,9	4,9	0,0	11	0,21	0,340	0,16	-0,2	1,0	0,0
	Pre-cycle 13 (n=10)	4,66	0,299	4,64	4,0	5,0	9,1	10	0,30	0,349	0,28	-0,3	0,9	9,1
	Pre-cycle 25 (n=5)	4,67	0,216	4,62	4,4	5,0	54,5	5	0,28	0,527	0,30	-0,4	1,1	54,5
	Pre-cycle 37 (n=1)	NC	NC	NC	5,0	5,0	90,9	1	NC	NC	NC	0,3	0,3	90,9
Strength MMT - Unilateral Lower	Baseline (n=7)	4,33	0,561	4,24	3,6	4,9	36,4							
	Pre-cycle 5 (n=7)	4,63	0,293	4,59	4,1	5,0	36,4	7	0,30	0,567	0,28	-0,3	1,4	36,4
	Pre-cycle 9 (n=7)	4,55	0,333	4,59	3,9	4,9	36,4	7	0,21	0,418	0,12	-0,2	1,0	36,4
	Pre-cycle 13 (n=6)	4,57	0,337	4,56	4,0	4,9	45,5	6	0,34	0,443	0,28	-0,3	0,9	45,5
	Pre-cycle 25 (n=3)	4,54	0,113	4,59	4,4	4,6	72,7	3	0,34	0,730	0,35	-0,4	1,1	72,7
Strength MMT - Unilateral Upper	Baseline (n=3)	4,49	0,298	4,63	4,2	4,7	72,7							
	Pre-cycle 5 (n=3)	4,69	0,171	4,66	4,5	4,9	72,7	3	0,20	0,298	0,18	-0,1	0,5	72,7
	Pre-cycle 9 (n=3)	4,72	0,170	4,63	4,6	4,9	72,7	3	0,23	0,232	0,21	0,0	0,5	72,7
	Pre-cycle 13 (n=3)	4,76	0,211	4,66	4,6	5,0	72,7	3	0,27	0,214	0,30	0,0	0,5	72,7
	Pre-cycle 25 (n=2)	NC	NC	NC	4,7	5,0	81,8	2	NC	NC	NC	0,1	0,3	81,8
	Pre-cycle 37 (n=1)	NC	NC	NC	5,0	5,0	90,9	1	NC	NC	NC	0,3	0,3	90,9
Strength MMT - Bilateral Lower	Baseline (n=1)	NC	NC	NC	4,7	4,7	90,9							
	Pre-cycle 5 (n=1)	NC	NC	NC	4,9	4,9	90,9	1	NC	NC	NC	0,2	0,2	90,9
	Pre-cycle 9 (n=1)	NC	NC	NC	4,9	4,9	90,9	1	NC	NC	NC	0,2	0,2	90,9
	Pre-cycle 13 (n=1)	NC	NC	NC	4,9	4,9	90,9	1	NC	NC	NC	0,2	0,2	90,9

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
MMT - Manual muscle test. NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.4.2.1.3 Motor function primary outcome scores and change from baseline over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Range of motion (degrees) - Total	Baseline (n=11)	584,82	189,346	498,00	345,0	908,0	0,0							
	Pre-cycle 5 (n=11)	650,36	229,312	510,00	427,0	965,0	0,0	11	65,55	97,194	44,00	-28,0	309,0	0,0
	Pre-cycle 9 (n=11)	648,45	238,460	507,00	430,0	985,0	0,0	11	63,64	102,504	19,00	-25,0	336,0	0,0
	Pre-cycle 13 (n=10)	671,20	234,032	524,00	470,0	977,0	9,1	10	77,70	99,899	24,50	13,0	328,0	9,1
	Pre-cycle 25 (n=5)	695,20	245,650	530,00	502,0	1000,0	54,5	5	93,40	144,206	34,00	16,0	351,0	54,5
	Pre-cycle 37 (n=1)	NC	NC	NC	969,0	969,0	90,9	1	NC	NC	NC	320,0	320,0	90,9
Range of motion (degrees) - Unilateral Lower	Baseline (n=7)	460,71	54,720	471,00	345,0	503,0	36,4							
	Pre-cycle 5 (n=7)	487,00	35,889	488,00	427,0	542,0	36,4	7	26,29	59,382	7,00	-28,0	150,0	36,4
	Pre-cycle 9 (n=7)	478,14	30,808	478,00	430,0	519,0	36,4	7	17,43	41,537	9,00	-25,0	105,0	36,4
	Pre-cycle 13 (n=6)	491,33	26,013	480,00	470,0	529,0	45,5	6	36,83	43,462	21,00	13,0	125,0	45,5
	Pre-cycle 25 (n=3)	517,00	14,107	519,00	502,0	530,0	72,7	3	27,00	9,644	31,00	16,0	34,0	72,7
Range of motion (degrees) - Unilateral Upper	Baseline (n=3)	766,67	120,600	761,00	649,0	890,0	72,7							
	Pre-cycle 5 (n=3)	926,67	40,452	941,00	881,0	958,0	72,7	3	160,00	133,570	120,00	51,0	309,0	72,7
	Pre-cycle 9 (n=3)	939,00	44,136	935,00	897,0	985,0	72,7	3	172,33	148,863	136,00	45,0	336,0	72,7
	Pre-cycle 13 (n=3)	947,67	43,247	968,00	898,0	977,0	72,7	3	181,00	130,679	137,00	78,0	328,0	72,7
	Pre-cycle 25 (n=2)	NC	NC	NC	925,0	1000,0	81,8	2	NC	NC	NC	35,0	351,0	81,8
	Pre-cycle 37 (n=1)	NC	NC	NC	969,0	969,0	90,9	1	NC	NC	NC	320,0	320,0	90,9
Range of motion (degrees) - Bilateral Lower	Baseline (n=1)	NC	NC	NC	908,0	908,0	90,9							
	Pre-cycle 5 (n=1)	NC	NC	NC	965,0	965,0	90,9	1	NC	NC	NC	57,0	57,0	90,9
	Pre-cycle 9 (n=1)	NC	NC	NC	969,0	969,0	90,9	1	NC	NC	NC	61,0	61,0	90,9
	Pre-cycle 13 (n=1)	NC	NC	NC	921,0	921,0	90,9	1	NC	NC	NC	13,0	13,0	90,9

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
MMT - Manual muscle test. NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.4.2.1.4 Motor function primary outcome scores and change from baseline over time - PN status at enrollm. = Non-progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Strength MMT - Total	Baseline (n=10)	4,24	0,950	4,56	1,8	5,0	9,1							
	Pre-cycle 5 (n=10)	4,28	0,936	4,56	2,0	5,0	9,1	10	0,03	0,142	0,00	-0,2	0,4	9,1
	Pre-cycle 9 (n=9)	4,44	0,934	4,91	2,2	5,0	18,2	9	0,17	0,254	0,14	-0,2	0,6	18,2
	Pre-cycle 13 (n=8)	4,49	0,971	4,78	2,1	5,0	27,3	8	0,13	0,155	0,15	-0,1	0,3	27,3
	Pre-cycle 25 (n=8)	4,49	0,990	4,90	2,1	5,0	27,3	8	0,14	0,259	0,15	-0,3	0,6	27,3
Strength MMT - Unilateral Lower	Baseline (n=4)	4,39	0,584	4,49	3,6	5,0	63,6							
	Pre-cycle 5 (n=4)	4,47	0,639	4,67	3,6	5,0	63,6	4	0,08	0,188	0,00	0,0	0,4	63,6
	Pre-cycle 9 (n=4)	4,69	0,628	5,00	3,7	5,0	63,6	4	0,29	0,266	0,30	0,0	0,6	63,6
	Pre-cycle 13 (n=3)	4,84	0,142	4,77	4,7	5,0	72,7	3	0,18	0,162	0,22	0,0	0,3	72,7
	Pre-cycle 25 (n=3)	4,92	0,135	5,00	4,8	5,0	72,7	3	0,26	0,288	0,22	0,0	0,6	72,7
Strength MMT - Unilateral Upper	Baseline (n=4)	3,97	1,423	4,64	1,8	4,8	63,6							
	Pre-cycle 5 (n=4)	3,98	1,358	4,56	2,0	4,8	63,6	4	0,01	0,140	0,04	-0,2	0,1	63,6
	Pre-cycle 9 (n=4)	4,05	1,243	4,54	2,2	4,9	63,6	4	0,08	0,248	0,06	-0,2	0,4	63,6
	Pre-cycle 13 (n=4)	4,10	1,333	4,64	2,1	5,0	63,6	4	0,13	0,175	0,16	-0,1	0,3	63,6
	Pre-cycle 25 (n=4)	4,05	1,319	4,53	2,1	5,0	63,6	4	0,08	0,273	0,17	-0,3	0,3	63,6
Strength MMT - Bilateral Upper	Baseline (n=2)	NC	NC	NC	4,0	5,0	81,8							
	Pre-cycle 5 (n=2)	NC	NC	NC	4,0	5,0	81,8	2	NC	NC	NC	0,0	0,0	81,8
	Pre-cycle 9 (n=1)	NC	NC	NC	5,0	5,0	90,9	1	NC	NC	NC	0,0	0,0	90,9
	Pre-cycle 13 (n=1)	NC	NC	NC	5,0	5,0	90,9	1	NC	NC	NC	0,0	0,0	90,9
	Pre-cycle 25 (n=1)	NC	NC	NC	5,0	5,0	90,9	1	NC	NC	NC	0,0	0,0	90,9

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
MMT - Manual muscle test. NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.4.2.1.4 Motor function primary outcome scores and change from baseline over time - PN status at enrollm. = Non-progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Range of motion (degrees) - Total	Baseline (n=11)	857,91	421,563	800,00	455,0	1833,0	0,0							
	Pre-cycle 5 (n=9)	870,67	469,834	760,00	445,0	1842,0	18,2	9	61,00	132,449	9,00	-40,0	384,0	18,2
	Pre-cycle 9 (n=8)	889,25	498,620	714,50	475,0	1837,0	27,3	8	78,38	142,814	26,00	-26,0	401,0	27,3
	Pre-cycle 13 (n=8)	920,50	489,033	849,00	470,0	1887,0	27,3	8	73,38	128,158	24,00	-36,0	351,0	27,3
	Pre-cycle 25 (n=8)	914,25	476,474	858,50	465,0	1872,0	27,3	8	67,13	106,346	23,00	-10,0	292,0	27,3
Range of motion (degrees) - Unilateral Lower	Baseline (n=4)	494,50	32,624	496,50	455,0	530,0	63,6							
	Pre-cycle 5 (n=4)	494,25	35,985	502,00	445,0	528,0	63,6	4	-0,25	7,932	0,00	-10,0	9,0	63,6
	Pre-cycle 9 (n=4)	500,00	17,340	505,00	475,0	515,0	63,6	4	5,50	25,788	8,00	-26,0	32,0	63,6
	Pre-cycle 13 (n=3)	487,67	15,503	494,00	470,0	499,0	72,7	3	-1,67	29,738	15,00	-36,0	16,0	72,7
	Pre-cycle 25 (n=3)	491,33	27,574	489,00	465,0	520,0	72,7	3	2,00	10,583	6,00	-10,0	10,0	72,7
Range of motion (degrees) - Unilateral Upper	Baseline (n=4)	821,75	47,836	818,00	770,0	881,0	63,6							
	Pre-cycle 5 (n=3)	891,33	117,134	929,00	760,0	985,0	72,7	3	52,33	94,574	48,00	-40,0	149,0	72,7
	Pre-cycle 9 (n=2)	NC	NC	NC	914,0	1003,0	81,8	2	NC	NC	NC	33,0	167,0	81,8
	Pre-cycle 13 (n=3)	901,33	110,961	913,00	785,0	1006,0	72,7	3	62,33	96,158	32,00	-15,0	170,0	72,7
	Pre-cycle 25 (n=3)	905,67	100,481	917,00	800,0	1000,0	72,7	3	66,67	86,194	36,00	0,0	164,0	72,7
Range of motion (degrees) - Bilateral Upper	Baseline (n=3)	1390,67	437,098	1380,00	959,0	1833,0	72,7							
	Pre-cycle 5 (n=2)	NC	NC	NC	1343,0	1842,0	81,8	2	NC	NC	NC	9,0	384,0	81,8
	Pre-cycle 9 (n=2)	NC	NC	NC	1360,0	1837,0	81,8	2	NC	NC	NC	4,0	401,0	81,8
	Pre-cycle 13 (n=2)	NC	NC	NC	1310,0	1887,0	81,8	2	NC	NC	NC	54,0	351,0	81,8
	Pre-cycle 25 (n=2)	NC	NC	NC	1251,0	1872,0	81,8	2	NC	NC	NC	39,0	292,0	81,8

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
MMT - Manual muscle test. NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.4.2.1.5 Motor function primary outcome scores and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Strength MMT - Total	Baseline (n=10)	4,36	0,532	4,54	3,7	5,0	9,1							
	Pre-cycle 5 (n=9)	4,32	0,530	4,48	3,4	5,0	18,2	9	0,02	0,207	0,00	-0,3	0,4	18,2
	Pre-cycle 9 (n=9)	4,25	0,640	4,08	3,3	5,0	18,2	9	-0,05	0,650	0,13	-1,7	0,4	18,2
	Pre-cycle 13 (n=9)	4,50	0,536	4,84	3,7	5,0	18,2	9	0,20	0,222	0,20	-0,3	0,4	18,2
	Pre-cycle 25 (n=7)	4,59	0,457	4,84	3,9	5,0	36,4	7	0,30	0,234	0,34	0,0	0,7	36,4
Strength MMT - Unilateral Lower	Baseline (n=1)	NC	NC	NC	3,7	3,7	90,9							
	Pre-cycle 5 (n=1)	NC	NC	NC	3,4	3,4	90,9	1	NC	NC	NC	-0,3	-0,3	90,9
	Pre-cycle 9 (n=1)	NC	NC	NC	3,8	3,8	90,9	1	NC	NC	NC	0,1	0,1	90,9
	Pre-cycle 13 (n=1)	NC	NC	NC	4,1	4,1	90,9	1	NC	NC	NC	0,4	0,4	90,9
	Pre-cycle 25 (n=1)	NC	NC	NC	4,4	4,4	90,9	1	NC	NC	NC	0,7	0,7	90,9
Strength MMT - Unilateral Upper	Baseline (n=4)	4,39	0,456	4,54	3,7	4,8	63,6							
	Pre-cycle 5 (n=4)	4,45	0,231	4,53	4,1	4,6	63,6	4	0,06	0,229	-0,01	-0,1	0,4	63,6
	Pre-cycle 9 (n=4)	4,67	0,408	4,81	4,1	5,0	63,6	4	0,28	0,104	0,28	0,2	0,4	63,6
	Pre-cycle 13 (n=4)	4,72	0,408	4,88	4,1	5,0	63,6	4	0,33	0,113	0,36	0,2	0,4	63,6
	Pre-cycle 25 (n=3)	4,64	0,494	4,84	4,1	5,0	72,7	3	0,37	0,040	0,35	0,3	0,4	72,7
Strength MMT - Bilateral Upper	Baseline (n=5)	4,46	0,598	4,83	3,7	5,0	54,5							
	Pre-cycle 5 (n=4)	4,43	0,620	4,43	3,9	5,0	63,6	4	0,06	0,164	0,05	-0,1	0,3	63,6
	Pre-cycle 9 (n=4)	3,96	0,709	3,81	3,3	5,0	63,6	4	-0,41	0,894	-0,01	-1,7	0,1	63,6
	Pre-cycle 13 (n=4)	4,38	0,685	4,41	3,7	5,0	63,6	4	0,02	0,196	0,06	-0,3	0,2	63,6
	Pre-cycle 25 (n=3)	4,61	0,600	4,95	3,9	5,0	72,7	3	0,11	0,144	0,12	0,0	0,2	72,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
MMT - Manual muscle test. NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

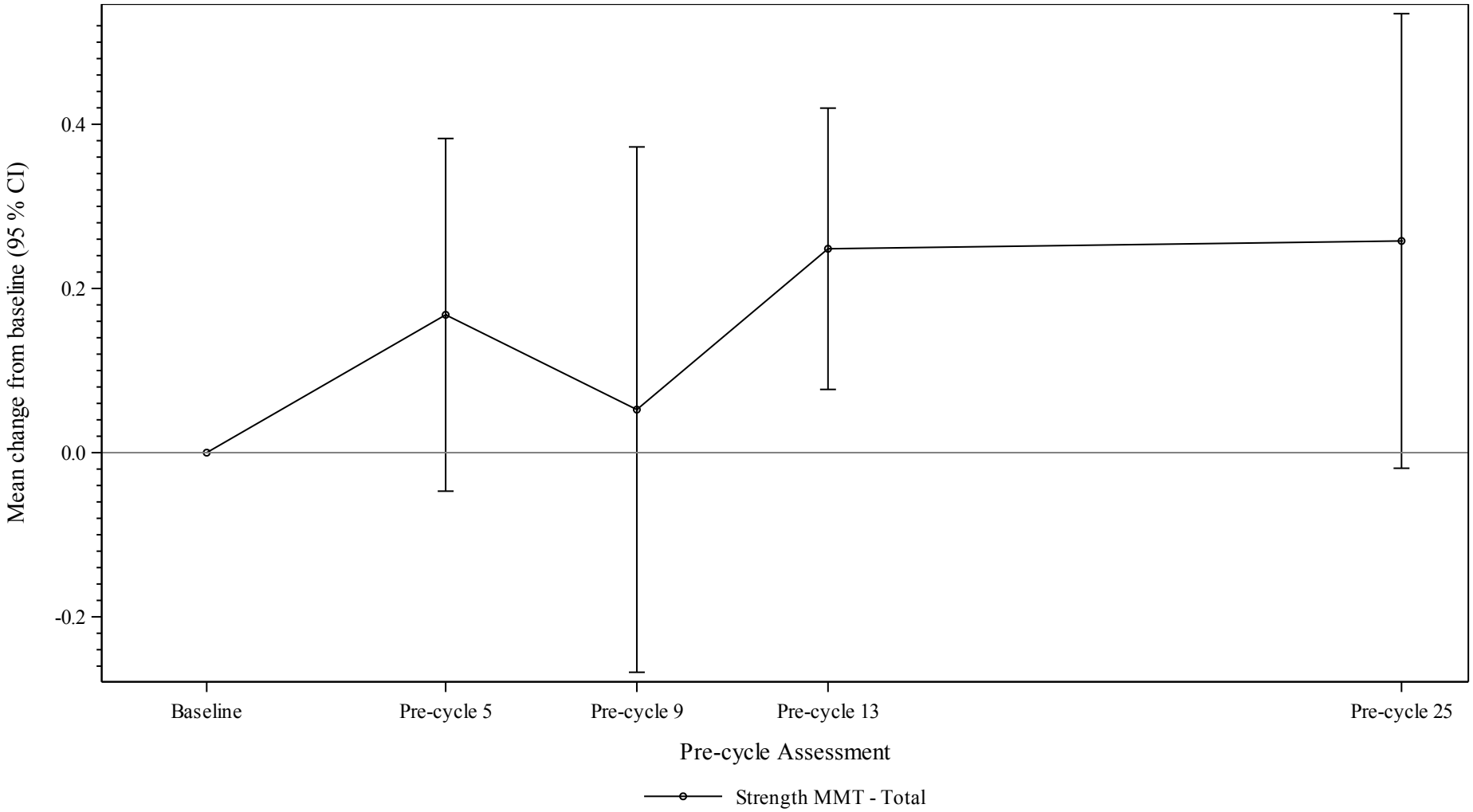
Table 2.4.2.1.5 Motor function primary outcome scores and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Range of motion (degrees) - Total	Baseline (n=11)	1103,45	470,768	886,00	360,0	1853,0	0,0							
	Pre-cycle 5 (n=8)	1145,00	504,044	982,50	416,0	1920,0	27,3	8	64,50	74,168	41,00	-11,0	184,0	27,3
	Pre-cycle 9 (n=10)	1133,30	481,573	971,00	393,0	1892,0	9,1	10	65,50	92,631	36,00	-54,0	229,0	9,1
	Pre-cycle 13 (n=8)	1107,50	523,170	948,50	355,0	1895,0	27,3	8	74,63	96,905	76,50	-73,0	241,0	27,3
	Pre-cycle 25 (n=7)	1140,57	567,061	898,00	356,0	1916,0	36,4	7	86,71	92,197	63,00	-9,0	237,0	36,4
Range of motion (degrees) - Unilateral Lower	Baseline (n=1)	NC	NC	NC	360,0	360,0	90,9							
	Pre-cycle 5 (n=1)	NC	NC	NC	416,0	416,0	90,9	1	NC	NC	NC	56,0	56,0	90,9
	Pre-cycle 9 (n=1)	NC	NC	NC	393,0	393,0	90,9	1	NC	NC	NC	33,0	33,0	90,9
	Pre-cycle 13 (n=1)	NC	NC	NC	355,0	355,0	90,9	1	NC	NC	NC	-5,0	-5,0	90,9
	Pre-cycle 25 (n=1)	NC	NC	NC	356,0	356,0	90,9	1	NC	NC	NC	-4,0	-4,0	90,9
Range of motion (degrees) - Unilateral Upper	Baseline (n=4)	780,00	145,536	842,50	565,0	870,0	63,6							
	Pre-cycle 5 (n=3)	860,00	48,218	880,00	805,0	895,0	72,7	3	8,33	18,556	10,00	-11,0	26,0	72,7
	Pre-cycle 9 (n=4)	823,25	44,342	805,50	794,0	888,0	63,6	4	43,25	127,380	-1,00	-54,0	229,0	63,6
	Pre-cycle 13 (n=3)	816,00	78,479	806,00	743,0	899,0	72,7	3	66,00	160,066	30,00	-73,0	241,0	72,7
	Pre-cycle 25 (n=3)	835,67	54,040	807,00	802,0	898,0	72,7	3	85,67	132,429	29,00	-9,0	237,0	72,7
Range of motion (degrees) - Bilateral Upper	Baseline (n=6)	1443,00	312,961	1464,50	886,0	1853,0	45,5							
	Pre-cycle 5 (n=4)	1541,00	351,850	1587,00	1070,0	1920,0	63,6	4	108,75	82,561	119,00	13,0	184,0	63,6
	Pre-cycle 9 (n=5)	1529,40	301,774	1550,00	1054,0	1892,0	54,5	5	89,80	75,098	81,00	-2,0	168,0	54,5
	Pre-cycle 13 (n=4)	1514,25	374,465	1582,00	998,0	1895,0	63,6	4	101,00	41,417	111,50	42,0	139,0	63,6
	Pre-cycle 25 (n=3)	1707,00	182,392	1625,00	1580,0	1916,0	72,7	3	118,00	48,775	135,00	63,0	156,0	72,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
MMT - Manual muscle test. NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Figure 2.4.3.1.1 Mean change from baseline of Motor function primary outcome test scores - Gender = Male
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

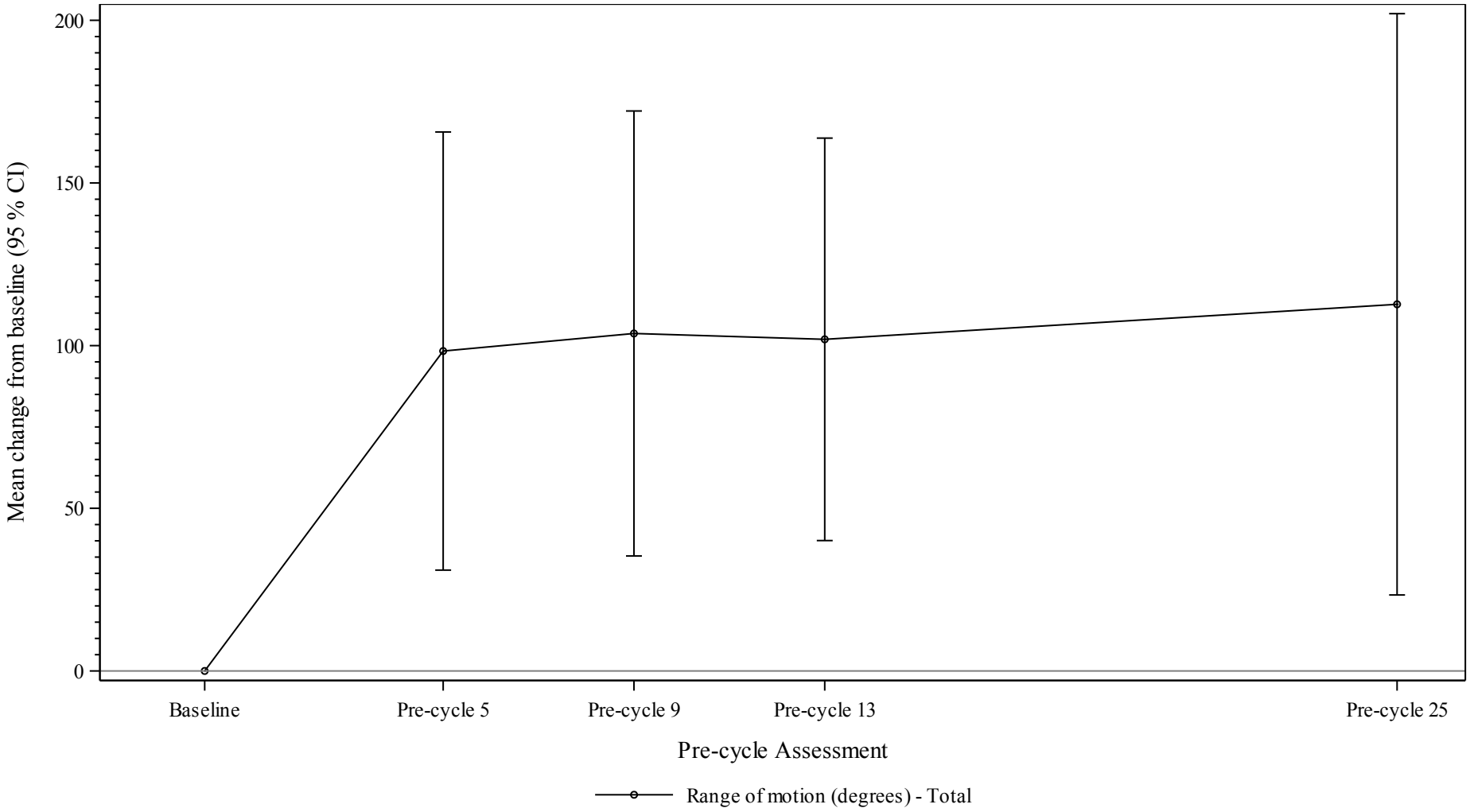
N = 19



CI = Confidence interval.

Figure 2.4.3.1.1 Mean change from baseline of Motor function primary outcome test scores - Gender = Male
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

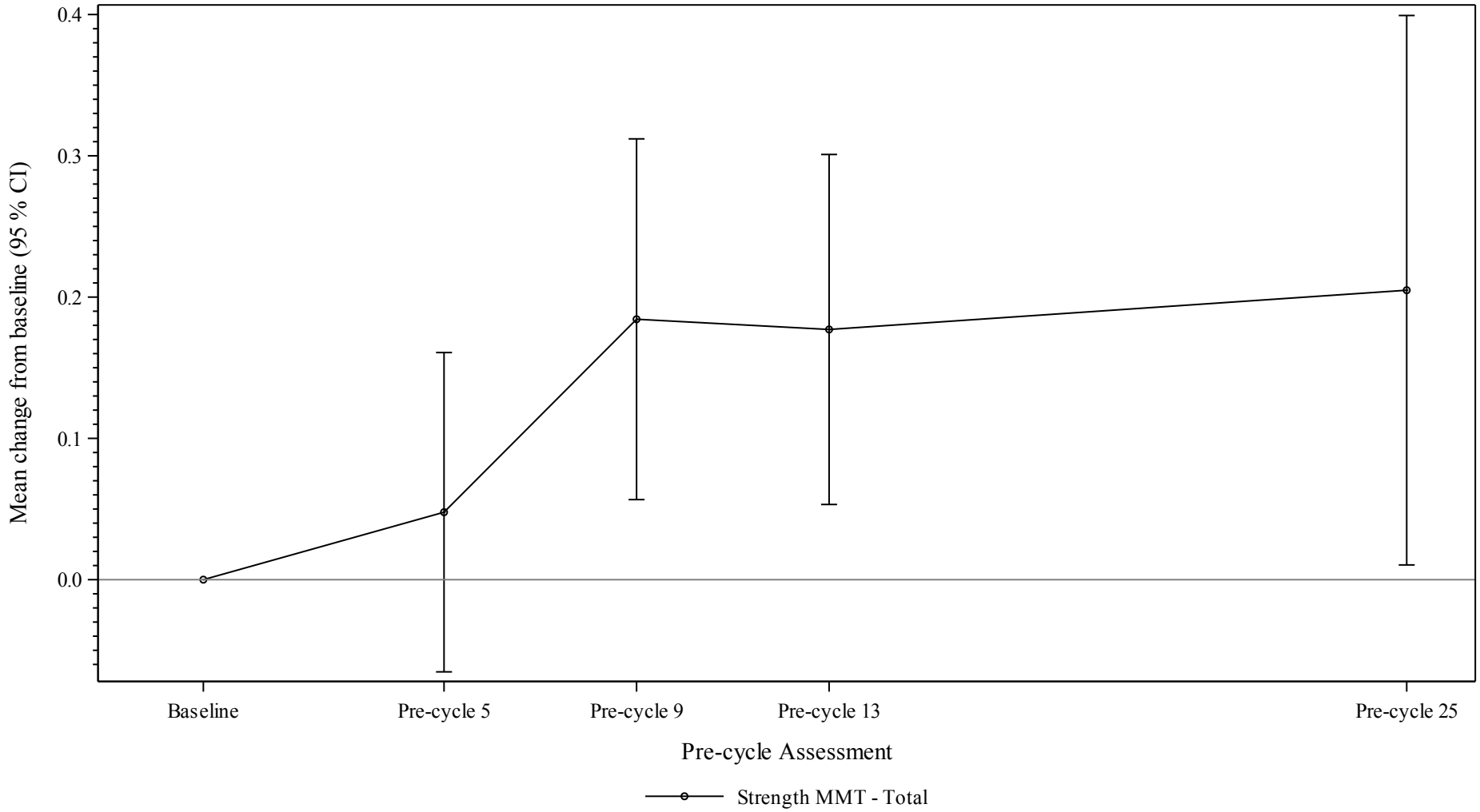
N = 19



CI = Confidence interval.

Figure 2.4.3.1.2 Mean change from baseline of Motor function primary outcome test scores - Gender = Female
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

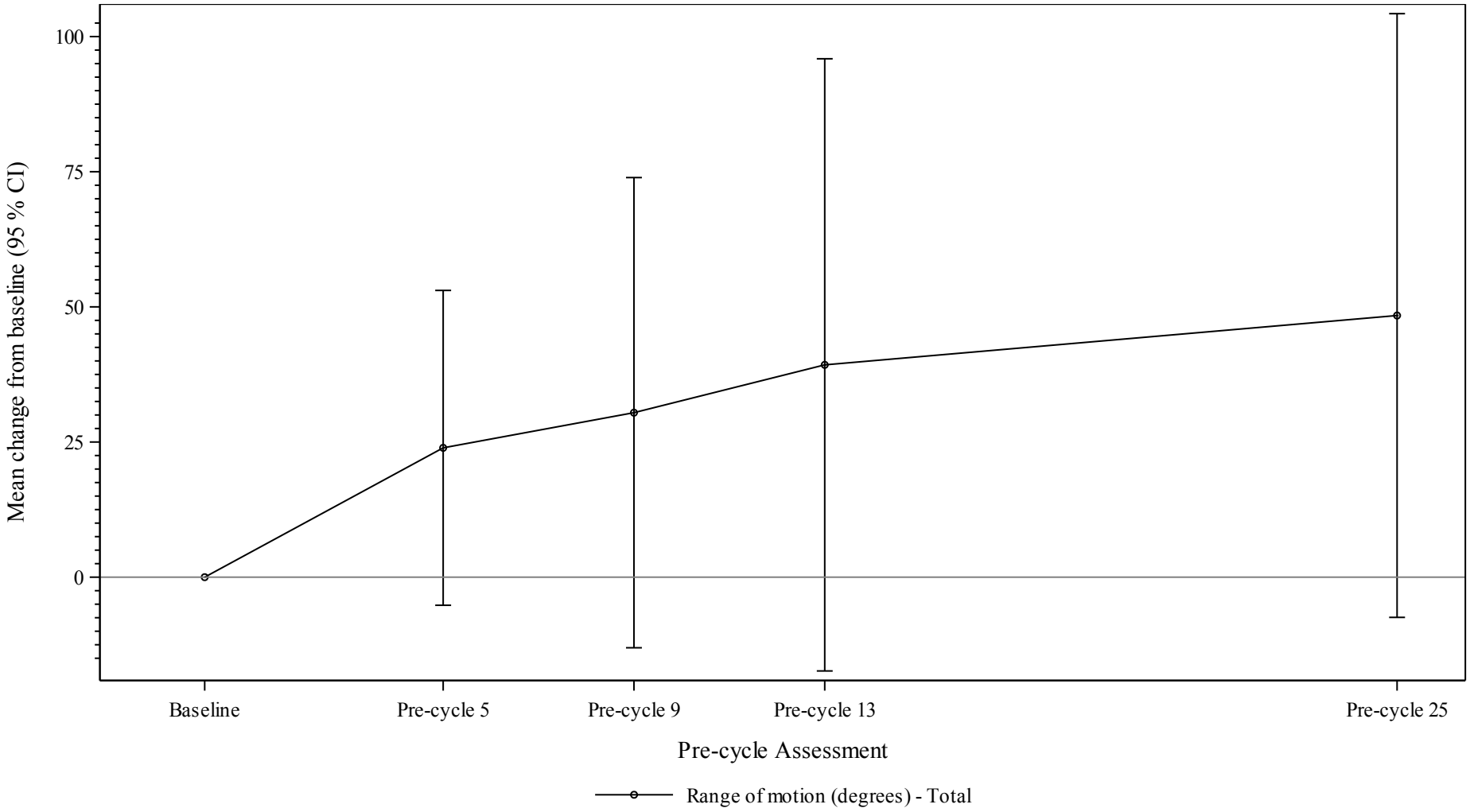
N = 14



CI = Confidence interval.

Figure 2.4.3.1.2 Mean change from baseline of Motor function primary outcome test scores - Gender = Female
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

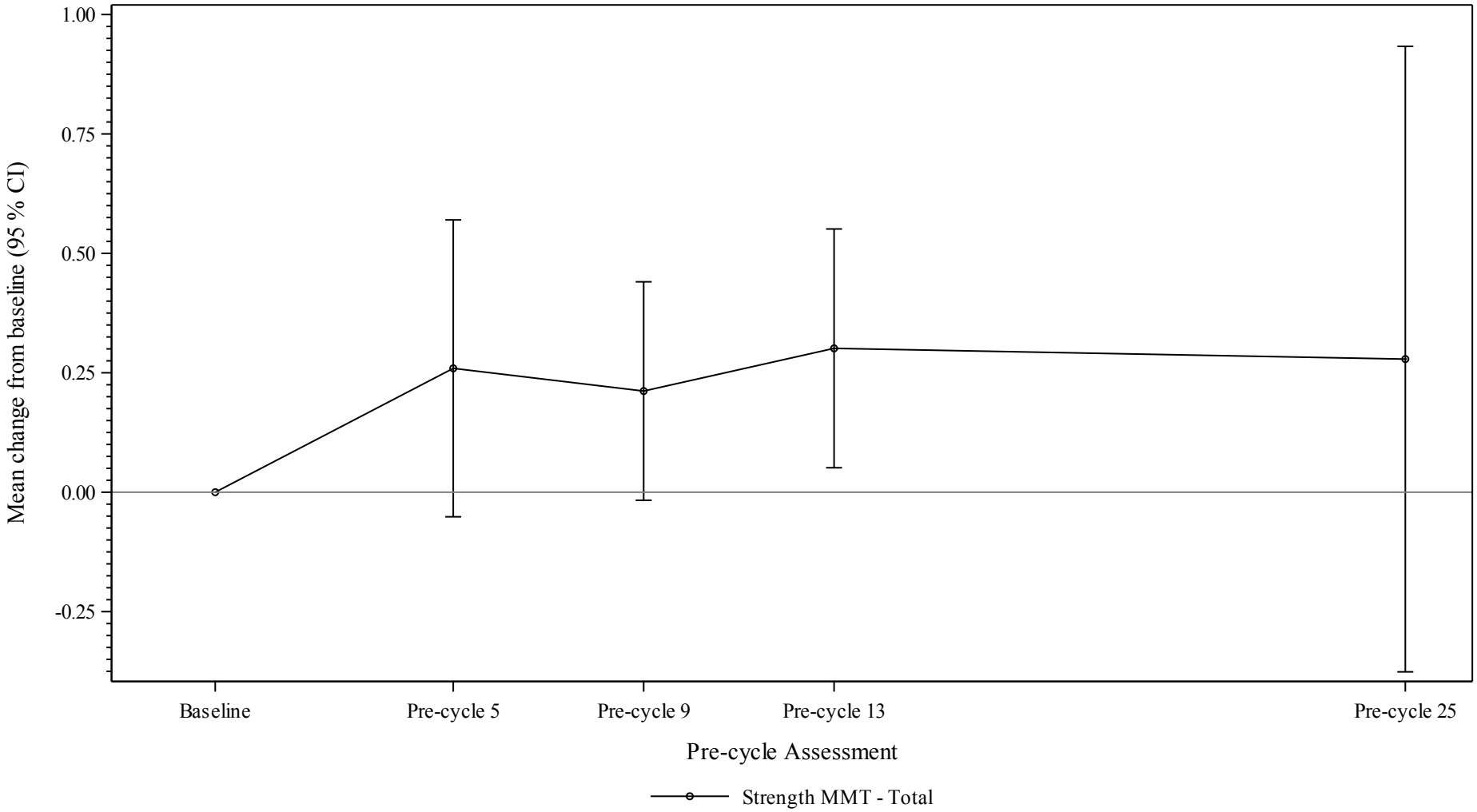
N = 14



CI = Confidence interval.

Figure 2.4.3.1.3 Mean change from baseline of Motor function primary outcome test scores - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

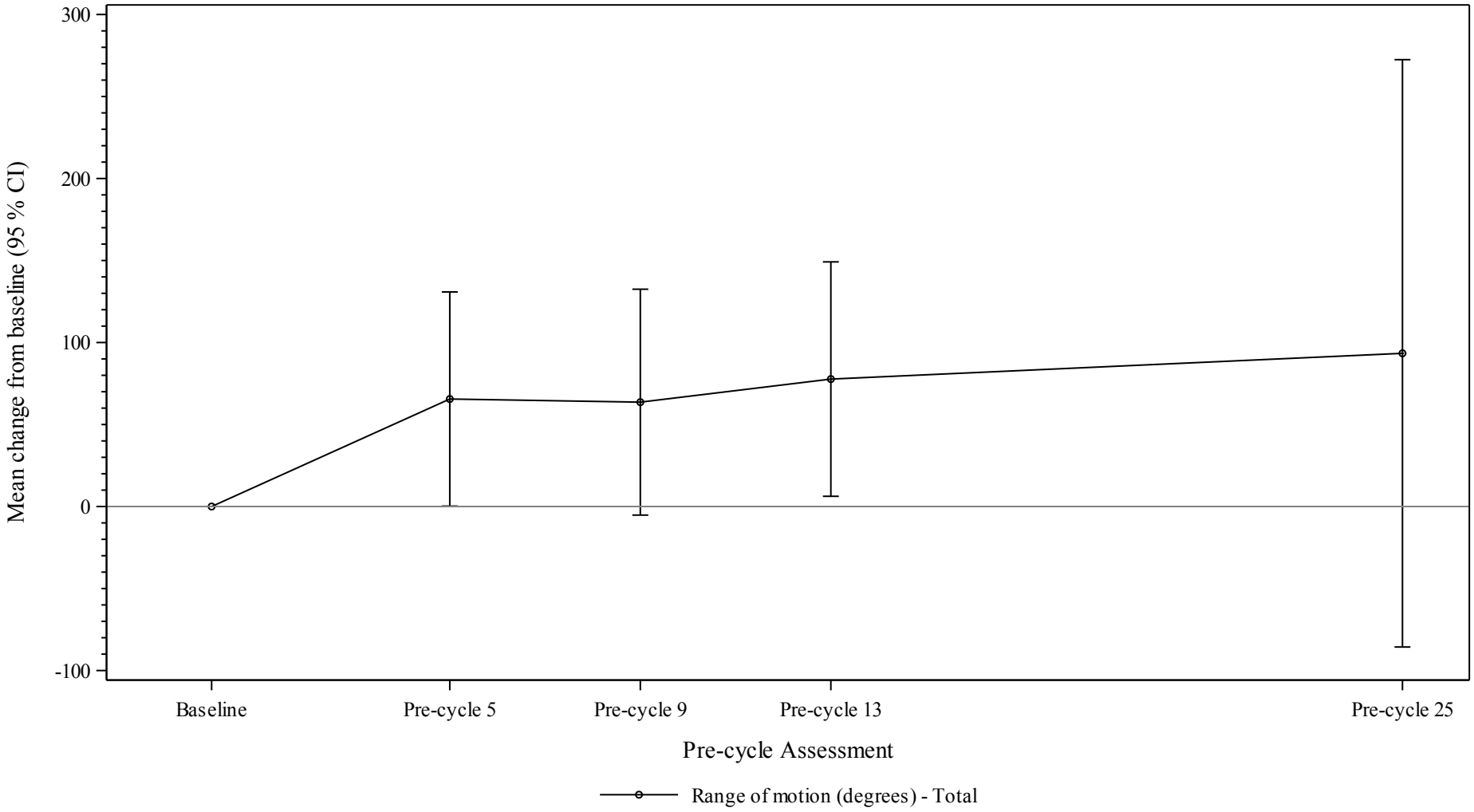
N = 11



CI = Confidence interval.

Figure 2.4.3.1.3 Mean change from baseline of Motor function primary outcome test scores - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

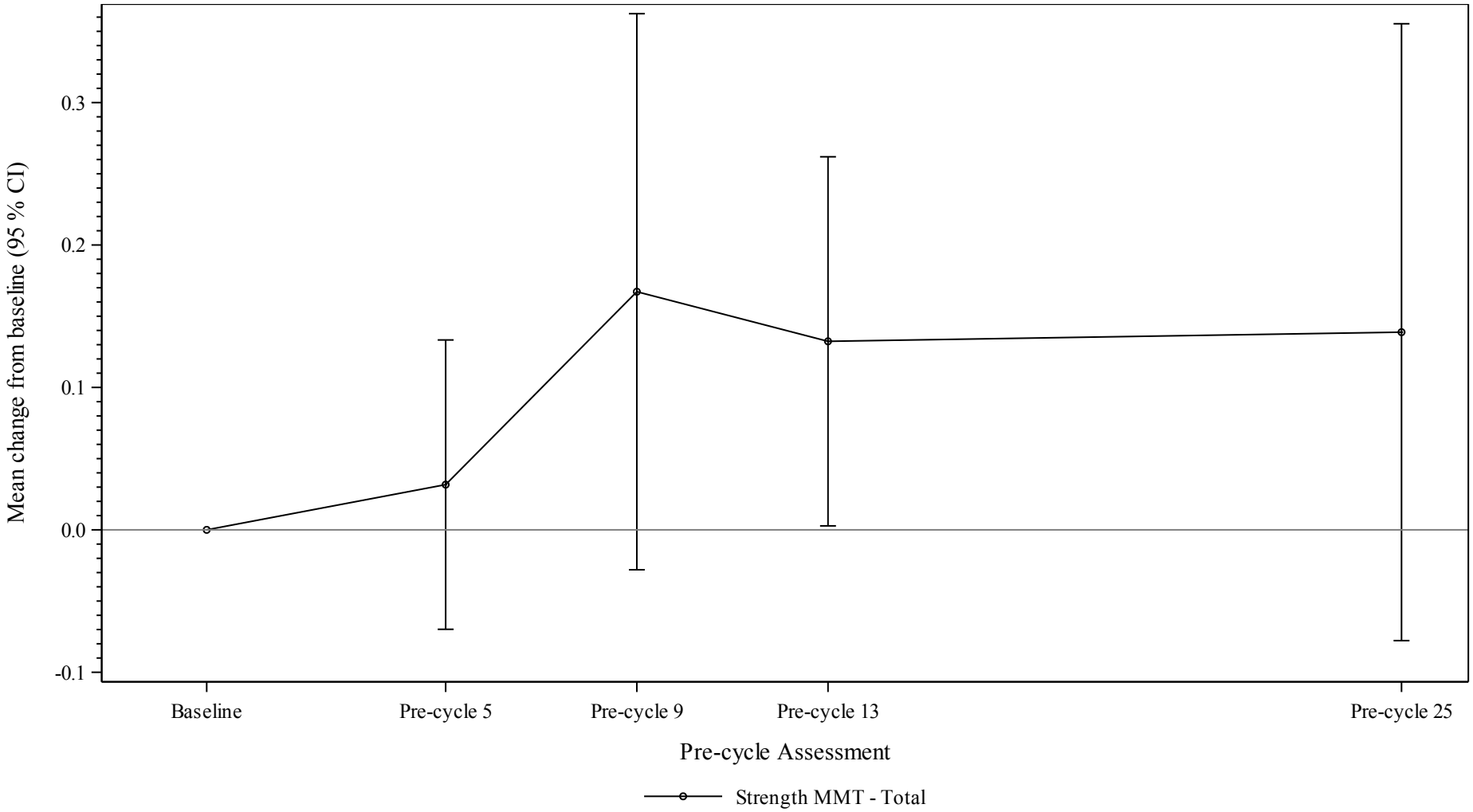
N = 11



CI = Confidence interval.

Figure 2.4.3.1.4 Mean change from baseline of Motor function primary outcome test scores - PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

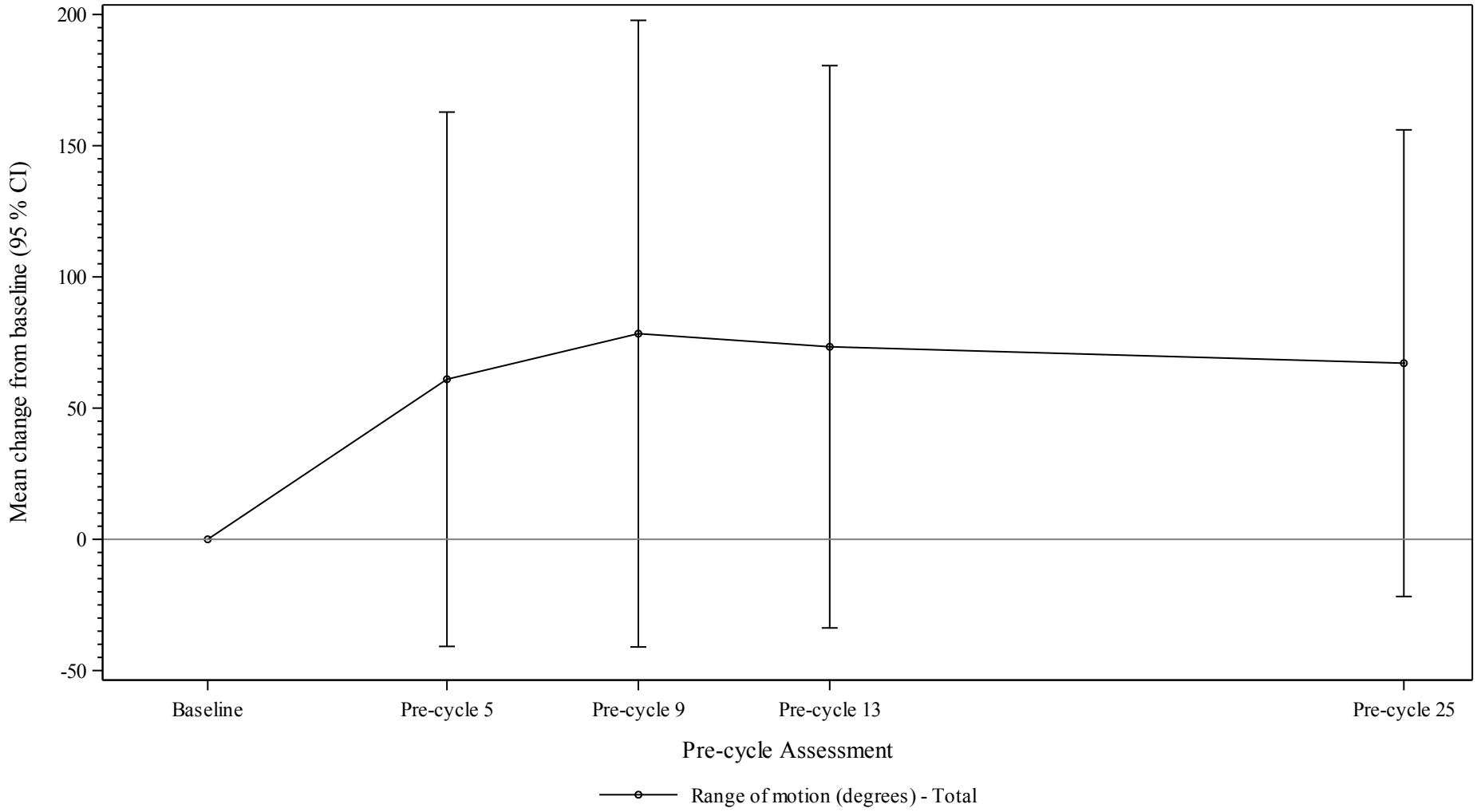
N = 11



CI = Confidence interval.

Figure 2.4.3.1.4 Mean change from baseline of Motor function primary outcome test scores - PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

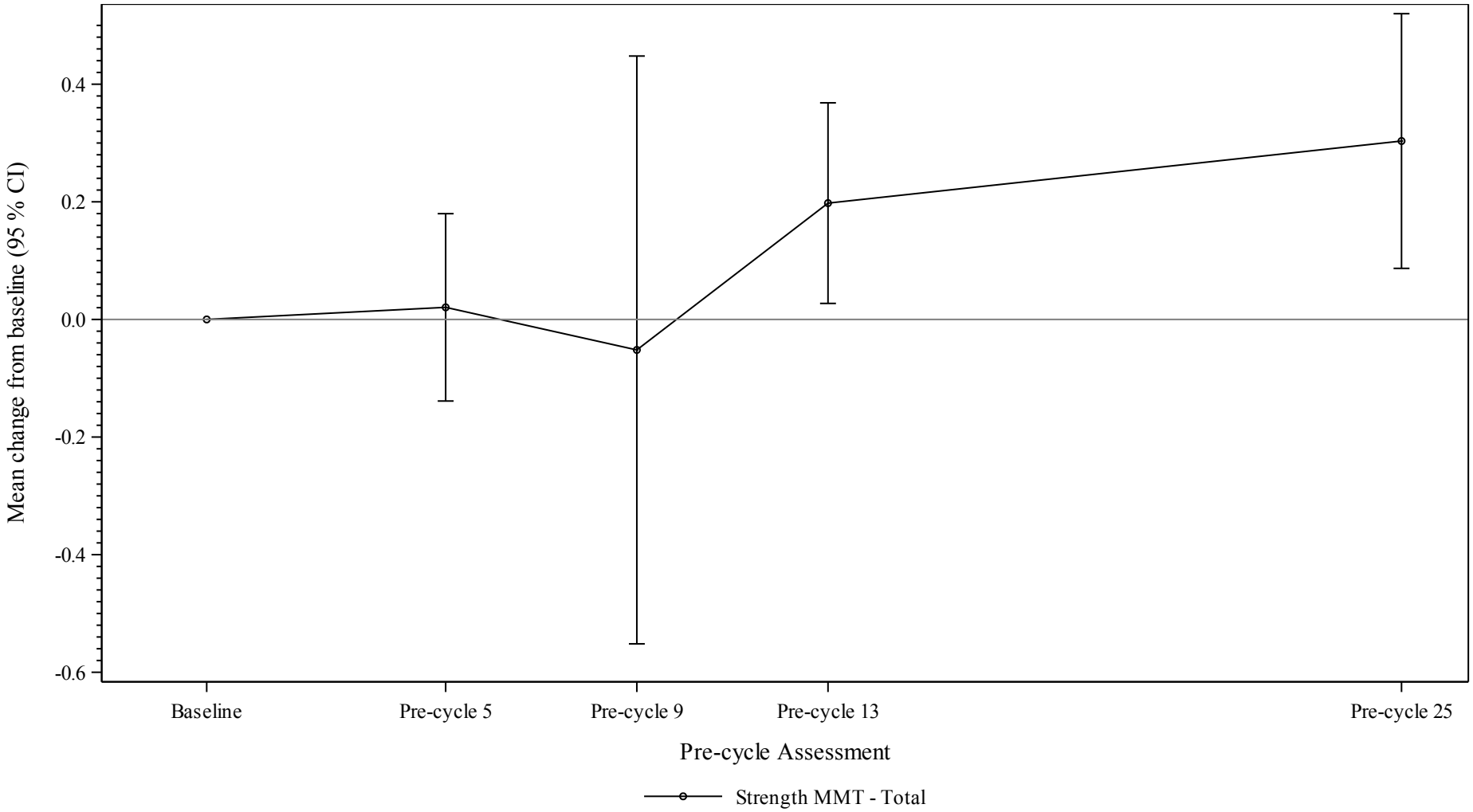
N = 11



CI = Confidence interval.

Figure 2.4.3.1.5 Mean change from baseline of Motor function primary outcome test scores PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

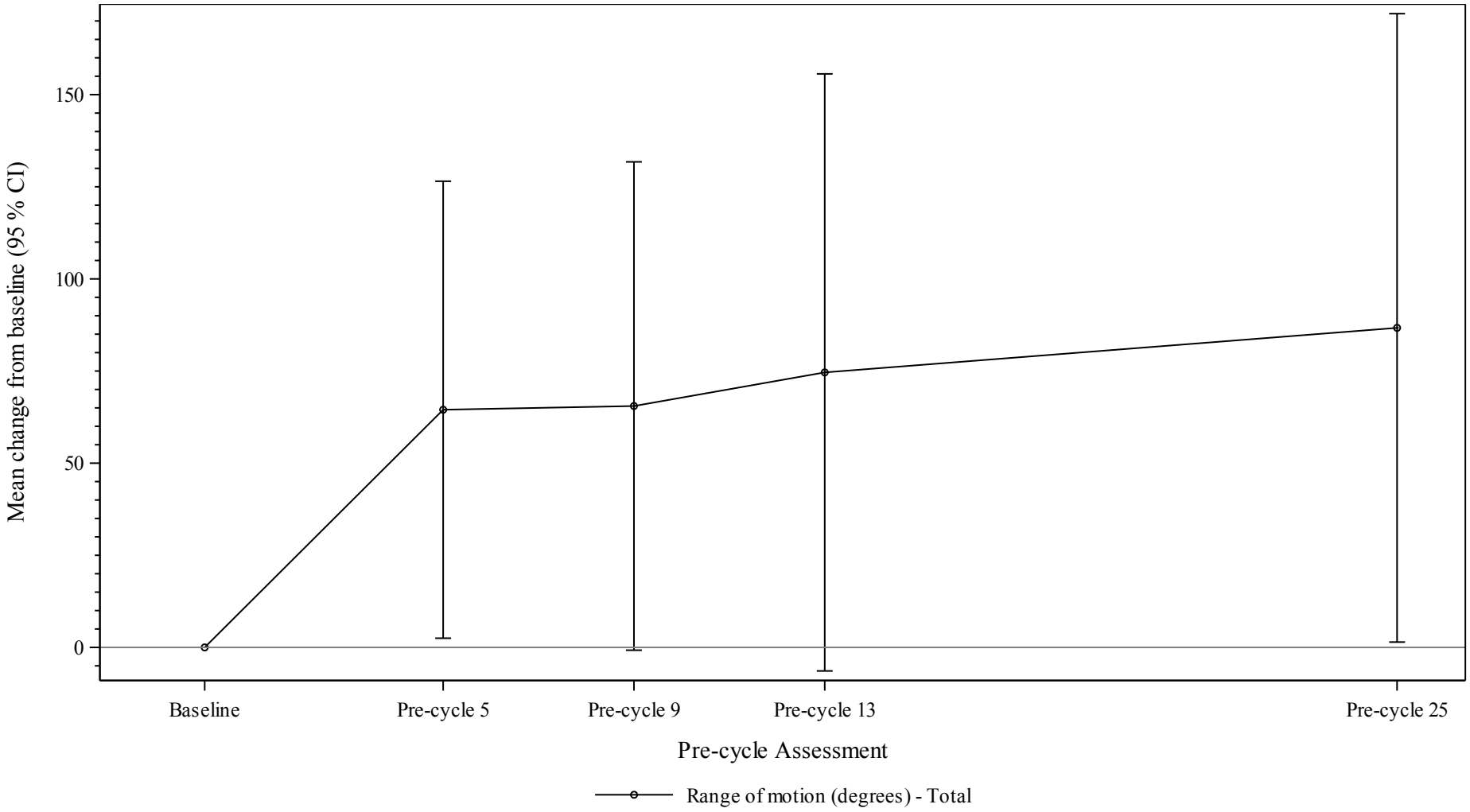
N = 11



CI = Confidence interval.

Figure 2.4.3.1.5 Mean change from baseline of Motor function primary outcome test scores PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

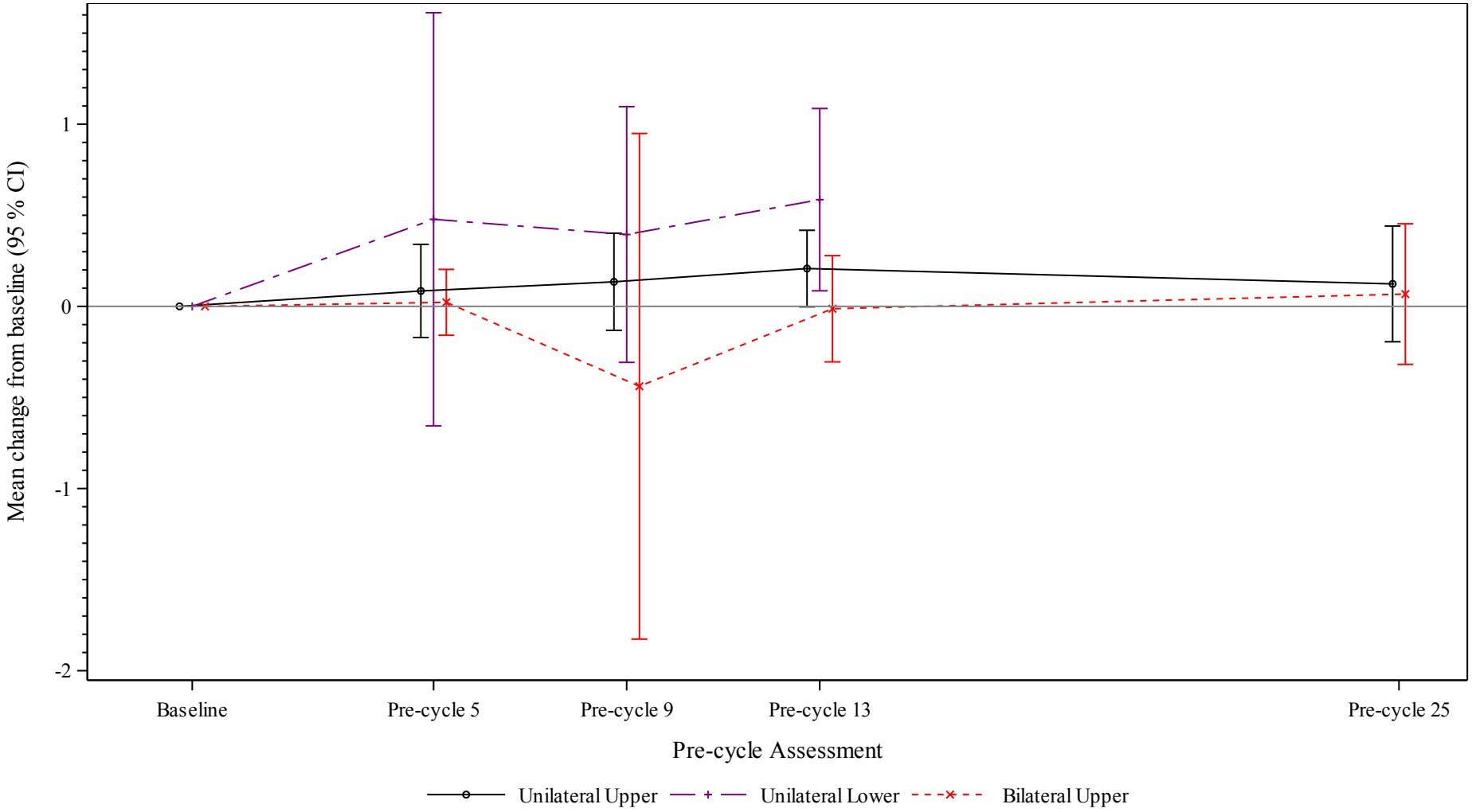
N = 11



CI = Confidence interval.

Figure 2.4.3.2.1 Mean change from baseline of Motor function primary outcome scores by PN Quadrant - Gender = Male
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

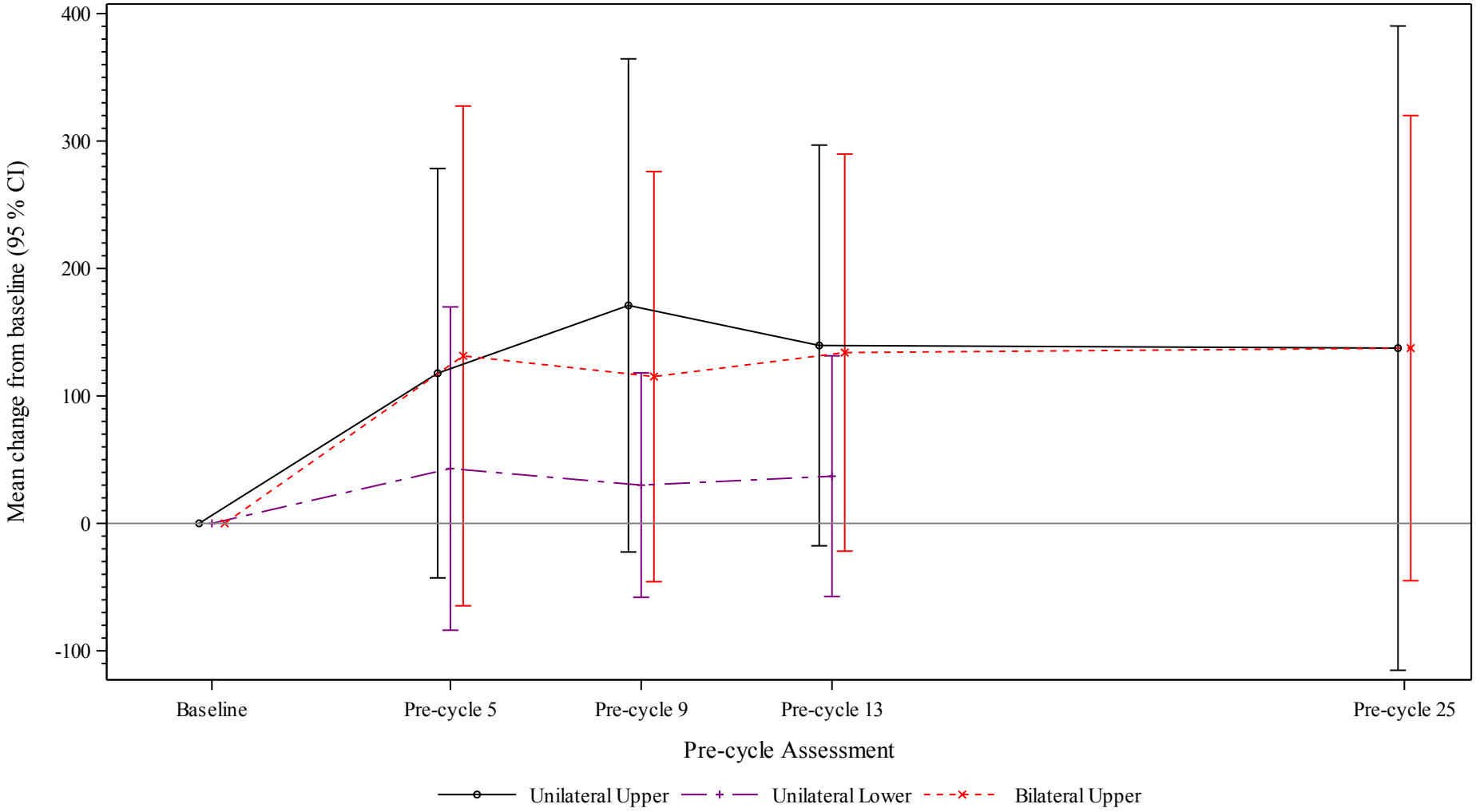
Strength MMT
N = 19



CI = Confidence interval.
Bilateral Lower group omitted owing to insufficient data.

Figure 2.4.3.2.1 Mean change from baseline of Motor function primary outcome scores by PN Quadrant - Gender = Male
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

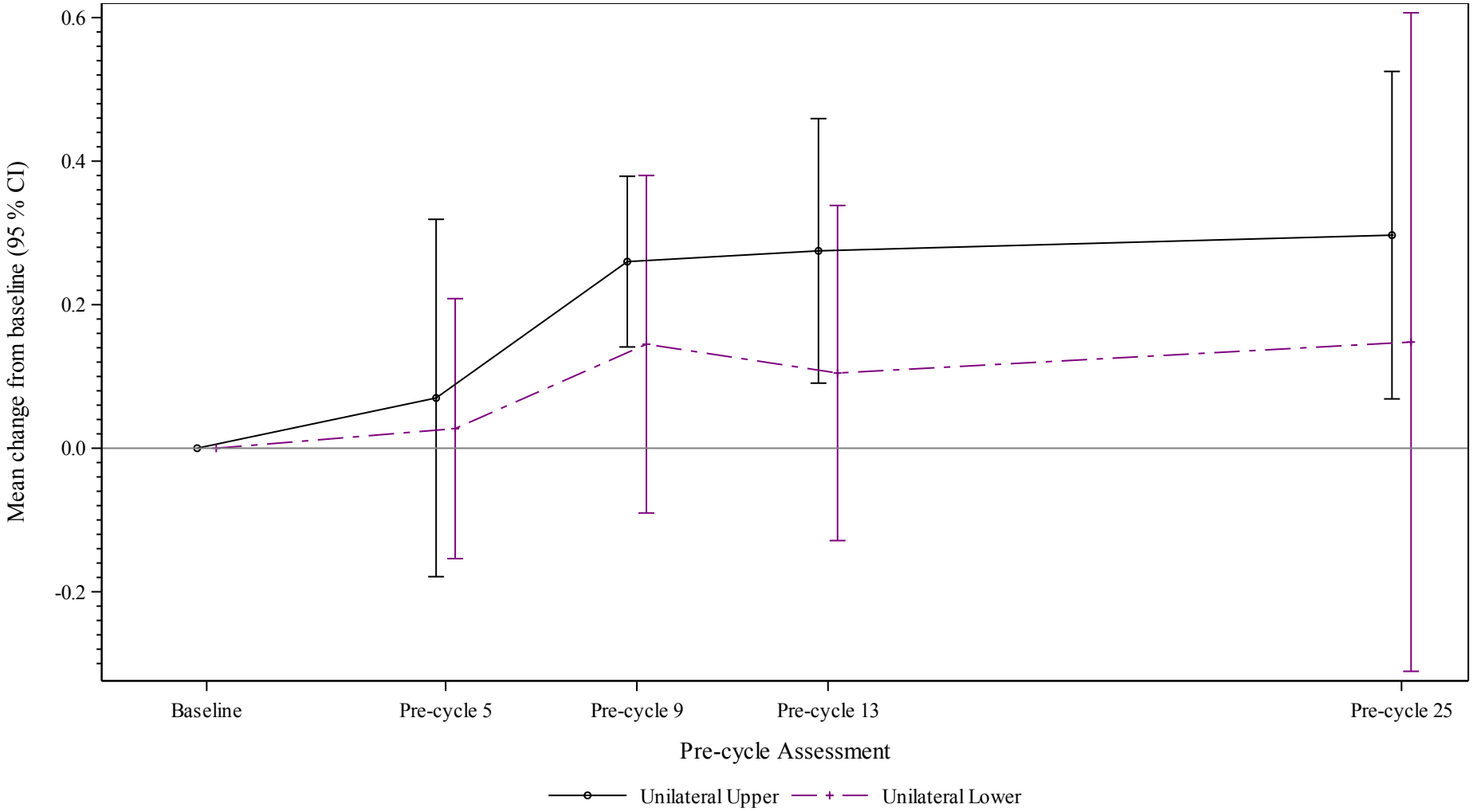
Range of motion (degrees)
N = 19



CI = Confidence interval.
Bilateral Lower group omitted owing to insufficient data.

Figure 2.4.3.2.2 Mean change from baseline of Motor function primary outcome scores by PN Quadrant - Gender = Female
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

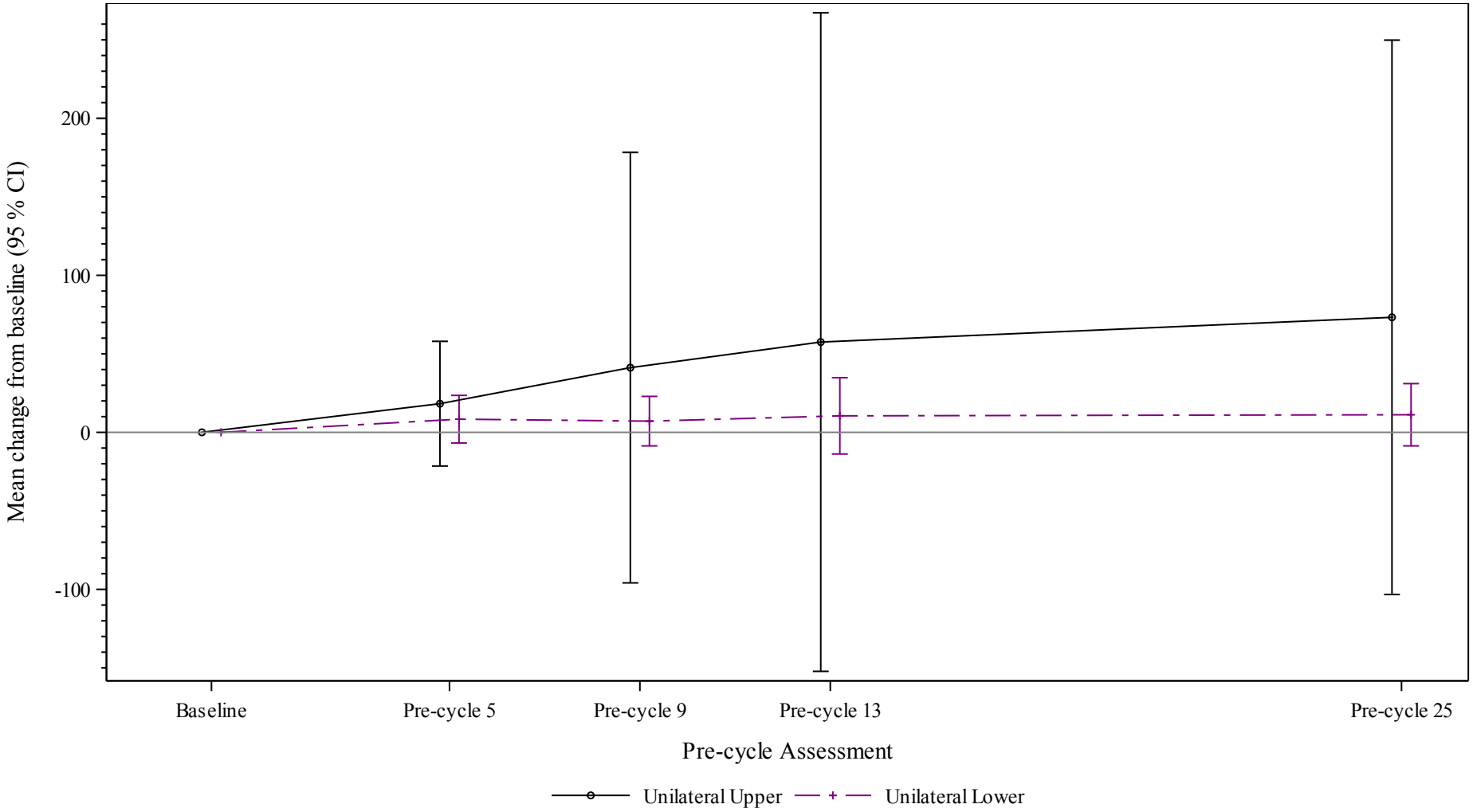
Strength MMT
N = 14



CI = Confidence interval.
Bilateral Lower/Upper group omitted owing to insufficient data.

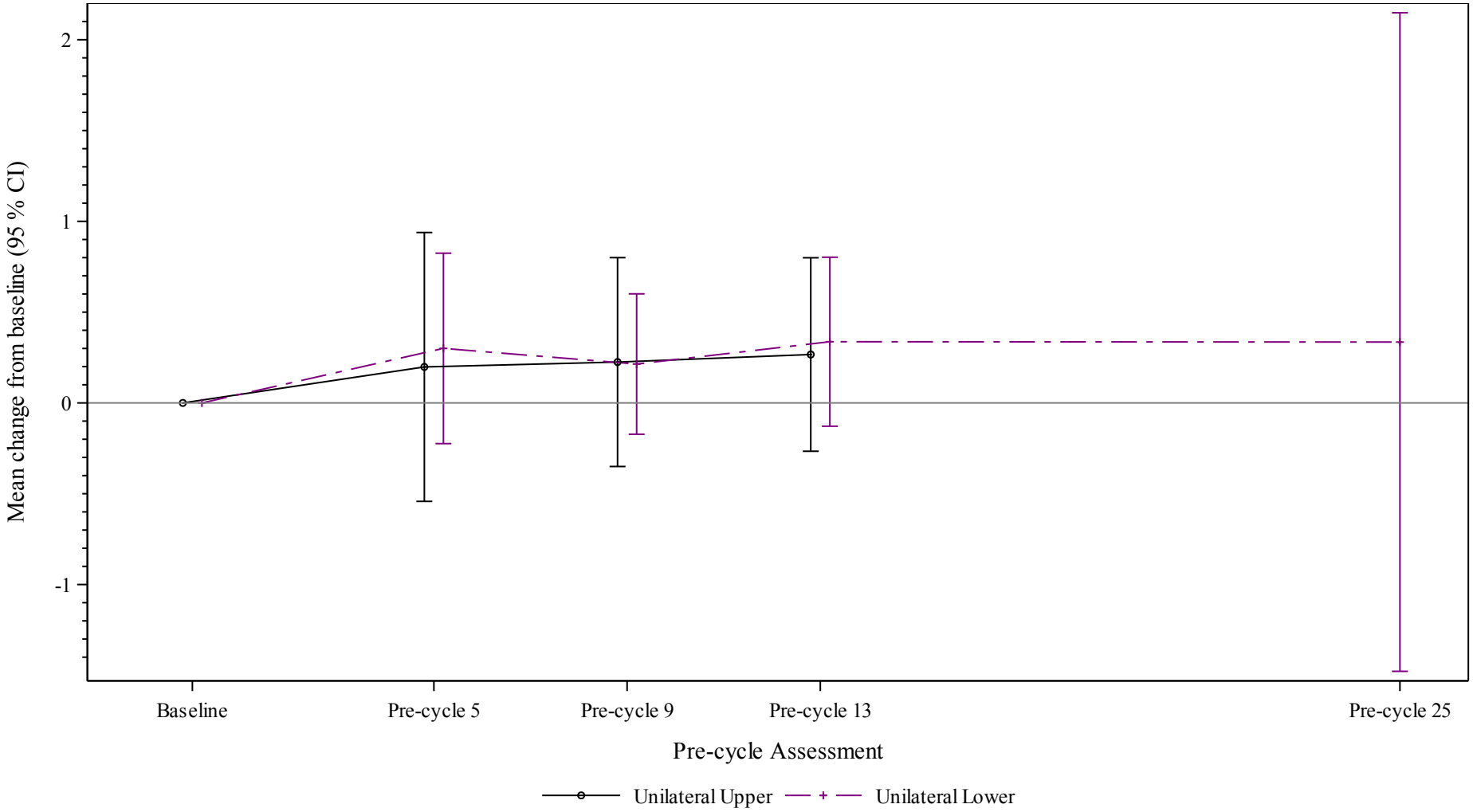
Figure 2.4.3.2.2 Mean change from baseline of Motor function primary outcome scores by PN Quadrant - Gender = Female
(Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1, Data cut-off: 29th June 2018

Range of motion (degrees)
N = 14



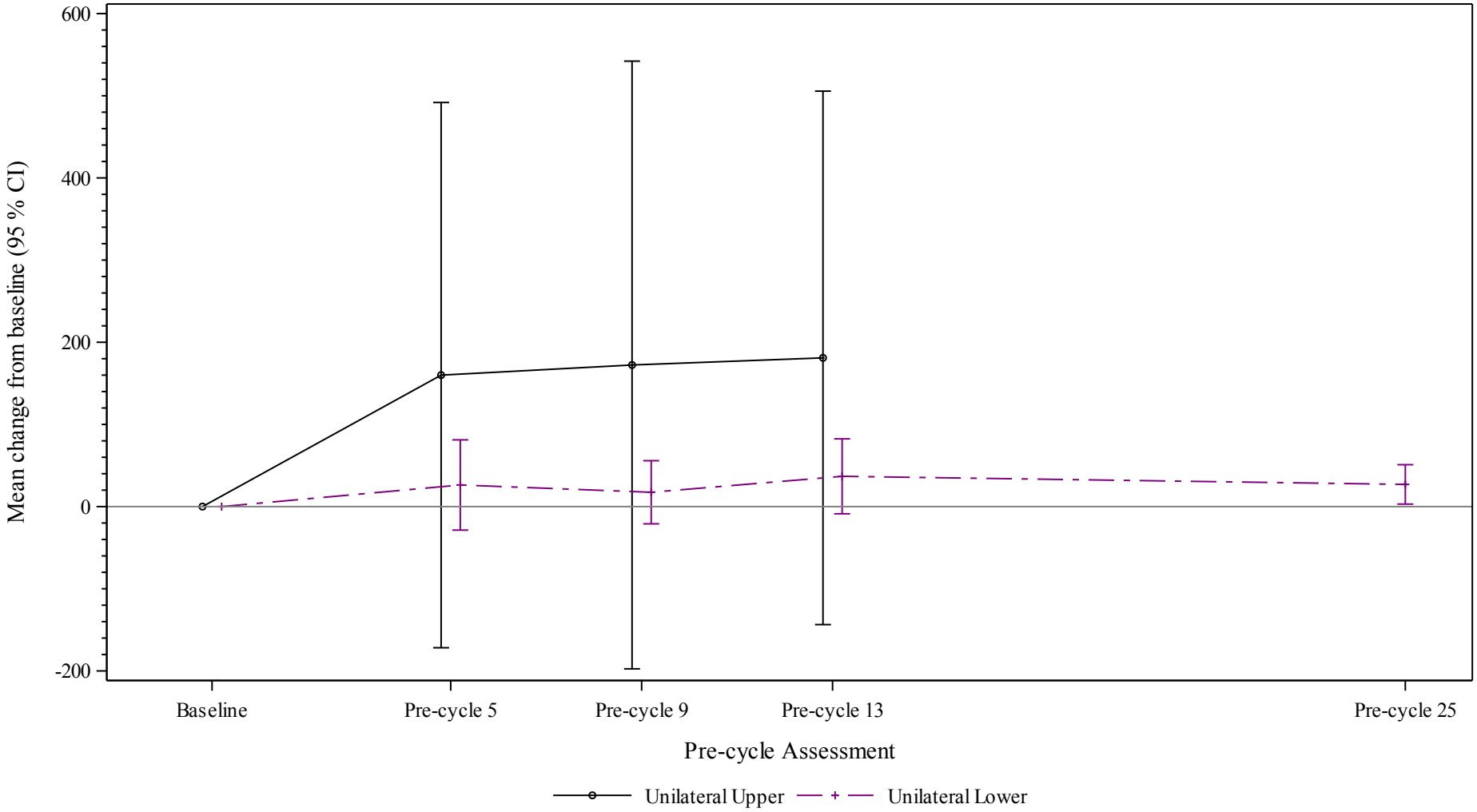
CI = Confidence interval.
Bilateral Lower/Upper group omitted owing to insufficient data.

Figure 2.4.3.2.3 Mean change from baseline of Motor function primary outcome scores by PN Quadrant
PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1
Data cut-off: 29th June 2018
Strength MMT
N = 11



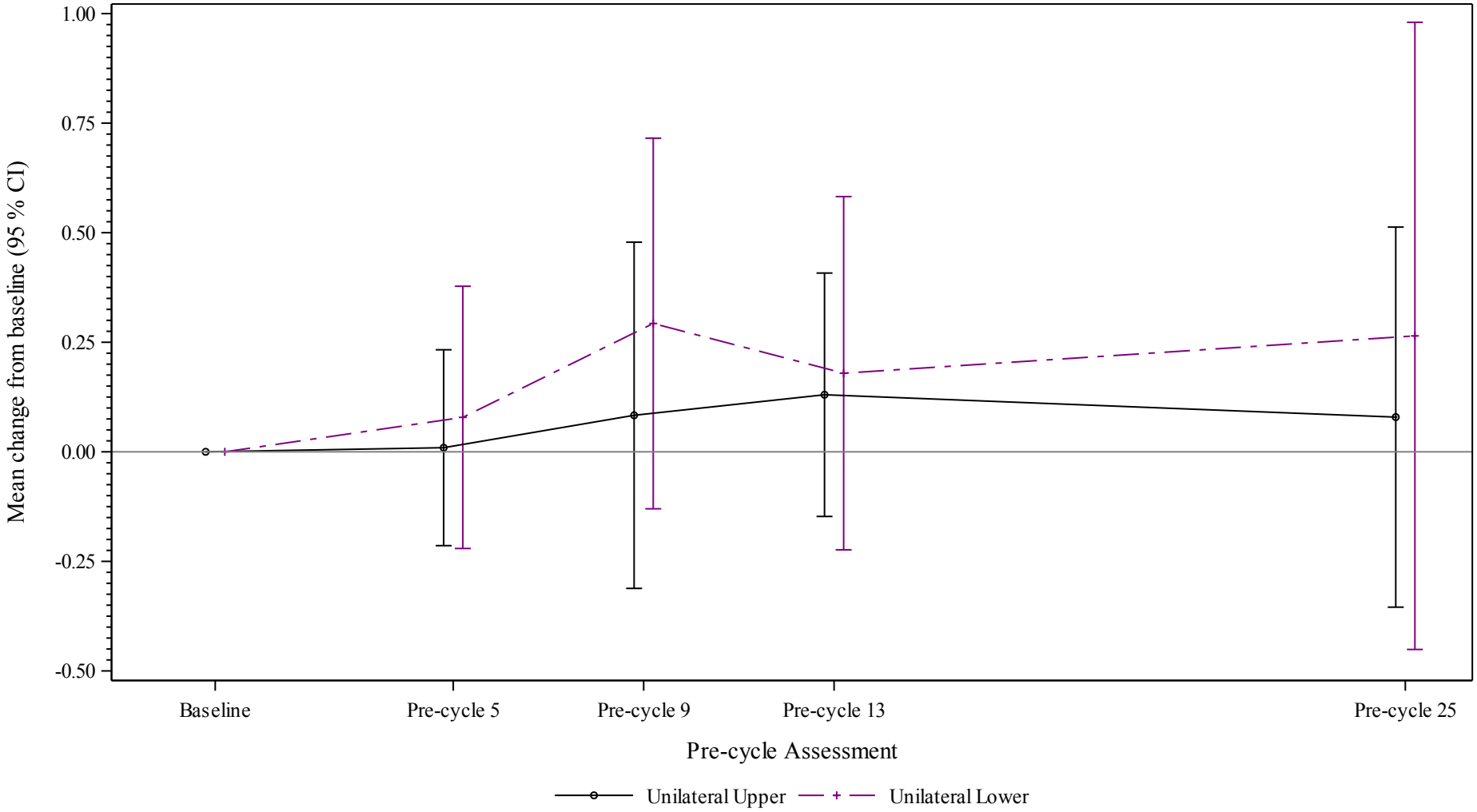
CI = Confidence interval.
Bilateral Lower/Upper group omitted owing to insufficient data.

Figure 2.4.3.2.3 Mean change from baseline of Motor function primary outcome scores by PN Quadrant
PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1
Data cut-off: 29th June 2018
Range of motion (degrees)
N = 11



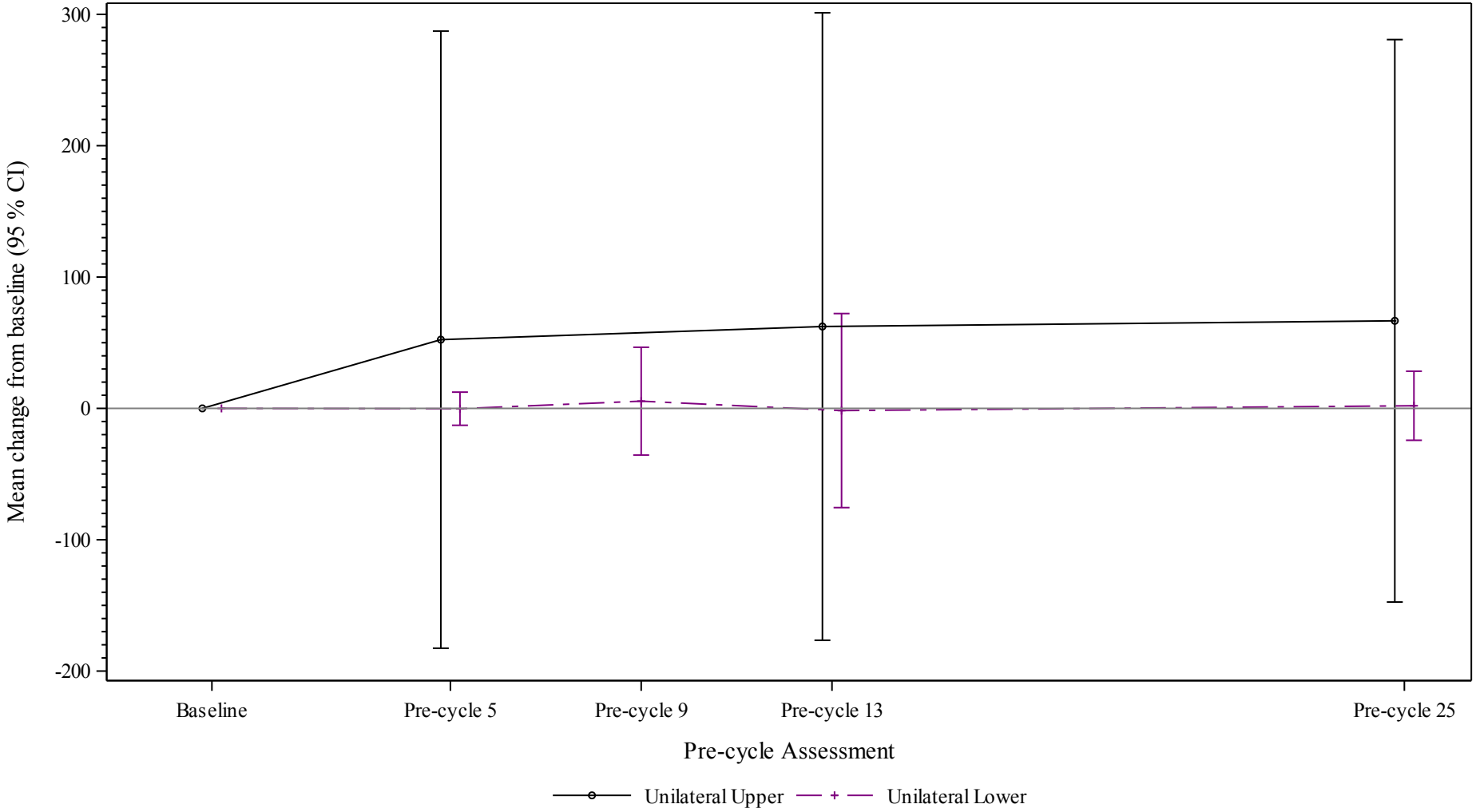
CI = Confidence interval.
Bilateral Lower/Upper group omitted owing to insufficient data.

Figure 2.4.3.2.4 Mean change from baseline of Motor function primary outcome scores by PN Quadrant
PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1
Data cut-off: 29th June 2018
Strength MMT
N = 11



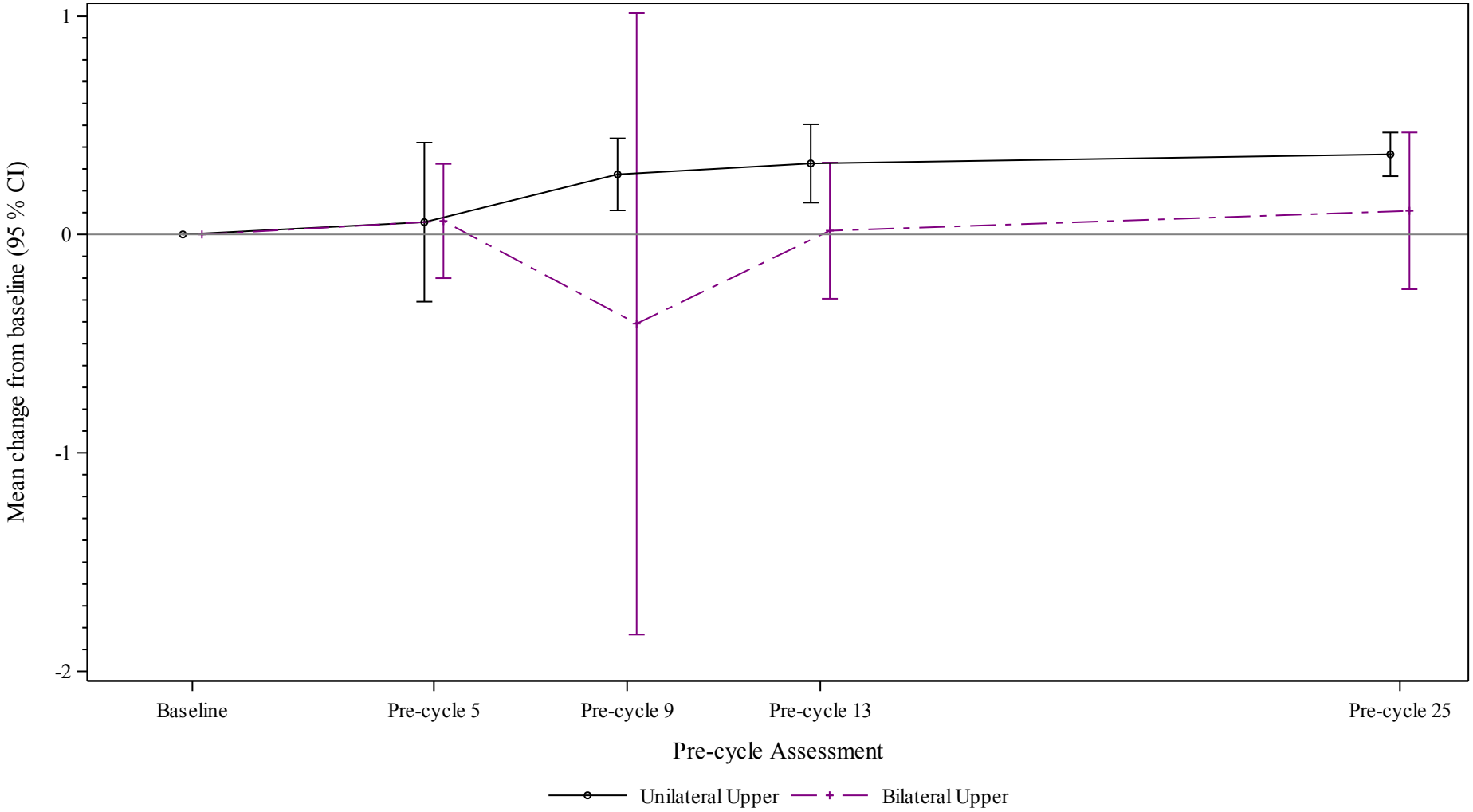
CI = Confidence interval.
Bilateral Lower/Upper group omitted owing to insufficient data.

Figure 2.4.3.2.4 Mean change from baseline of Motor function primary outcome scores by PN Quadrant
PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1
Data cut-off: 29th June 2018
Range of motion (degrees)
N = 11



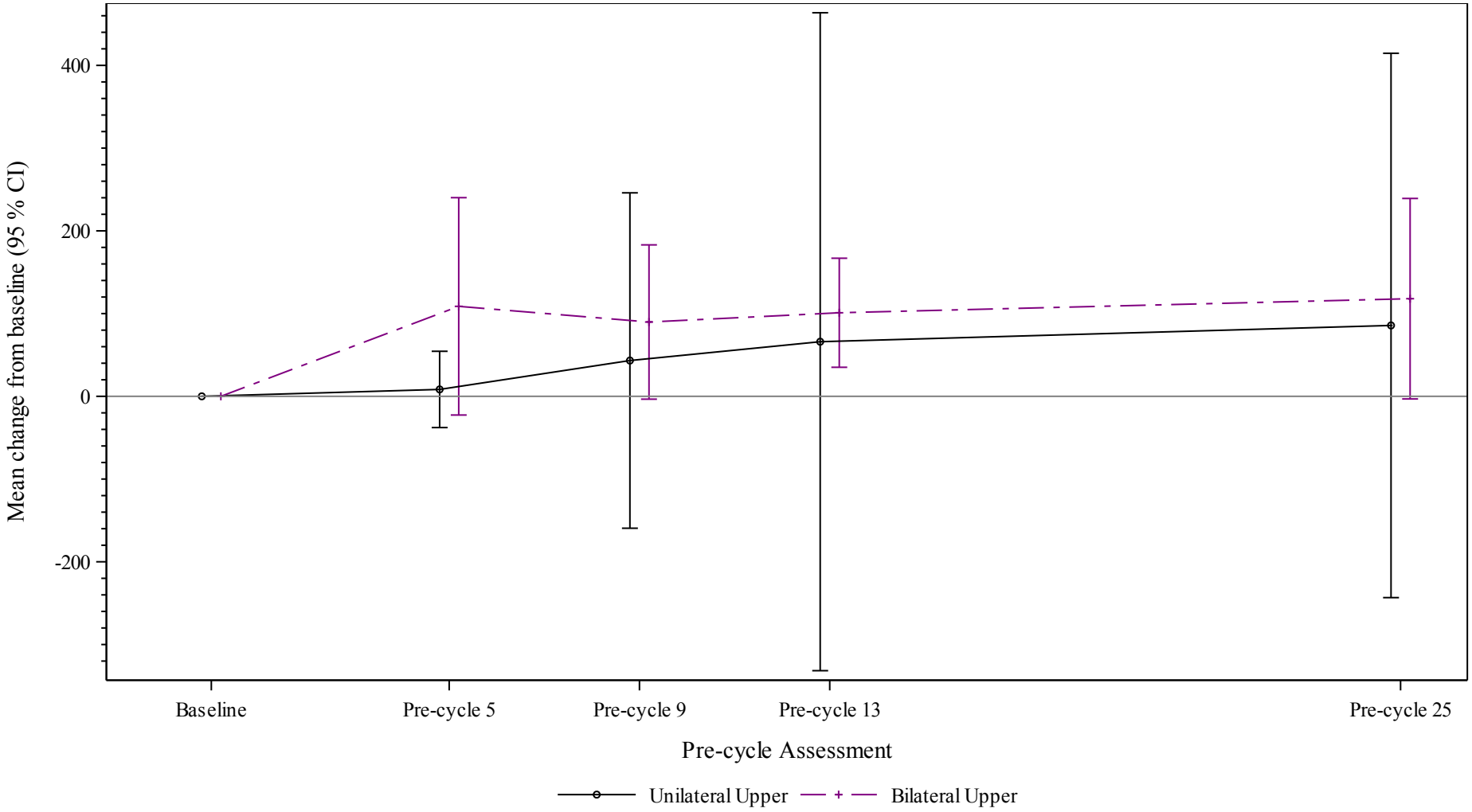
CI = Confidence interval.
Bilateral Lower/Upper group omitted owing to insufficient data.

Figure 2.4.3.2.5 Mean change from baseline of Motor function primary outcome test scores by PN Quadrant
PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1
Data cut-off: 29th June 2018
Strength MMT
N = 11



CI = Confidence interval.
Bilateral/Unilateral Lower group omitted owing to insufficient data.

Figure 2.4.3.2.5 Mean change from baseline of Motor function primary outcome test scores by PN Quadrant
PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) SPRINT Phase II Stratum 1
Data cut-off: 29th June 2018
Range of motion (degrees)
N = 11



CI = Confidence interval.
Bilateral/Unilateral Lower group omitted owing to insufficient data.

Table 2.4.4.1 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=19) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 5 (N=16)	Categories of change [d]			
		Improvement	1	6,3	0,2, 30,2
		No improvement	15	93,8	69,8, 99,8
	Pre-cycle 9 (N=15)	Categories of change [d]			
		Improvement	1	6,7	0,2, 31,9
		No improvement	14	93,3	68,1, 99,8
	Pre-cycle 13 (N=15)	Categories of change [d]			
		Improvement	1	6,7	0,2, 31,9
		No improvement	14	93,3	68,1, 99,8
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=16)	Categories of change [d]			
		Improvement	1	6,3	0,2, 30,2
		No improvement	15	93,8	69,8, 99,8

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.1 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=19) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Lower	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Pre-cycle 13 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
	Overall (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.1 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=19) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Upper	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100
	Pre-cycle 9 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100
	Pre-cycle 25 (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.1 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=19) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral Lower	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.1 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=19) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral Upper	Pre-cycle 5 (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 13 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Overall (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.2 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=14) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 5 (N=14)	Categories of change [d]			
		Improvement	0	0	0, 23,2
		No improvement	14	100	76,8, 100
	Pre-cycle 9 (N=14)	Categories of change [d]			
		Improvement	0	0	0, 23,2
		No improvement	14	100	76,8, 100
	Pre-cycle 13 (N=12)	Categories of change [d]			
		Improvement	0	0	0, 26,5
		No improvement	12	100	73,5, 100
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100
	Overall (N=14)	Categories of change [d]			
		Improvement	0	0	0, 23,2
		No improvement	14	100	76,8, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.2 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=14) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Lower	Pre-cycle 5 (N=8)	Categories of change [d]			
		Improvement	0	0	0, 36,9
		No improvement	8	100	63,1, 100
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	0	0	0, 36,9
		No improvement	8	100	63,1, 100
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100
	Pre-cycle 25 (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100
	Overall (N=8)	Categories of change [d]			
		Improvement	0	0	0, 36,9
		No improvement	8	100	63,1, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.2 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=14) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Upper	Pre-cycle 5 (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100
	Pre-cycle 9 (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100
	Pre-cycle 13 (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100
	Pre-cycle 25 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Overall (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.2 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=14) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral Upper	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.3 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	1	9,1	0,2, 41,3
		No improvement	10	90,9	58,7, 99,8
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	1	9,1	0,2, 41,3
		No improvement	10	90,9	58,7, 99,8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7
	Pre-cycle 25 (N=5)	Categories of change [d]			
		Improvement	1	20,0	0,5, 71,6
		No improvement	4	80,0	28,4, 99,5
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=11)	Categories of change [d]			
		Improvement	1	9,1	0,2, 41,3
		No improvement	10	90,9	58,7, 99,8

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.3 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Lower	Pre-cycle 5 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Pre-cycle 9 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
	Overall (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.3 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Upper	Pre-cycle 5 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Pre-cycle 9 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Pre-cycle 13 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.3 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral Lower	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.4 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100
	Pre-cycle 9 (N=9)	Categories of change [d]			
		Improvement	0	0	0, 33,6
		No improvement	9	100	66,4, 100
	Pre-cycle 13 (N=8)	Categories of change [d]			
		Improvement	0	0	0, 36,9
		No improvement	8	100	63,1, 100
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	0	0	0, 36,9
		No improvement	8	100	63,1, 100
	Overall (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.4 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Lower	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 13 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Overall (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.4 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Upper	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 13 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 25 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Overall (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.4 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral Upper	Pre-cycle 5 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.5 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	0	0	0, 33,6
		No improvement	9	100	66,4, 100
	Pre-cycle 9 (N=9)	Categories of change [d]			
		Improvement	0	0	0, 33,6
		No improvement	9	100	66,4, 100
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	0	0	0, 33,6
		No improvement	9	100	66,4, 100
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	0	0	0, 41,0
		No improvement	7	100	59,0, 100
	Overall (N=9)	Categories of change [d]			
		Improvement	0	0	0, 33,6
		No improvement	9	100	66,4, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.5 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Lower	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.5 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral Upper	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 13 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Overall (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.4.4.5 Motor function primary outcome test score (Strength MMT) categories of change over time - percentage of patients with Improvement by >= 0.75 points - PN status at enrollment = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral Upper	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 13 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Overall (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100

MMT - Manual Muscle Test.
[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 0.75. NC - not calculated.

Table 2.5.1 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=24) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=21)	Categories of change [d]			
		Improvement	3	14,3	3,0, 36,3
		No improvement	18	85,7	63,7, 97,0
	Pre-cycle 5 (N=22)	Categories of change [d]			
		Improvement	3	13,6	2,9, 34,9
		No improvement	19	86,4	65,1, 97,1
	Pre-cycle 9 (N=22)	Categories of change [d]			
		Improvement	4	18,2	5,2, 40,3
		No improvement	18	81,8	59,7, 94,8
	Pre-cycle 13 (N=20)	Categories of change [d]			
		Improvement	2	10,0	1,2, 31,7
		No improvement	18	90,0	68,3, 98,8
	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	1	7,1	0,2, 33,9
		No improvement	13	92,9	66,1, 99,8
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
	Overall (N=22)	Categories of change [d]			
		Improvement	6	27,3	10,7, 50,2
		No improvement	16	72,7	49,8, 89,3

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=24) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=21)	Categories of change [d]			
		Improvement	4	19,0	5,4, 41,9
		No improvement	17	81,0	58,1, 94,6
	Pre-cycle 5 (N=21)	Categories of change [d]			
		Improvement	3	14,3	3,0, 36,3
		No improvement	18	85,7	63,7, 97,0
	Pre-cycle 9 (N=21)	Categories of change [d]			
		Improvement	2	9,5	1,2, 30,4
		No improvement	19	90,5	69,6, 98,8
	Pre-cycle 13 (N=19)	Categories of change [d]			
		Improvement	3	15,8	3,4, 39,6
		No improvement	16	84,2	60,4, 96,6
	Pre-cycle 25 (N=13)	Categories of change [d]			
		Improvement	3	23,1	5,0, 53,8
		No improvement	10	76,9	46,2, 95,0
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=21)	Categories of change [d]			
		Improvement	7	33,3	14,6, 57,0
		No improvement	14	66,7	43,0, 85,4

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1.1.1 PROMIS self-report scores over time and change from baseline over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]											
		Absolute values						Change from baseline					
PROMIS self-report score: Mobility	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=13)	46,05	6,610	44,10	38,4	58,5	7,1							
	Pre-cycle 3 (n=12)	44,76	5,325	44,65	35,5	52,3	14,3	12	-0,26	7,459	0,00	-18,0	9,2	14,3
	Pre-cycle 5 (n=12)	47,55	6,981	45,75	40,0	58,5	14,3	12	2,53	6,985	2,25	-14,1	14,4	14,3
	Pre-cycle 9 (n=12)	46,43	6,925	44,35	38,5	58,5	14,3	12	1,42	10,065	2,75	-20,0	15,7	14,3
	Pre-cycle 13 (n=11)	47,43	7,180	45,40	38,3	58,5	21,4	11	1,91	8,442	1,90	-17,9	14,4	21,4
	Pre-cycle 25 (n=7)	52,64	8,349	58,50	37,4	58,5	50,0	7	7,10	7,473	6,20	-6,1	15,5	50,0
	Pre-cycle 37 (n=2)	NC	NC	NC	33,2	45,0	85,7	2	NC	NC	NC	-10,3	-0,8	85,7
Raw Score	Baseline (n=13)	26,7	4,23	27,0	19	32	7,1							
	Pre-cycle 3 (n=12)	27,0	3,64	27,5	19	31	14,3	12	0,8	4,73	0,0	-8	9	14,3
	Pre-cycle 5 (n=12)	27,7	3,31	27,0	23	32	14,3	12	1,4	2,91	1,5	-5	6	14,3
	Pre-cycle 9 (n=12)	28,2	3,04	28,0	23	32	14,3	12	1,9	5,02	3,5	-9	6	14,3
	Pre-cycle 13 (n=11)	28,1	3,67	29,0	22	32	21,4	11	1,6	3,23	3,0	-7	5	21,4
	Pre-cycle 25 (n=7)	29,6	4,39	32,0	20	32	50,0	7	2,6	2,23	3,0	-1	6	50,0
	Pre-cycle 37 (n=2)	NC	NC	NC	17	29	85,7	2	NC	NC	NC	-4	2	85,7

[a] Children, ages 8 to 18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.1.1.1 PROMIS self-report scores over time and change from baseline over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
PROMIS self-report score: Upper extremity	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=13)	43,62	15,152	56,70	20,4	56,7	7,1							
	Pre-cycle 3 (n=12)	44,19	13,811	46,10	18,7	56,7	14,3	12	1,67	7,113	0,00	-9,0	14,1	14,3
	Pre-cycle 5 (n=12)	43,33	13,402	44,20	21,9	56,7	14,3	12	0,81	3,701	0,00	-7,9	5,7	14,3
	Pre-cycle 9 (n=12)	40,00	10,484	37,50	24,8	56,7	14,3	12	-2,53	10,830	0,00	-25,8	11,1	14,3
	Pre-cycle 13 (n=11)	44,86	12,649	48,80	25,5	56,7	21,4	11	1,80	6,293	0,00	-7,9	11,4	21,4
	Pre-cycle 25 (n=7)	48,27	11,337	56,70	29,6	56,7	50,0	7	4,80	6,178	0,00	0,0	14,2	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	42,2	42,2	92,9	1	NC	NC	NC	15,2	15,2	92,9
Raw Score	Baseline (n=13)	24,8	8,82	32,0	9	32	7,1							
	Pre-cycle 3 (n=12)	25,8	8,72	30,5	9	32	14,3	12	1,6	4,76	0,0	-8	10	14,3
	Pre-cycle 5 (n=12)	24,8	7,76	26,0	10	32	14,3	12	0,6	3,65	0,0	-8	6	14,3
	Pre-cycle 9 (n=12)	24,3	6,29	24,0	13	32	14,3	12	0,1	5,48	0,0	-11	11	14,3
	Pre-cycle 13 (n=11)	25,8	7,47	30,0	14	32	21,4	11	1,6	4,11	0,0	-4	10	21,4
	Pre-cycle 25 (n=7)	28,7	5,62	32,0	17	32	50,0	7	4,1	5,24	0,0	0	11	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	29	29	92,9	1	NC	NC	NC	13	13	92,9

[a] Children, ages 8 to 18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.1.1.2 PROMIS self-report scores over time and change from baseline over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=10) [a]											
		Absolute values						Change from baseline					
PROMIS self-report score: Mobility	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=10)	47,23	6,732	47,30	32,3	58,5	0,0							
	Pre-cycle 3 (n=9)	48,41	9,524	47,40	30,3	58,5	10,0	9	1,74	5,243	0,10	-5,5	11,2	10,0
	Pre-cycle 5 (n=10)	48,38	7,660	46,15	36,9	58,5	0,0	10	1,15	4,422	0,00	-3,4	8,5	0,0
	Pre-cycle 9 (n=10)	48,06	7,840	48,60	30,9	58,5	0,0	10	0,83	5,599	0,35	-8,5	11,2	0,0
	Pre-cycle 13 (n=9)	48,74	6,368	48,70	40,7	58,5	10,0	9	1,70	5,017	0,00	-3,5	11,2	10,0
	Pre-cycle 25 (n=7)	47,97	5,732	45,80	41,9	58,5	30,0	7	-1,14	7,600	-0,10	-14,0	11,2	30,0
Raw Score	Baseline (n=10)	28,4	4,93	30,0	15	32	0,0							
	Pre-cycle 3 (n=9)	28,1	5,35	30,0	15	32	10,0	9	0,0	1,66	0,0	-4	2	10,0
	Pre-cycle 5 (n=10)	28,8	3,61	29,5	20	32	0,0	10	0,4	2,27	0,0	-3	5	0,0
	Pre-cycle 9 (n=10)	28,6	4,99	30,0	15	32	0,0	10	0,2	1,69	0,0	-3	3	0,0
	Pre-cycle 13 (n=9)	29,4	2,30	30,0	26	32	10,0	9	1,2	3,80	0,0	-1	11	10,0
	Pre-cycle 25 (n=7)	29,6	1,62	29,0	27	32	30,0	7	-0,3	1,89	0,0	-3	2	30,0

[a] Children, ages 8 to 18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.1.1.2 PROMIS self-report scores over time and change from baseline over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=10) [a]											
		Absolute values						Change from baseline					
PROMIS self-report score: Upper extremity	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=9)	49,32	8,447	48,30	35,7	56,7	10,0							
	Pre-cycle 3 (n=9)	48,03	10,132	50,00	29,3	56,7	10,0	9	-1,29	6,613	0,00	-15,8	8,4	10,0
	Pre-cycle 5 (n=10)	47,83	6,826	46,15	40,2	56,7	0,0	9	-1,13	7,016	0,00	-16,5	7,9	10,0
	Pre-cycle 9 (n=10)	50,32	9,519	56,70	31,4	56,7	0,0	9	0,29	9,678	0,00	-19,9	13,5	10,0
	Pre-cycle 13 (n=9)	50,46	7,772	56,70	40,0	56,7	10,0	8	1,28	8,091	2,35	-16,7	8,4	20,0
	Pre-cycle 25 (n=7)	51,61	8,687	56,70	38,6	56,7	30,0	6	1,63	10,301	5,55	-18,1	8,4	40,0
Raw Score	Baseline (n=9)	29,8	3,67	31,0	22	32	10,0							
	Pre-cycle 3 (n=9)	29,4	4,07	31,0	20	32	10,0	9	-0,3	1,32	0,0	-3	1	10,0
	Pre-cycle 5 (n=10)	30,1	1,66	30,0	28	32	0,0	9	0,4	3,09	0,0	-4	7	10,0
	Pre-cycle 9 (n=10)	29,8	4,24	32,0	19	32	0,0	9	-0,2	3,23	0,0	-6	6	10,0
	Pre-cycle 13 (n=9)	30,3	2,40	32,0	26	32	10,0	8	0,6	2,83	0,5	-5	4	20,0
	Pre-cycle 25 (n=7)	30,7	2,21	32,0	27	32	30,0	6	0,2	2,71	1,0	-5	3	40,0

[a] Children, ages 8 to 18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.1.1.3 PROMIS self-report scores over time and change from baseline over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=6) [a]											
		Absolute values						Change from baseline					
PROMIS self-report score: Mobility	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=6)	45,08	8,817	45,60	32,3	58,5	0,0							
	Pre-cycle 3 (n=6)	41,90	7,631	41,10	30,3	52,1	0,0	6	-3,18	9,132	-2,85	-18,0	8,6	0,0
	Pre-cycle 5 (n=6)	44,30	4,227	45,40	36,9	48,9	0,0	6	-0,78	6,734	0,95	-14,1	4,6	0,0
	Pre-cycle 9 (n=6)	43,20	7,611	44,35	30,9	52,2	0,0	6	-1,88	9,537	-0,70	-20,0	6,8	0,0
	Pre-cycle 13 (n=5)	43,80	4,544	41,50	40,6	51,3	16,7	5	-0,52	10,292	1,90	-17,9	8,4	16,7
	Pre-cycle 25 (n=1)	NC	NC	NC	51,3	51,3	83,3	1	NC	NC	NC	5,5	5,5	83,3
	Pre-cycle 37 (n=1)	NC	NC	NC	45,0	45,0	83,3	1	NC	NC	NC	-0,8	-0,8	83,3
Raw Score	Baseline (n=6)	25,8	6,31	28,0	15	32	0,0							
	Pre-cycle 3 (n=6)	24,7	5,28	25,5	15	30	0,0	6	-1,2	4,58	-1,0	-8	6	0,0
	Pre-cycle 5 (n=6)	27,2	3,76	28,0	20	30	0,0	6	1,3	3,72	1,5	-5	5	0,0
	Pre-cycle 9 (n=6)	25,8	5,98	28,0	15	31	0,0	6	0,0	4,94	0,5	-9	6	0,0
	Pre-cycle 13 (n=5)	27,0	2,35	26,0	25	30	16,7	5	2,0	6,48	3,0	-7	11	16,7
	Pre-cycle 25 (n=1)	NC	NC	NC	30	30	83,3	1	NC	NC	NC	3	3	83,3
	Pre-cycle 37 (n=1)	NC	NC	NC	29	29	83,3	1	NC	NC	NC	2	2	83,3

[a] Children, ages 8 to 18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.1.1.3 PROMIS self-report scores over time and change from baseline over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=6) [a]												
		Absolute values						Change from baseline						
PROMIS self-report score: Upper extremity	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=6)	42,92	15,538	46,20	24,7	56,7	0,0							
	Pre-cycle 3 (n=6)	43,47	11,983	42,30	29,3	56,7	0,0	6	0,55	7,729	0,00	-8,7	11,9	0,0
	Pre-cycle 5 (n=6)	44,67	11,671	46,20	29,5	56,7	0,0	6	1,75	5,692	2,40	-7,9	7,9	0,0
	Pre-cycle 9 (n=6)	41,05	9,586	37,50	31,4	56,7	0,0	6	-1,87	10,583	-2,15	-17,5	11,1	0,0
	Pre-cycle 13 (n=5)	43,64	9,083	40,40	33,9	56,7	16,7	5	3,48	7,722	4,70	-7,9	11,4	16,7
	Pre-cycle 25 (n=1)	NC	NC	NC	37,2	37,2	83,3	1	NC	NC	NC	10,2	10,2	83,3
	Pre-cycle 37 (n=1)	NC	NC	NC	42,2	42,2	83,3	1	NC	NC	NC	15,2	15,2	83,3
Raw Score	Baseline (n=6)	24,3	8,98	27,0	12	32	0,0							
	Pre-cycle 3 (n=6)	26,0	6,23	26,0	20	32	0,0	6	1,7	3,93	0,0	-2	8	0,0
	Pre-cycle 5 (n=6)	27,2	5,81	29,5	18	32	0,0	6	2,8	3,92	3,0	-2	7	0,0
	Pre-cycle 9 (n=6)	25,0	5,48	24,0	19	32	0,0	6	0,7	6,22	-0,5	-7	11	0,0
	Pre-cycle 13 (n=5)	26,6	4,98	26,0	19	32	16,7	5	3,8	4,92	4,0	-2	10	16,7
	Pre-cycle 25 (n=1)	NC	NC	NC	26	26	83,3	1	NC	NC	NC	10	10	83,3
	Pre-cycle 37 (n=1)	NC	NC	NC	29	29	83,3	1	NC	NC	NC	13	13	83,3

[a] Children, ages 8 to 18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.1.1.4 PROMIS self-report scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=8) [a]											
		Absolute values						Change from baseline					
PROMIS self-report score: Mobility	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=8)	47,48	6,381	45,70	39,5	58,5	0,0							
	Pre-cycle 3 (n=7)	48,90	5,789	47,40	42,6	58,5	12,5	7	2,11	3,661	0,10	-1,5	9,2	12,5
	Pre-cycle 5 (n=8)	50,79	8,507	52,85	40,0	58,5	0,0	8	3,31	5,713	2,35	-3,4	14,4	0,0
	Pre-cycle 9 (n=8)	50,14	7,596	48,65	39,1	58,5	0,0	8	2,66	10,036	3,35	-13,2	15,7	0,0
	Pre-cycle 13 (n=7)	51,93	4,939	50,00	45,4	58,5	12,5	7	3,31	5,856	2,60	-3,5	14,4	12,5
	Pre-cycle 25 (n=7)	53,79	6,343	58,50	44,5	58,5	12,5	7	5,17	10,241	6,20	-14,0	15,5	12,5
Raw Score	Baseline (n=8)	28,5	2,93	29,0	24	32	0,0							
	Pre-cycle 3 (n=7)	29,1	2,79	30,0	24	32	12,5	7	1,0	2,94	0,0	-4	5	12,5
	Pre-cycle 5 (n=8)	29,0	3,59	30,5	23	32	0,0	8	0,5	1,60	0,0	-1	4	0,0
	Pre-cycle 9 (n=8)	29,8	2,76	30,5	24	32	0,0	8	1,3	4,06	2,0	-7	6	0,0
	Pre-cycle 13 (n=7)	30,9	1,07	31,0	29	32	12,5	7	1,7	2,29	1,0	-1	5	12,5
	Pre-cycle 25 (n=7)	31,0	1,41	32,0	29	32	12,5	7	1,9	2,91	2,0	-3	6	12,5

[a] Children, ages 8 to 18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.1.1.4 PROMIS self-report scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=8) [a]											
		Absolute values						Change from baseline					
PROMIS self-report score: Upper extremity	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=7)	48,83	11,169	56,70	30,1	56,7	12,5							
	Pre-cycle 3 (n=7)	53,03	6,273	56,70	43,5	56,7	12,5	7	4,20	5,679	0,00	0,0	14,1	12,5
	Pre-cycle 5 (n=8)	49,21	8,801	52,20	35,0	56,7	0,0	7	1,04	2,072	0,00	-0,6	4,9	12,5
	Pre-cycle 9 (n=8)	47,64	10,965	52,35	30,9	56,7	0,0	7	-2,49	11,607	0,00	-25,8	8,4	12,5
	Pre-cycle 13 (n=7)	53,20	9,260	56,70	32,2	56,7	12,5	6	1,75	3,364	0,00	0,0	8,4	25,0
	Pre-cycle 25 (n=7)	54,93	4,687	56,70	44,3	56,7	12,5	6	3,77	6,117	0,00	0,0	14,2	25,0
Raw Score	Baseline (n=7)	29,0	5,10	32,0	19	32	12,5							
	Pre-cycle 3 (n=7)	31,3	1,25	32,0	29	32	12,5	7	2,3	3,86	0,0	0	10	12,5
	Pre-cycle 5 (n=8)	28,4	5,73	31,5	17	32	0,0	7	-0,7	3,40	0,0	-8	3	12,5
	Pre-cycle 9 (n=8)	28,4	4,98	31,5	21	32	0,0	7	-1,1	4,45	0,0	-11	2	12,5
	Pre-cycle 13 (n=7)	30,4	4,16	32,0	21	32	12,5	6	0,5	0,84	0,0	0	2	25,0
	Pre-cycle 25 (n=7)	31,7	0,76	32,0	30	32	12,5	6	2,0	4,43	0,0	0	11	25,0

[a] Children, ages 8 to 18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.1.1.5 PROMIS self-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=10) [a]											
		Absolute values						Change from baseline					
PROMIS self-report score: Mobility	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=9)	46,74	5,548	47,30	38,4	58,5	10,0							
	Pre-cycle 3 (n=8)	47,39	7,938	45,95	35,5	58,5	20,0	8	2,11	5,793	0,85	-5,5	11,2	20,0
	Pre-cycle 5 (n=8)	47,79	6,840	45,05	41,6	58,5	20,0	8	2,51	5,422	2,40	-3,3	11,2	20,0
	Pre-cycle 9 (n=8)	47,19	5,813	46,45	40,4	58,5	20,0	8	1,91	4,786	1,50	-5,4	11,2	20,0
	Pre-cycle 13 (n=8)	47,24	7,734	45,70	38,3	58,5	20,0	8	1,96	5,874	-0,45	-3,1	11,2	20,0
	Pre-cycle 25 (n=6)	46,08	7,177	45,00	37,4	58,5	40,0	6	0,00	6,275	-1,15	-6,1	11,2	40,0
	Pre-cycle 37 (n=1)	NC	NC	NC	33,2	33,2	90,0	1	NC	NC	NC	-10,3	-10,3	90,0
Raw Score	Baseline (n=9)	27,6	4,56	30,0	19	32	10,0							
	Pre-cycle 3 (n=8)	28,1	4,22	29,0	19	32	20,0	8	1,1	3,64	0,5	-4	9	20,0
	Pre-cycle 5 (n=8)	28,1	3,23	28,0	23	32	20,0	8	1,1	2,80	1,5	-3	6	20,0
	Pre-cycle 9 (n=8)	28,9	2,36	28,5	25	32	20,0	8	1,9	3,14	1,5	-3	6	20,0
	Pre-cycle 13 (n=8)	27,9	3,87	29,0	22	32	20,0	8	0,9	1,55	1,0	-1	3	20,0
	Pre-cycle 25 (n=6)	27,8	4,17	29,0	20	32	40,0	6	0,0	1,67	-0,5	-2	2	40,0
	Pre-cycle 37 (n=1)	NC	NC	NC	17	17	90,0	1	NC	NC	NC	-4	-4	90,0

[a] Children, ages 8 to 18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

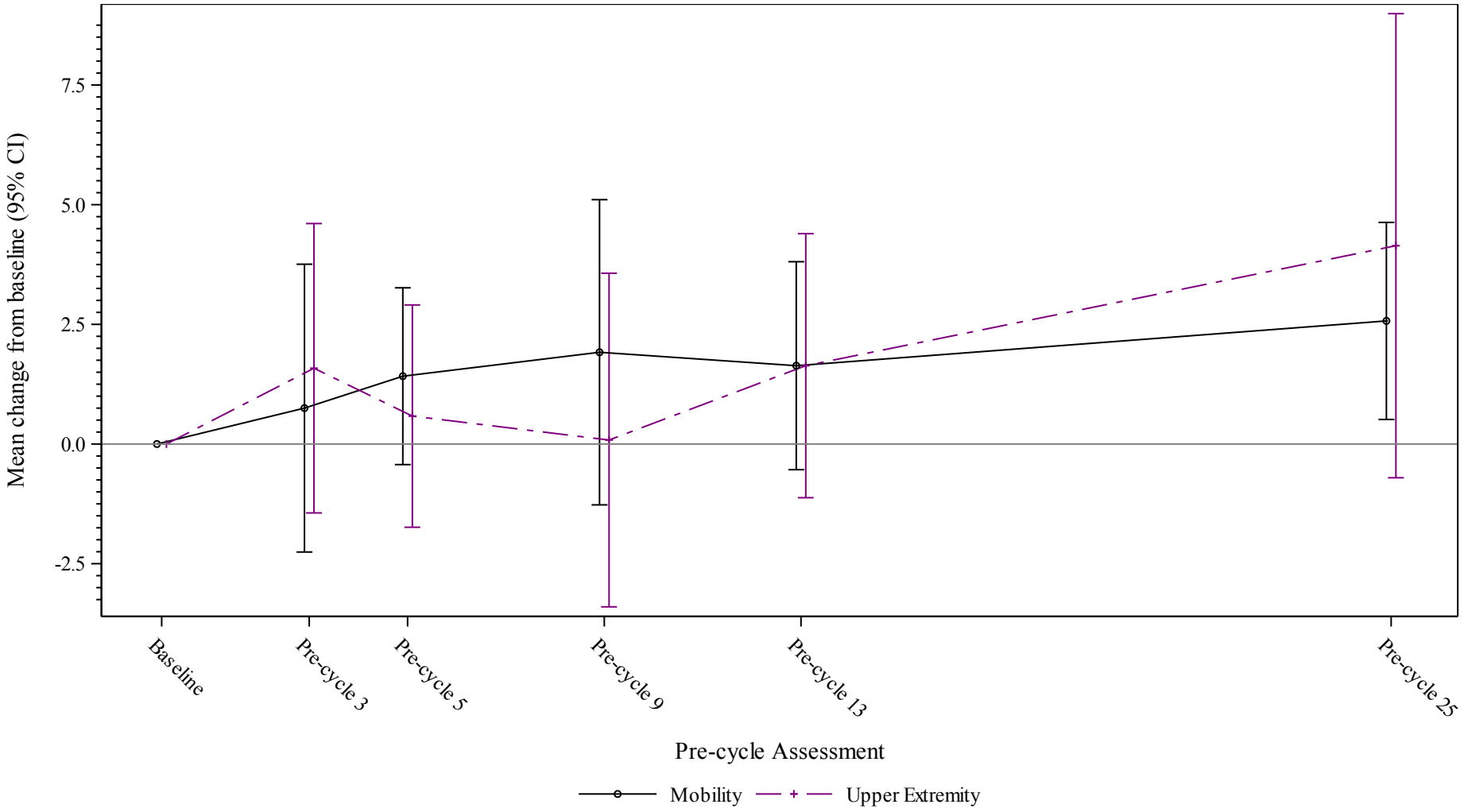
Table 2.5.1.1.5 PROMIS self-report scores over time and change from baseline over time - PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=10) [a]											
		Absolute values						Change from baseline					
PROMIS self-report score: Upper extremity	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=9)	45,73	13,368	48,30	20,4	56,7	10,0							
	Pre-cycle 3 (n=8)	41,33	14,554	44,45	18,7	56,7	20,0	8	-3,04	6,133	-0,15	-15,8	1,7	20,0
	Pre-cycle 5 (n=8)	42,08	12,388	41,05	21,9	56,7	20,0	8	-2,29	6,637	0,00	-16,5	4,3	20,0
	Pre-cycle 9 (n=8)	44,48	12,847	47,40	24,8	56,7	20,0	8	0,11	9,887	0,00	-19,9	13,5	20,0
	Pre-cycle 13 (n=8)	44,63	12,105	45,10	25,5	56,7	20,0	8	0,26	8,688	0,00	-16,7	10,8	20,0
	Pre-cycle 25 (n=6)	46,25	11,942	47,95	29,6	56,7	40,0	6	1,77	10,411	5,55	-18,1	9,2	40,0
Raw Score	Baseline (n=9)	26,9	8,22	31,0	9	32	10,0							
	Pre-cycle 3 (n=8)	25,0	9,77	30,0	9	32	20,0	8	-1,3	2,96	0,0	-8	1	20,0
	Pre-cycle 5 (n=8)	26,1	7,74	28,5	10	32	20,0	8	-0,1	2,10	0,0	-4	3	20,0
	Pre-cycle 9 (n=8)	26,6	7,52	30,5	13	32	20,0	8	0,4	3,58	0,0	-6	6	20,0
	Pre-cycle 13 (n=8)	26,4	7,84	30,0	14	32	20,0	8	0,1	3,44	0,0	-5	5	20,0
	Pre-cycle 25 (n=6)	28,0	5,83	30,0	17	32	40,0	6	1,3	4,23	1,0	-5	8	40,0

[a] Children, ages 8 to 18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Figure 2.5.1.2.1 Mean change from baseline of PROMIS self-report raw scores over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

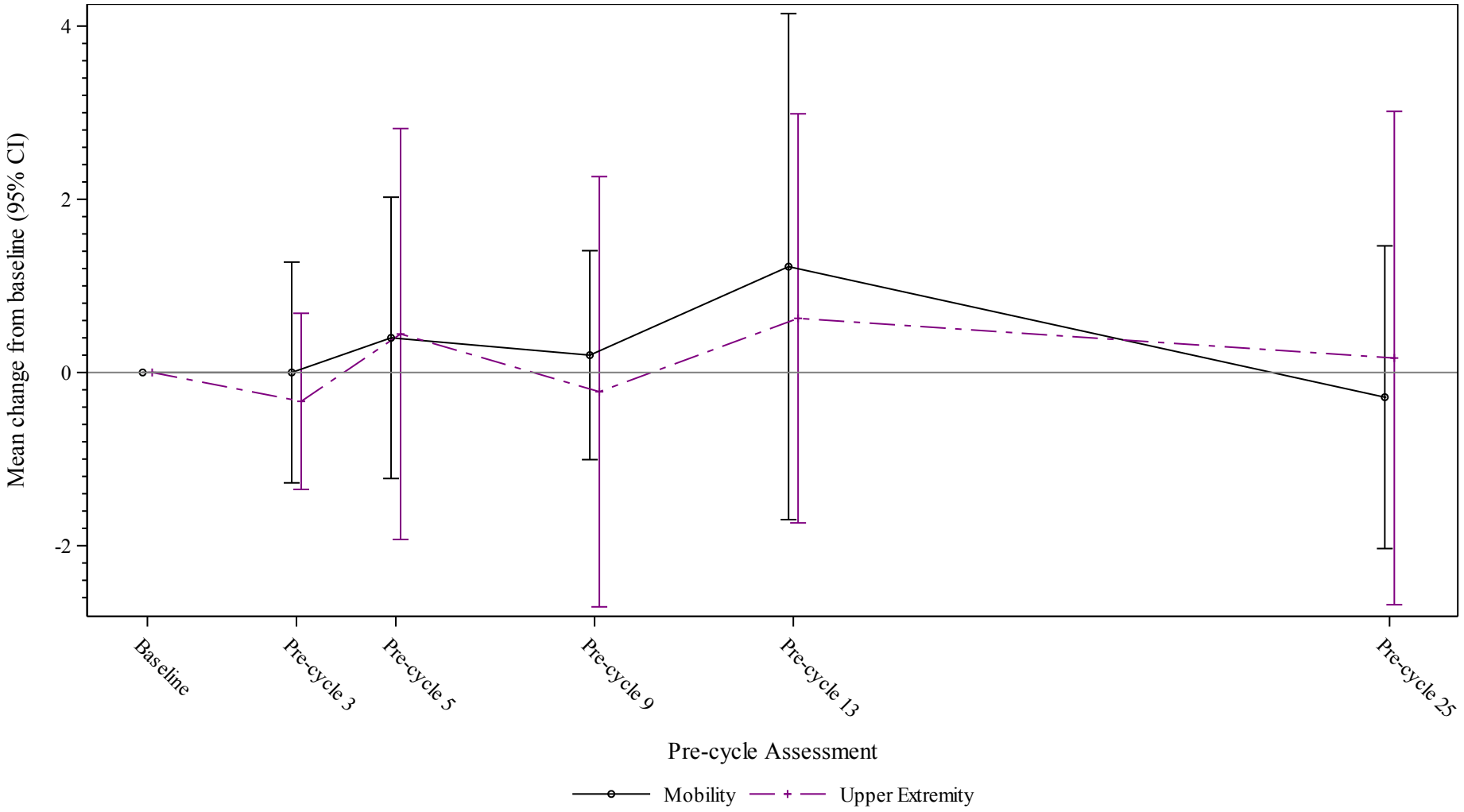
N = 14



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PROMIS.
CI = Confidence interval.

Figure 2.5.1.2.2 Mean change from baseline of PROMIS self-report raw scores over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

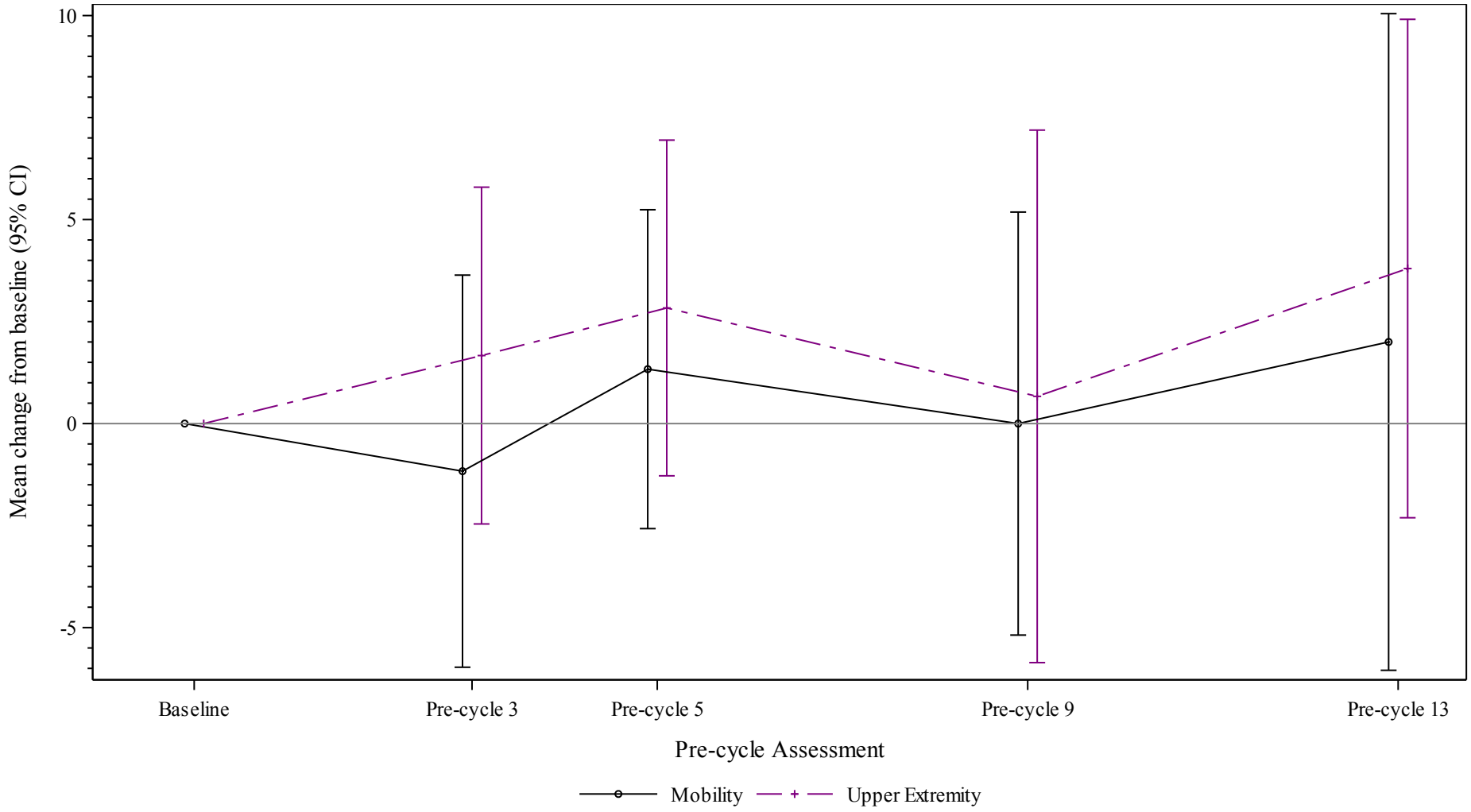
N = 10



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PROMIS.
CI = Confidence interval.

Figure 2.5.1.2.3 Mean change from baseline of PROMIS self-report raw scores over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

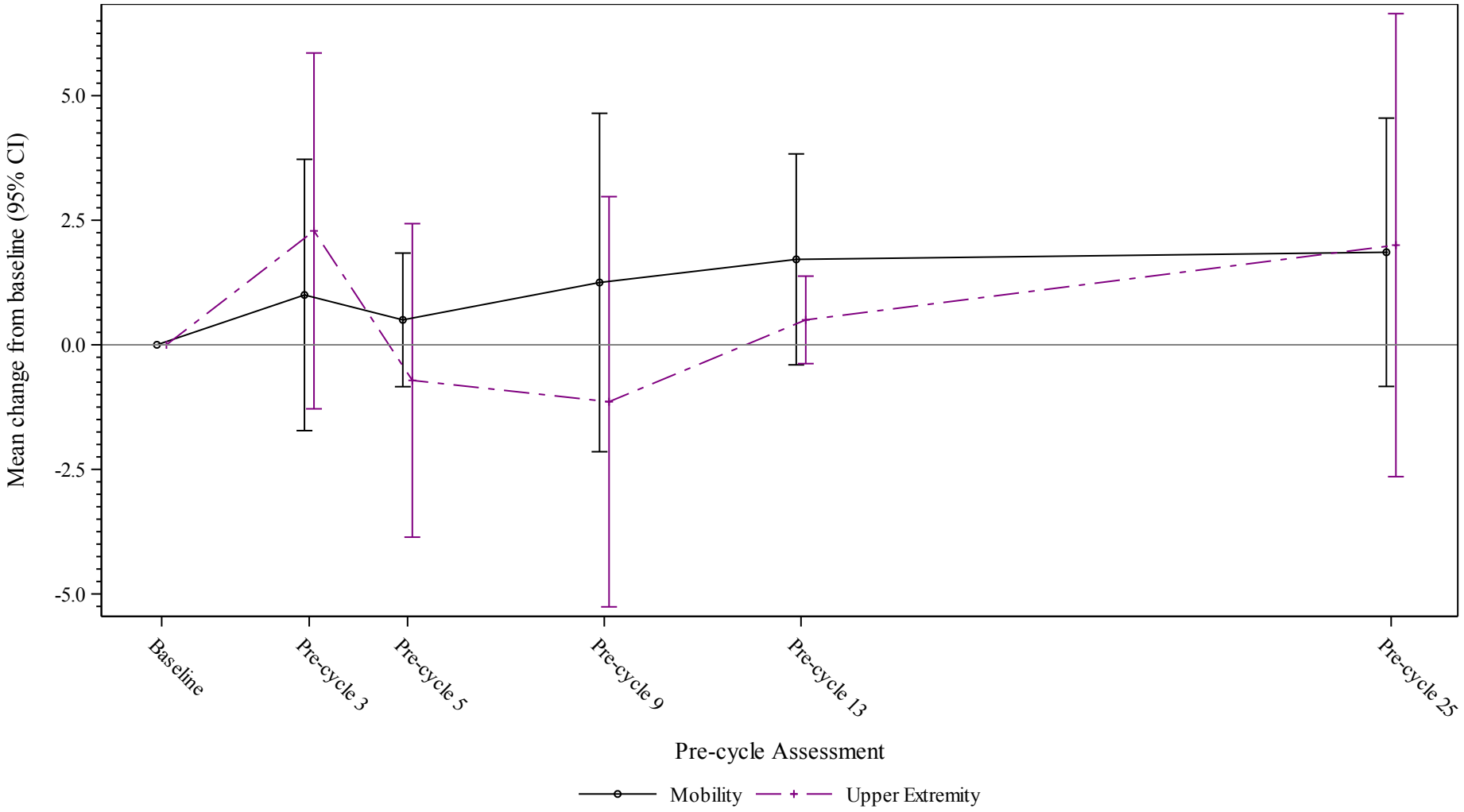
N = 6



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PROMIS.
CI = Confidence interval.

Figure 2.5.1.2.4 Mean change from baseline of PROMIS self-report raw scores over time - PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

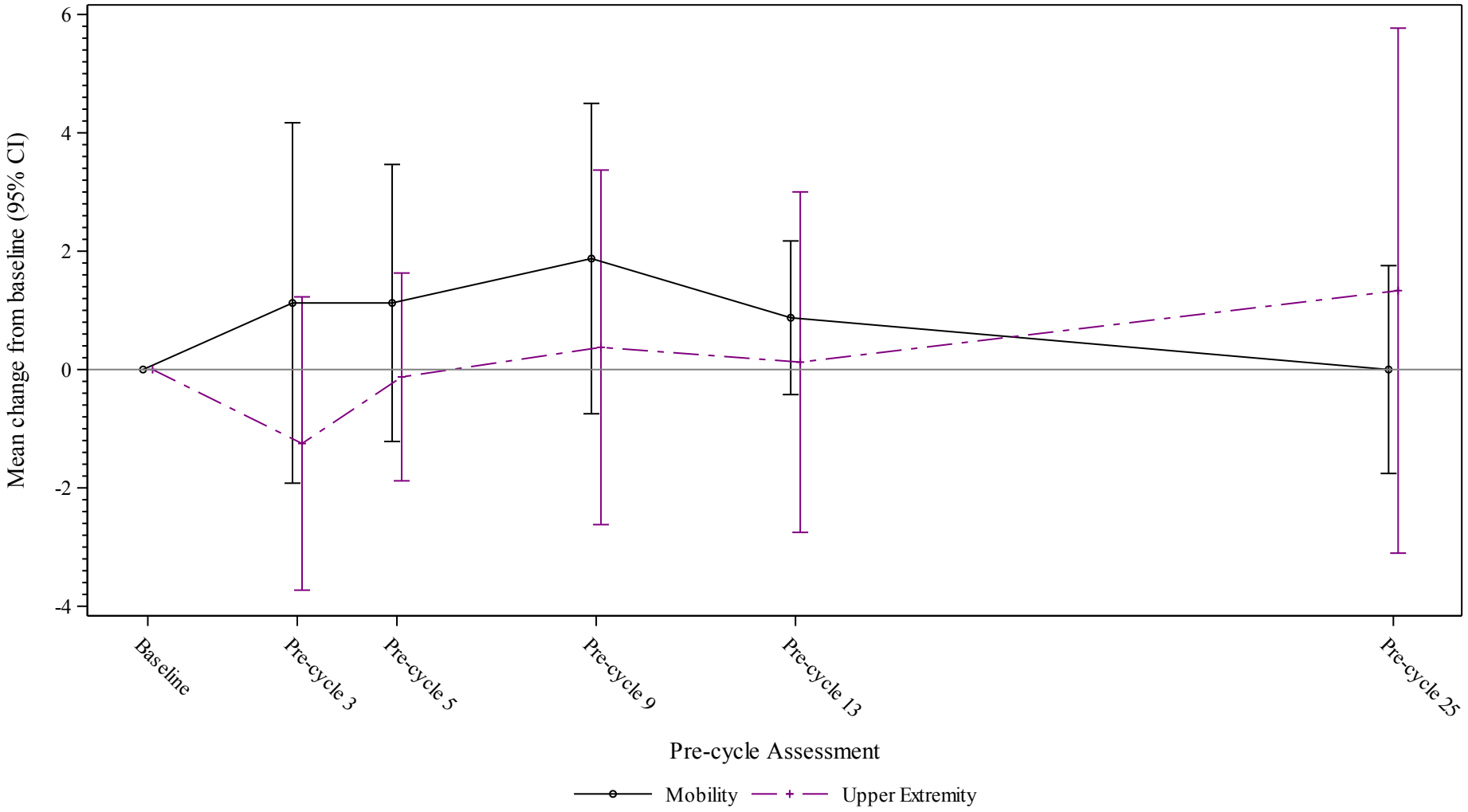
N = 8



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PROMIS.
CI = Confidence interval.

Figure 2.5.1.2.5 Mean change from baseline of PROMIS self-report raw scores over time - PN status at enrollment = Unknown
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 10



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PROMIS.
CI = Confidence interval.

Table 2.5.1.3.1 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=14) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=12)	Categories of change [d]			
		Improvement	3	25,0	5,5, 57,2
		No improvement	9	75,0	42,8, 94,5
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	2	16,7	2,1, 48,4
		No improvement	10	83,3	51,6, 97,9
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	1	9,1	0,2, 41,3
		No improvement	10	90,9	58,7, 99,8
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
	Overall (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1.3.1 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=14) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	2	16,7	2,1, 48,4
		No improvement	10	83,3	51,6, 97,9
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	1	8,3	0,2, 38,5
		No improvement	11	91,7	61,5, 99,8
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	3	42,9	9,9, 81,6
		No improvement	4	57,1	18,4, 90,1
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1.3.2 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=10) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=9)	Categories of change [d]			
		Improvement	0	0	0, 33,6
		No improvement	9	100	66,4, 100
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	1	11,1	0,3, 48,2
		No improvement	8	88,9	51,8, 99,7
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	0	0	0, 41,0
		No improvement	7	100	59,0, 100
	Overall (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1.3.2 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=10) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=9)	Categories of change [d]			
		Improvement	0	0	0, 33,6
		No improvement	9	100	66,4, 100
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	1	11,1	0,3, 48,2
		No improvement	8	88,9	51,8, 99,7
	Pre-cycle 9 (N=9)	Categories of change [d]			
		Improvement	1	11,1	0,3, 48,2
		No improvement	8	88,9	51,8, 99,7
	Pre-cycle 13 (N=8)	Categories of change [d]			
		Improvement	0	0	0, 36,9
		No improvement	8	100	63,1, 100
	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100
	Overall (N=9)	Categories of change [d]			
		Improvement	2	22,2	2,8, 60,0
		No improvement	7	77,8	40,0, 97,2

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1.3.3 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrollment = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=6) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	2	33,3	4,3, 77,7
		No improvement	4	66,7	22,3, 95,7
	Pre-cycle 9 (N=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Pre-cycle 13 (N=5)	Categories of change [d]			
		Improvement	1	20,0	0,5, 71,6
		No improvement	4	80,0	28,4, 99,5
	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=6)	Categories of change [d]			
		Improvement	2	33,3	4,3, 77,7
		No improvement	4	66,7	22,3, 95,7

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1.3.3 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrollment = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=6) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=6)	Categories of change [d]			
		Improvement	2	33,3	4,3, 77,7
		No improvement	4	66,7	22,3, 95,7
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	3	50,0	11,8, 88,2
		No improvement	3	50,0	11,8, 88,2
	Pre-cycle 9 (N=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Pre-cycle 13 (N=5)	Categories of change [d]			
		Improvement	2	40,0	5,3, 85,3
		No improvement	3	60,0	14,7, 94,7
	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=6)	Categories of change [d]			
		Improvement	3	50,0	11,8, 88,2
		No improvement	3	50,0	11,8, 88,2

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1.3.4 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrol. = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=8) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Pre-cycle 5 (N=8)	Categories of change [d]			
		Improvement	0	0	0, 36,9
		No improvement	8	100	63,1, 100
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	1	12,5	0,3, 52,7
		No improvement	7	87,5	47,3, 99,7
	Pre-cycle 13 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Overall (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1.3.4 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrol. = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=8) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=7)	Categories of change [d]			
		Improvement	2	28,6	3,7, 71,0
		No improvement	5	71,4	29,0, 96,3
	Pre-cycle 5 (N=7)	Categories of change [d]			
		Improvement	0	0	0, 41,0
		No improvement	7	100	59,0, 100
	Pre-cycle 9 (N=7)	Categories of change [d]			
		Improvement	0	0	0, 41,0
		No improvement	7	100	59,0, 100
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100
	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Overall (N=7)	Categories of change [d]			
		Improvement	2	28,6	3,7, 71,0
		No improvement	5	71,4	29,0, 96,3

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1.3.5 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrollment = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=10) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=8)	Categories of change [d]			
		Improvement	1	12,5	0,3, 52,7
		No improvement	7	87,5	47,3, 99,7
	Pre-cycle 5 (N=8)	Categories of change [d]			
		Improvement	1	12,5	0,3, 52,7
		No improvement	7	87,5	47,3, 99,7
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8
	Pre-cycle 13 (N=8)	Categories of change [d]			
		Improvement	0	0	0, 36,9
		No improvement	8	100	63,1, 100
	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.1.3.5 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrollment = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=10) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=8)	Categories of change [d]			
		Improvement	0	0	0, 36,9
		No improvement	8	100	63,1, 100
	Pre-cycle 5 (N=8)	Categories of change [d]			
		Improvement	0	0	0, 36,9
		No improvement	8	100	63,1, 100
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	1	12,5	0,3, 52,7
		No improvement	7	87,5	47,3, 99,7
	Pre-cycle 13 (N=8)	Categories of change [d]			
		Improvement	1	12,5	0,3, 52,7
		No improvement	7	87,5	47,3, 99,7
	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Overall (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. [d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=33) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=30)	Categories of change [d]			
		Improvement	5	16,7	5,6, 34,7
		No improvement	25	83,3	65,3, 94,4
	Pre-cycle 5 (N=30)	Categories of change [d]			
		Improvement	9	30,0	14,7, 49,4
		No improvement	21	70,0	50,6, 85,3
	Pre-cycle 9 (N=31)	Categories of change [d]			
		Improvement	10	32,3	16,7, 51,4
		No improvement	21	67,7	48,6, 83,3
	Pre-cycle 13 (N=28)	Categories of change [d]			
		Improvement	9	32,1	15,9, 52,4
		No improvement	19	67,9	47,6, 84,1
	Pre-cycle 25 (N=19)	Categories of change [d]			
		Improvement	6	31,6	12,6, 56,6
		No improvement	13	68,4	43,4, 87,4
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=31)	Categories of change [d]			
		Improvement	16	51,6	33,1, 69,8
		No improvement	15	48,4	30,2, 66,9

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=33) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=30)	Categories of change [d]			
		Improvement	2	6,7	0,8, 22,1
		No improvement	28	93,3	77,9, 99,2
	Pre-cycle 5 (N=29)	Categories of change [d]			
		Improvement	3	10,3	2,2, 27,4
		No improvement	26	89,7	72,6, 97,8
	Pre-cycle 9 (N=30)	Categories of change [d]			
		Improvement	5	16,7	5,6, 34,7
		No improvement	25	83,3	65,3, 94,4
	Pre-cycle 13 (N=27)	Categories of change [d]			
		Improvement	6	22,2	8,6, 42,3
		No improvement	21	77,8	57,7, 91,4
	Pre-cycle 25 (N=18)	Categories of change [d]			
		Improvement	3	16,7	3,6, 41,4
		No improvement	15	83,3	58,6, 96,4
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=30)	Categories of change [d]			
		Improvement	10	33,3	17,3, 52,8
		No improvement	20	66,7	47,2, 82,7

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2.1.1 PROMIS parent-report scores over time and change from baseline over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=19) [a]												
		Absolute values						Change from baseline						
PROMIS parent-report score: Mobility	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=18)	35,75	6,440	36,75	19,8	44,9	5,3							
	Pre-cycle 3 (n=18)	38,38	6,012	40,35	27,5	48,6	5,3	17	2,87	2,331	2,40	-0,5	7,7	10,5
	Pre-cycle 5 (n=18)	39,37	9,271	38,35	17,5	56,5	5,3	17	3,79	5,344	3,40	-2,7	16,0	10,5
	Pre-cycle 9 (n=18)	39,38	8,917	39,00	17,5	56,5	5,3	17	3,59	5,866	2,60	-4,1	18,5	10,5
	Pre-cycle 13 (n=17)	40,24	9,862	38,30	21,1	56,5	10,5	16	3,72	4,926	2,75	-3,4	15,4	15,8
	Pre-cycle 25 (n=11)	41,44	7,566	41,20	28,0	56,5	42,1	10	4,36	4,687	3,10	0,1	13,5	47,4
	Pre-cycle 37 (n=1)	NC	NC	NC	38,9	38,9	94,7	1	NC	NC	NC	4,5	4,5	94,7
Raw Score	Baseline (n=18)	21,2	7,45	21,0	3	30	5,3							
	Pre-cycle 3 (n=18)	24,0	6,05	25,5	10	31	5,3	17	3,1	2,49	3,0	-1	8	10,5
	Pre-cycle 5 (n=18)	24,1	7,82	24,5	0	32	5,3	17	3,1	3,73	4,0	-3	9	10,5
	Pre-cycle 9 (n=18)	24,3	7,42	25,5	1	32	5,3	17	3,2	3,95	3,0	-5	11	10,5
	Pre-cycle 13 (n=17)	24,0	7,50	23,0	4	32	10,5	16	2,8	2,93	2,5	-3	8	15,8
	Pre-cycle 25 (n=11)	26,1	6,43	28,0	11	32	42,1	10	3,2	2,78	2,5	0	10	47,4
	Pre-cycle 37 (n=1)	NC	NC	NC	25	25	94,7	1	NC	NC	NC	5	5	94,7

[a] Parents/legal guardians of children from 5 to 18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.2.1.1 PROMIS parent-report scores over time and change from baseline over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=19) [a]											
		Absolute values						Change from baseline					
PROMIS parent-report score: Upper extremity	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=18)	35,18	12,934	31,40	14,0	54,8	5,3							
	Pre-cycle 3 (n=18)	36,18	12,370	34,30	16,6	54,8	5,3	17	1,83	7,615	2,30	-20,9	15,5	10,5
	Pre-cycle 5 (n=18)	36,03	12,234	34,70	16,6	54,8	5,3	17	2,08	3,712	0,10	-1,9	10,5	10,5
	Pre-cycle 9 (n=18)	34,81	11,201	34,00	15,8	54,8	5,3	17	-0,40	7,907	2,50	-25,3	6,9	10,5
	Pre-cycle 13 (n=17)	37,20	12,804	36,30	14,0	54,8	10,5	16	1,80	6,563	1,60	-16,7	12,9	15,8
	Pre-cycle 25 (n=11)	37,46	11,009	39,30	18,0	54,8	42,1	10	3,69	4,070	3,15	-1,4	10,5	47,4
	Pre-cycle 37 (n=1)	NC	NC	NC	29,7	29,7	94,7	1	NC	NC	NC	6,1	6,1	94,7
Raw Score	Baseline (n=18)	21,4	10,32	24,0	0	32	5,3							
	Pre-cycle 3 (n=18)	22,2	9,90	24,0	1	32	5,3	17	0,9	3,98	1,0	-8	8	10,5
	Pre-cycle 5 (n=18)	22,6	9,91	25,0	1	32	5,3	17	1,5	3,04	1,0	-3	11	10,5
	Pre-cycle 9 (n=18)	22,2	9,53	24,5	1	32	5,3	17	0,9	6,73	1,0	-17	10	10,5
	Pre-cycle 13 (n=17)	24,1	10,05	28,0	0	32	10,5	16	2,7	4,33	1,0	-4	10	15,8
	Pre-cycle 25 (n=11)	25,2	8,78	30,0	2	32	42,1	10	3,1	3,70	1,5	0	10	47,4
	Pre-cycle 37 (n=1)	NC	NC	NC	22	22	94,7	1	NC	NC	NC	11	11	94,7

[a] Parents/legal guardians of children from 5 to 18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.2.1.2 PROMIS parent-report scores over time and change from baseline over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
PROMIS parent-report score: Mobility	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=14)	39,60	8,042	38,30	30,7	56,5	0,0							
	Pre-cycle 3 (n=13)	39,25	6,468	39,40	29,9	56,5	7,1	13	0,95	3,383	0,80	-3,9	10,0	7,1
	Pre-cycle 5 (n=13)	39,23	6,457	39,70	27,7	48,6	7,1	13	-0,92	5,416	-0,70	-9,7	10,8	7,1
	Pre-cycle 9 (n=14)	40,47	5,142	41,15	30,9	46,8	0,0	14	0,87	5,449	2,50	-9,7	9,0	0,0
	Pre-cycle 13 (n=12)	42,43	7,725	41,30	30,8	56,5	14,3	12	2,12	3,454	1,15	-1,4	10,6	14,3
	Pre-cycle 25 (n=9)	44,96	7,234	42,70	34,8	56,5	35,7	9	4,68	6,055	3,40	-3,7	17,9	35,7
Raw Score	Baseline (n=14)	24,2	5,41	24,5	15	32	0,0							
	Pre-cycle 3 (n=13)	24,7	5,54	26,0	12	32	7,1	13	1,1	3,62	1,0	-3	10	7,1
	Pre-cycle 5 (n=13)	24,8	6,60	26,0	11	31	7,1	13	0,2	4,38	0,0	-7	9	7,1
	Pre-cycle 9 (n=14)	26,2	5,15	27,5	16	31	0,0	14	2,0	4,17	1,5	-8	10	0,0
	Pre-cycle 13 (n=12)	27,0	4,55	27,5	16	32	14,3	12	2,3	3,63	1,0	-2	11	14,3
	Pre-cycle 25 (n=9)	28,8	3,38	29,0	21	32	35,7	9	3,6	4,50	4,0	-5	10	35,7

[a] Parents/legal guardians of children from 5 to 18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.2.1.2 PROMIS parent-report scores over time and change from baseline over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]											
		Absolute values						Change from baseline					
PROMIS parent-report score: Upper extremity	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=13)	42,25	10,643	44,30	25,9	54,8	7,1							
	Pre-cycle 3 (n=13)	39,30	10,644	40,00	25,4	54,8	7,1	13	-2,95	5,100	-1,40	-13,5	6,8	7,1
	Pre-cycle 5 (n=13)	42,04	11,192	45,00	23,7	54,8	7,1	12	-1,04	6,059	-0,60	-13,5	8,9	14,3
	Pre-cycle 9 (n=14)	42,90	10,841	42,80	26,1	54,8	0,0	13	-0,26	6,180	0,00	-13,5	8,9	7,1
	Pre-cycle 13 (n=12)	45,37	10,889	50,35	27,5	54,8	14,3	11	1,92	6,839	0,70	-8,4	17,9	21,4
	Pre-cycle 25 (n=9)	48,11	10,527	54,80	30,1	54,8	35,7	8	5,50	6,950	4,55	-3,3	17,9	42,9
Raw Score	Baseline (n=13)	26,9	6,69	30,0	13	32	7,1							
	Pre-cycle 3 (n=13)	25,5	7,11	29,0	12	32	7,1	13	-1,5	2,85	-1,0	-9	2	7,1
	Pre-cycle 5 (n=13)	27,1	6,78	31,0	10	32	7,1	12	0,0	2,17	0,0	-3	5	14,3
	Pre-cycle 9 (n=14)	27,5	6,31	31,0	15	32	0,0	13	0,2	3,35	0,0	-8	5	7,1
	Pre-cycle 13 (n=12)	28,3	5,35	31,5	17	32	14,3	11	0,3	2,10	0,0	-3	4	21,4
	Pre-cycle 25 (n=9)	29,7	4,12	32,0	22	32	35,7	8	2,3	3,06	1,5	0	9	42,9

[a] Parents/legal guardians of children from 5 to 18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.2.1.3 PROMIS parent-report scores over time and change from baseline over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
PROMIS parent-report score: Mobility	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=10)	36,98	4,253	37,65	30,7	44,9	9,1							
	Pre-cycle 3 (n=11)	39,55	4,535	40,10	29,9	46,8	0,0	10	2,45	3,660	1,90	-2,6	10,0	9,1
	Pre-cycle 5 (n=10)	39,85	6,105	41,55	28,7	46,8	9,1	9	2,01	4,080	2,30	-5,8	6,4	18,2
	Pre-cycle 9 (n=11)	41,03	6,618	40,20	31,1	56,5	0,0	10	3,48	5,749	2,45	-4,8	16,1	9,1
	Pre-cycle 13 (n=10)	40,76	7,592	38,25	30,8	56,5	9,1	9	2,32	4,030	0,80	-2,0	10,6	18,2
	Pre-cycle 25 (n=5)	40,70	4,374	41,50	34,8	46,8	54,5	4	2,73	5,368	2,80	-3,7	9,0	63,6
	Pre-cycle 37 (n=1)	NC	NC	NC	38,9	38,9	90,9	1	NC	NC	NC	4,5	4,5	90,9
Raw Score	Baseline (n=10)	22,7	4,60	21,5	16	30	9,1							
	Pre-cycle 3 (n=11)	25,8	4,31	27,0	15	31	0,0	10	2,9	3,93	2,5	-3	10	9,1
	Pre-cycle 5 (n=10)	25,6	6,36	28,5	12	31	9,1	9	2,0	5,17	2,0	-7	9	18,2
	Pre-cycle 9 (n=11)	26,2	4,73	26,0	16	32	0,0	10	3,0	5,03	4,5	-8	10	9,1
	Pre-cycle 13 (n=10)	25,3	5,50	24,5	16	32	9,1	9	2,4	4,13	1,0	-2	11	18,2
	Pre-cycle 25 (n=5)	27,0	4,00	29,0	21	31	54,5	4	3,3	6,24	4,0	-5	10	63,6
	Pre-cycle 37 (n=1)	NC	NC	NC	25	25	90,9	1	NC	NC	NC	5	5	90,9

[a] Parents/legal guardians of children from 5 to 18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.2.1.3 PROMIS parent-report scores over time and change from baseline over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
PROMIS parent-report score: Upper extremity	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=10)	39,04	12,189	33,50	23,6	54,8	9,1							
	Pre-cycle 3 (n=11)	36,07	8,609	34,70	21,4	54,8	0,0	10	-3,52	8,409	-1,40	-20,9	7,8	9,1
	Pre-cycle 5 (n=10)	37,31	10,137	34,70	24,9	54,8	9,1	9	-0,78	5,734	0,00	-13,5	8,2	18,2
	Pre-cycle 9 (n=11)	37,91	9,363	35,00	28,0	54,8	0,0	10	-2,82	9,839	0,10	-25,3	6,1	9,1
	Pre-cycle 13 (n=10)	39,96	9,865	37,75	29,0	54,8	9,1	9	1,02	8,142	2,30	-16,7	12,9	18,2
	Pre-cycle 25 (n=5)	36,42	11,155	30,10	28,8	54,8	54,5	4	2,58	6,039	1,90	-3,3	9,8	63,6
	Pre-cycle 37 (n=1)	NC	NC	NC	29,7	29,7	90,9	1	NC	NC	NC	6,1	6,1	90,9
Raw Score	Baseline (n=10)	24,0	8,07	25,5	11	32	9,1							
	Pre-cycle 3 (n=11)	23,8	7,57	24,0	7	32	0,0	10	-0,9	5,34	-1,0	-9	8	9,1
	Pre-cycle 5 (n=10)	24,9	6,40	25,0	12	32	9,1	9	1,2	3,90	1,0	-3	11	18,2
	Pre-cycle 9 (n=11)	25,0	6,16	27,0	15	32	0,0	10	0,3	8,17	1,0	-17	9	9,1
	Pre-cycle 13 (n=10)	26,6	5,15	27,5	19	32	9,1	9	2,9	4,96	1,0	-3	10	18,2
	Pre-cycle 25 (n=5)	25,4	5,18	22,0	21	32	54,5	4	4,0	4,32	3,0	0	10	63,6
	Pre-cycle 37 (n=1)	NC	NC	NC	22	22	90,9	1	NC	NC	NC	11	11	90,9

[a] Parents/legal guardians of children from 5 to 18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.2.1.4 PROMIS parent-report scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
PROMIS parent-report score: Mobility	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=11)	37,80	8,043	35,90	27,3	56,5	0,0							
	Pre-cycle 3 (n=10)	37,49	6,091	37,20	28,9	48,6	9,1	10	1,56	2,854	1,45	-3,9	5,5	9,1
	Pre-cycle 5 (n=11)	38,15	5,983	37,80	27,7	46,8	0,0	11	0,35	5,220	0,00	-9,7	10,8	0,0
	Pre-cycle 9 (n=11)	40,38	7,440	40,20	30,9	56,5	0,0	11	2,58	6,899	2,70	-9,7	18,5	0,0
	Pre-cycle 13 (n=9)	42,98	8,907	40,30	30,6	56,5	18,2	9	3,91	4,650	3,20	-3,4	12,2	18,2
	Pre-cycle 25 (n=8)	44,59	9,386	44,15	28,0	56,5	27,3	8	4,90	5,083	3,30	0,0	13,5	27,3
Raw Score	Baseline (n=11)	22,5	6,64	21,0	10	32	0,0							
	Pre-cycle 3 (n=10)	22,7	6,34	23,0	12	31	9,1	10	1,1	2,47	1,0	-3	4	9,1
	Pre-cycle 5 (n=11)	23,9	6,14	24,0	11	31	0,0	11	1,4	4,11	0,0	-4	9	0,0
	Pre-cycle 9 (n=11)	25,2	5,19	25,0	16	32	0,0	11	2,6	3,67	3,0	-5	8	0,0
	Pre-cycle 13 (n=9)	26,4	5,53	27,0	15	32	18,2	9	2,8	3,31	2,0	-3	8	18,2
	Pre-cycle 25 (n=8)	27,1	7,06	29,5	11	32	27,3	8	3,1	3,31	2,0	0	10	27,3

[a] Parents/legal guardians of children from 5 to 18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.2.1.4 PROMIS parent-report scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
PROMIS parent-report score: Upper extremity	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=10)	35,89	11,761	38,75	14,0	54,8	9,1							
	Pre-cycle 3 (n=10)	39,25	13,529	40,80	16,6	54,8	9,1	10	3,36	6,170	2,45	-5,9	15,5	9,1
	Pre-cycle 5 (n=11)	40,13	13,887	39,30	17,6	54,8	0,0	10	2,77	4,526	1,00	-2,2	10,5	9,1
	Pre-cycle 9 (n=11)	38,85	12,701	37,00	16,6	54,8	0,0	10	1,36	6,257	1,35	-12,9	8,9	9,1
	Pre-cycle 13 (n=9)	42,58	13,928	39,90	14,0	54,8	18,2	8	3,14	4,466	0,85	-1,0	10,5	27,3
	Pre-cycle 25 (n=8)	42,49	12,693	41,80	18,0	54,8	27,3	7	3,96	3,803	3,80	0,0	10,5	36,4
Raw Score	Baseline (n=10)	22,9	10,72	29,0	0	32	9,1							
	Pre-cycle 3 (n=10)	24,1	10,29	29,5	1	32	9,1	10	1,2	1,55	1,0	-2	4	9,1
	Pre-cycle 5 (n=11)	24,4	10,46	30,0	2	32	0,0	10	0,7	1,83	0,5	-3	4	9,1
	Pre-cycle 9 (n=11)	24,6	9,76	29,0	1	32	0,0	10	1,0	4,67	1,0	-9	10	9,1
	Pre-cycle 13 (n=9)	26,7	10,34	30,0	0	32	18,2	8	1,3	2,76	0,0	0	8	27,3
	Pre-cycle 25 (n=8)	26,8	10,26	30,5	2	32	27,3	7	2,1	3,13	1,0	0	9	36,4

[a] Parents/legal guardians of children from 5 to 18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.5.2.1.5 PROMIS parent-report scores over time and change from baseline over time - PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
PROMIS parent-report score: Mobility	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=11)	37,48	9,215	38,60	19,8	56,5	0,0							
	Pre-cycle 3 (n=10)	39,11	7,876	40,40	27,5	56,5	9,1	10	2,11	2,437	2,20	-1,1	7,7	9,1
	Pre-cycle 5 (n=10)	40,06	11,761	39,25	17,5	56,5	9,1	10	3,06	7,652	2,25	-7,9	16,0	9,1
	Pre-cycle 9 (n=10)	38,00	8,569	41,45	17,5	46,8	9,1	10	1,00	4,574	2,00	-9,7	7,0	9,1
	Pre-cycle 13 (n=10)	39,88	10,779	39,50	21,1	56,5	9,1	10	2,88	4,693	1,80	-0,9	15,4	9,1
	Pre-cycle 25 (n=7)	42,89	7,217	42,70	32,0	56,5	36,4	7	5,09	5,887	3,20	0,1	17,9	36,4
Raw Score	Baseline (n=11)	22,3	8,74	25,0	3	32	0,0							
	Pre-cycle 3 (n=10)	24,2	6,63	26,5	10	32	9,1	10	2,6	2,84	3,0	-2	7	9,1
	Pre-cycle 5 (n=10)	23,7	9,44	26,0	0	32	9,1	10	2,1	3,78	3,0	-4	7	9,1
	Pre-cycle 9 (n=10)	24,0	9,37	28,0	1	31	9,1	10	2,4	3,69	1,5	-2	11	9,1
	Pre-cycle 13 (n=10)	24,1	8,49	27,0	4	32	9,1	10	2,5	2,37	2,5	-1	6	9,1
	Pre-cycle 25 (n=7)	27,7	4,57	29,0	18	32	36,4	7	3,7	2,50	4,0	0	8	36,4

[a] Parents/legal guardians of children from 5 to 18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

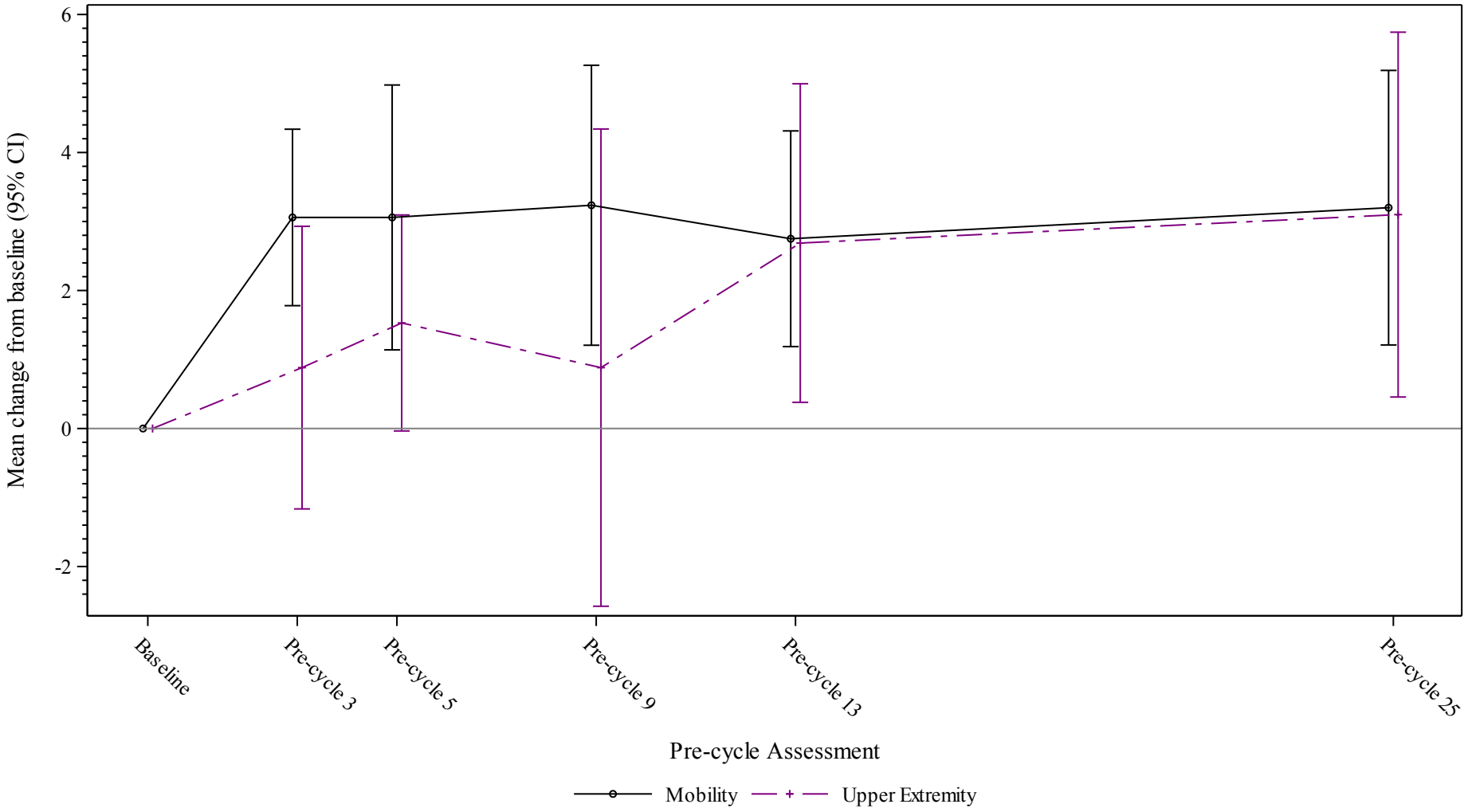
Table 2.5.2.1.5 PROMIS parent-report scores over time and change from baseline over time - PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
PROMIS parent-report score: Upper extremity	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Transformed Score	Baseline (n=11)	39,38	13,863	36,90	18,2	54,8	0,0							
	Pre-cycle 3 (n=10)	37,28	13,302	34,15	21,0	54,8	9,1	10	-0,56	4,603	0,00	-9,2	8,4	9,1
	Pre-cycle 5 (n=10)	38,06	12,567	38,00	16,6	54,8	9,1	10	0,22	4,483	0,00	-8,9	9,0	9,1
	Pre-cycle 9 (n=10)	38,28	13,671	37,20	15,8	54,8	9,1	10	0,44	3,925	0,00	-6,8	7,4	9,1
	Pre-cycle 13 (n=10)	39,40	14,586	36,10	14,0	54,8	9,1	10	1,56	6,861	0,35	-8,4	17,9	9,1
	Pre-cycle 25 (n=7)	46,16	11,231	54,80	30,9	54,8	36,4	7	6,13	6,710	5,30	0,0	17,9	36,4
Raw Score	Baseline (n=11)	24,2	9,74	28,0	4	32	0,0							
	Pre-cycle 3 (n=10)	22,7	9,53	26,0	7	32	9,1	10	-0,7	3,09	0,0	-6	4	9,1
	Pre-cycle 5 (n=10)	24,2	10,03	29,0	1	32	9,1	10	0,8	2,66	0,0	-3	5	9,1
	Pre-cycle 9 (n=10)	23,9	10,24	29,0	1	32	9,1	10	0,5	2,64	0,0	-3	4	9,1
	Pre-cycle 13 (n=10)	24,4	10,16	28,0	0	32	9,1	10	1,0	3,23	0,5	-4	7	9,1
	Pre-cycle 25 (n=7)	29,0	4,51	32,0	22	32	36,4	7	2,6	3,36	1,0	0	9	36,4

[a] Parents/legal guardians of children from 5 to 18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy PROMIS.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Figure 2.5.2.2.1 Mean change from baseline of PROMIS parent-report raw scores over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

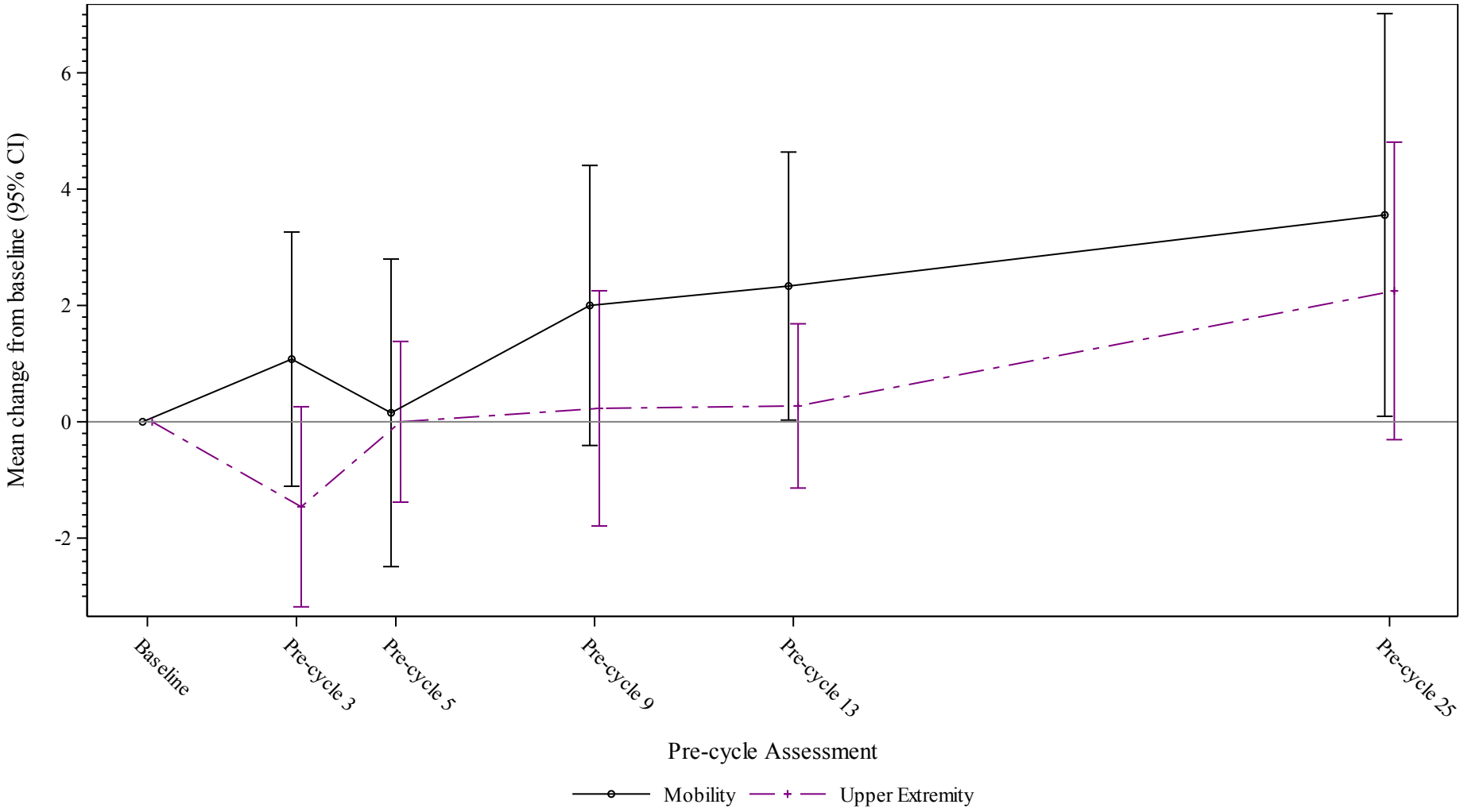
N = 19



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PROMIS.
CI = Confidence interval.

Figure 2.5.2.2.2 Mean change from baseline of PROMIS parent-report raw scores over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

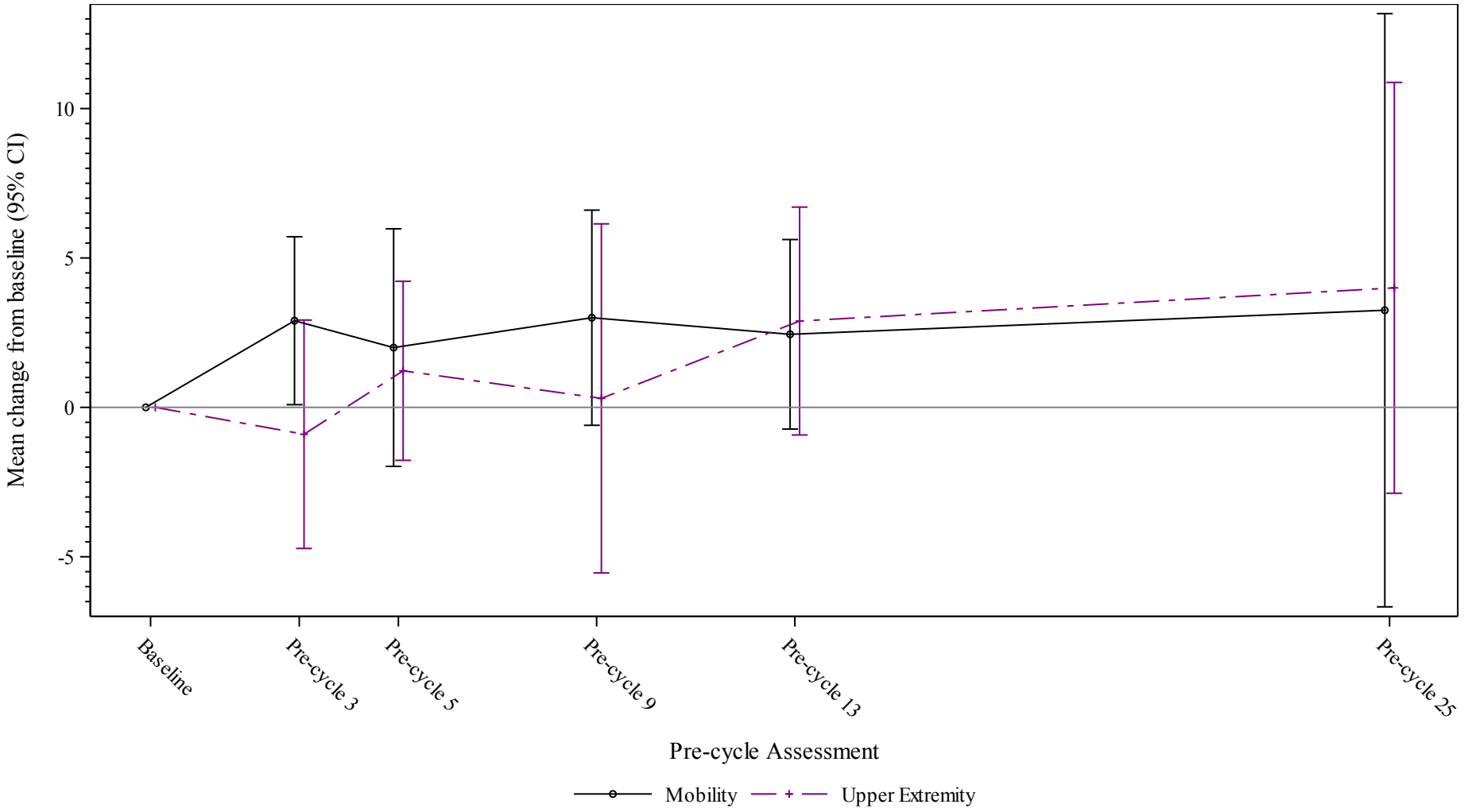
N = 14



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PROMIS.
CI = Confidence interval.

Figure 2.5.2.2.3 Mean change from baseline of PROMIS parent-report raw scores over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

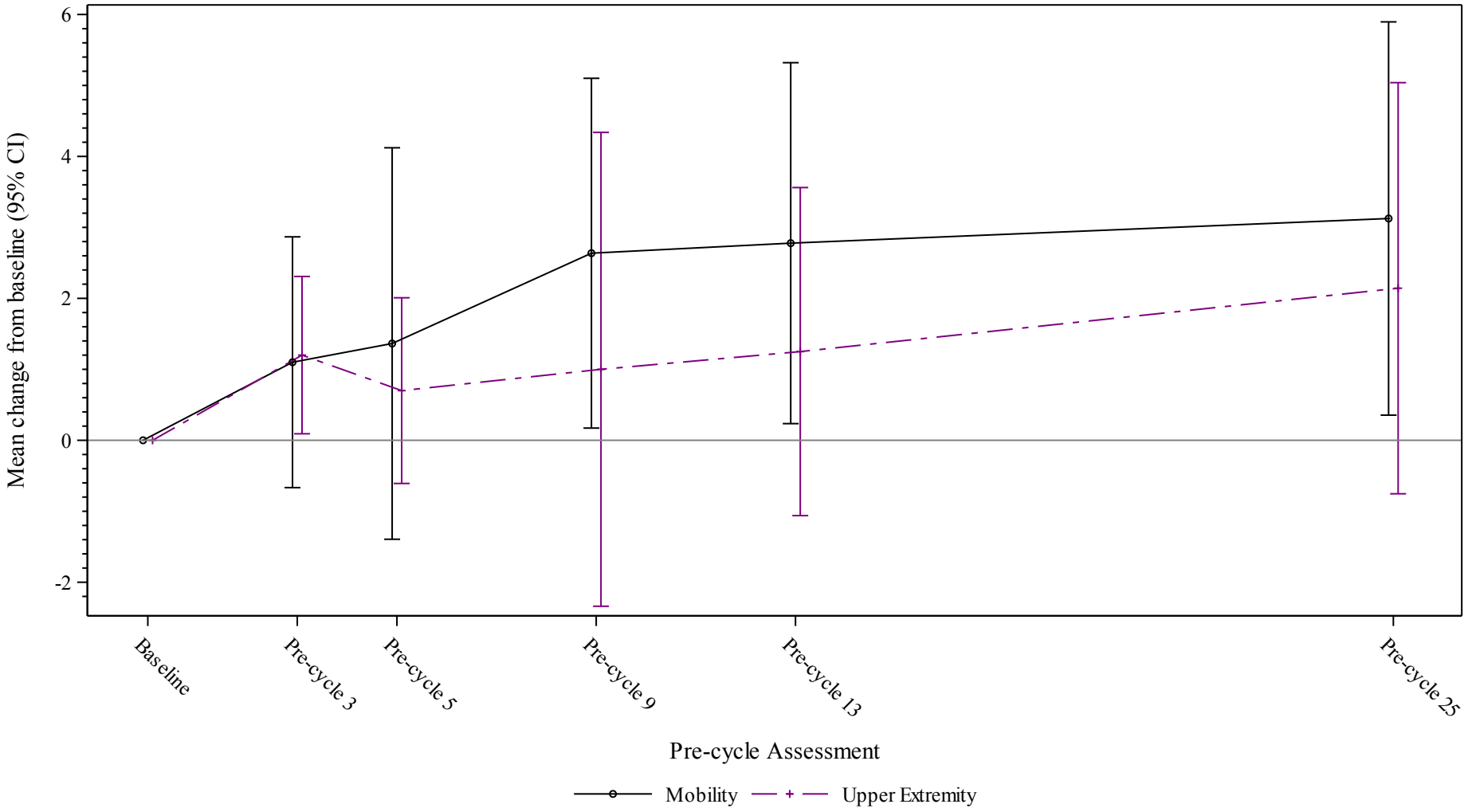
N = 11



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PROMIS.
CI = Confidence interval.

Figure 2.5.2.2.4 Mean change from baseline of PROMIS parent-report raw scores over time - PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 11

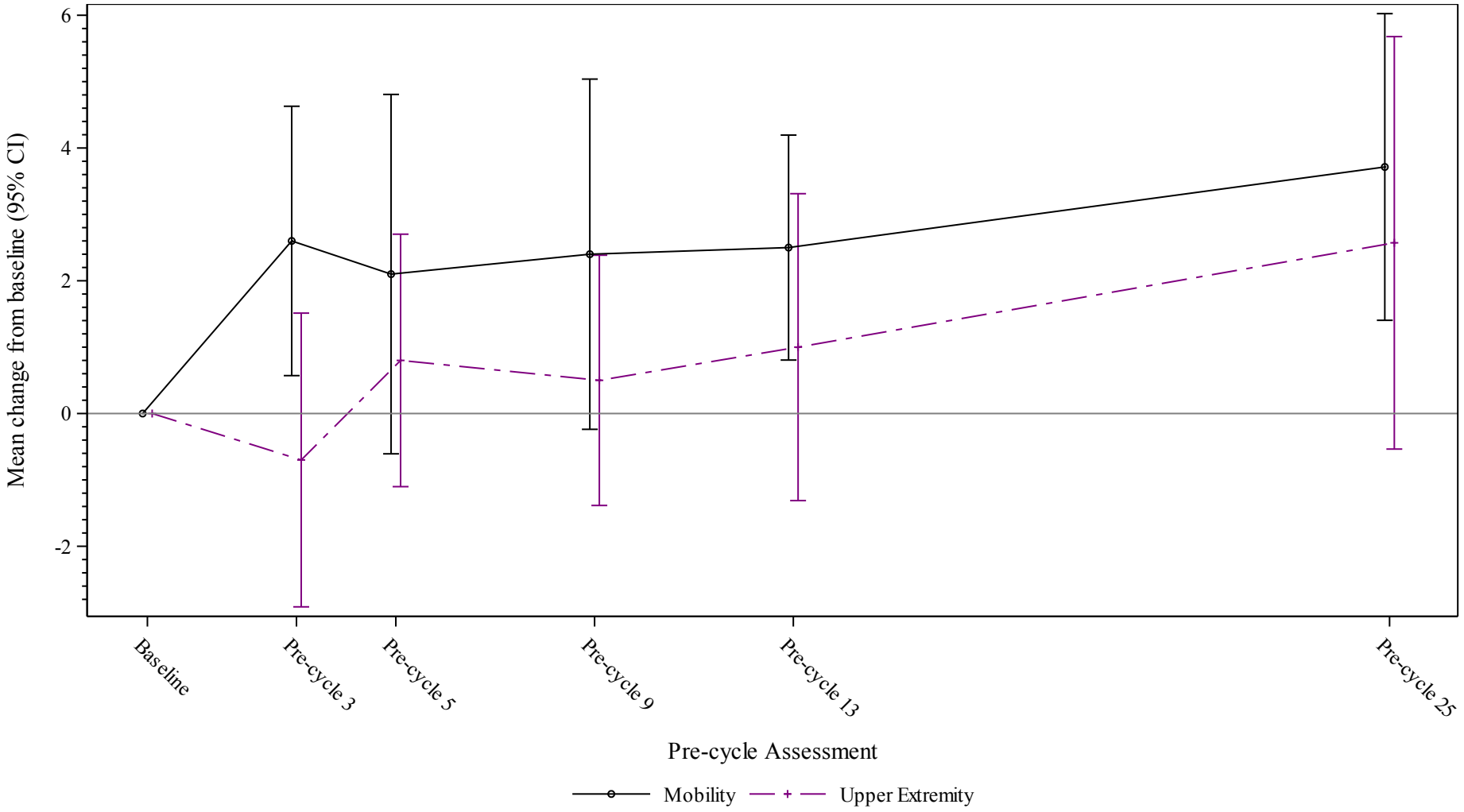


Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PROMIS.
CI = Confidence interval.

root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/promiscrplsub.sas promiscrplsubi.rtf 29APR2021:12:08 icesas457PD

Figure 2.5.2.2.5 Mean change from baseline of PROMIS parent-report raw scores over time - PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 11



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PROMIS.
CI = Confidence interval.

Table 2.5.2.3.1 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=19) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=17)	Categories of change [d]			
		Improvement	4	23,5	6,8, 49,9
		No improvement	13	76,5	50,1, 93,2
	Pre-cycle 5 (N=17)	Categories of change [d]			
		Improvement	7	41,2	18,4, 67,1
		No improvement	10	58,8	32,9, 81,6
	Pre-cycle 9 (N=17)	Categories of change [d]			
		Improvement	7	41,2	18,4, 67,1
		No improvement	10	58,8	32,9, 81,6
	Pre-cycle 13 (N=16)	Categories of change [d]			
		Improvement	6	37,5	15,2, 64,6
		No improvement	10	62,5	35,4, 84,8
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=17)	Categories of change [d]			
		Improvement	11	64,7	38,3, 85,8
		No improvement	6	35,3	14,2, 61,7

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2.3.1 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=19) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=17)	Categories of change [d]			
		Improvement	2	11,8	1,5, 36,4
		No improvement	15	88,2	63,6, 98,5
	Pre-cycle 5 (N=17)	Categories of change [d]			
		Improvement	2	11,8	1,5, 36,4
		No improvement	15	88,2	63,6, 98,5
	Pre-cycle 9 (N=17)	Categories of change [d]			
		Improvement	4	23,5	6,8, 49,9
		No improvement	13	76,5	50,1, 93,2
	Pre-cycle 13 (N=16)	Categories of change [d]			
		Improvement	6	37,5	15,2, 64,6
		No improvement	10	62,5	35,4, 84,8
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=17)	Categories of change [d]			
		Improvement	8	47,1	23,0, 72,2
		No improvement	9	52,9	27,8, 77,0

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2.3.2 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=14) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=13)	Categories of change [d]			
		Improvement	1	7,7	0,2, 36,0
		No improvement	12	92,3	64,0, 99,8
	Pre-cycle 5 (N=13)	Categories of change [d]			
		Improvement	2	15,4	1,9, 45,4
		No improvement	11	84,6	54,6, 98,1
	Pre-cycle 9 (N=14)	Categories of change [d]			
		Improvement	3	21,4	4,7, 50,8
		No improvement	11	78,6	49,2, 95,3
	Pre-cycle 13 (N=12)	Categories of change [d]			
		Improvement	3	25,0	5,5, 57,2
		No improvement	9	75,0	42,8, 94,5
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	4	44,4	13,7, 78,8
		No improvement	5	55,6	21,2, 86,3
	Overall (N=14)	Categories of change [d]			
		Improvement	5	35,7	12,8, 64,9
		No improvement	9	64,3	35,1, 87,2

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2.3.2 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=14) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=13)	Categories of change [d]			
		Improvement	0	0	0, 24,7
		No improvement	13	100	75,3, 100
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	1	8,3	0,2, 38,5
		No improvement	11	91,7	61,5, 99,8
	Pre-cycle 9 (N=13)	Categories of change [d]			
		Improvement	1	7,7	0,2, 36,0
		No improvement	12	92,3	64,0, 99,8
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	0	0	0, 28,5
		No improvement	11	100	71,5, 100
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	1	12,5	0,3, 52,7
		No improvement	7	87,5	47,3, 99,7
	Overall (N=13)	Categories of change [d]			
		Improvement	2	15,4	1,9, 45,4
		No improvement	11	84,6	54,6, 98,1

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2.3.3 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrollment = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	4	44,4	13,7, 78,8
		No improvement	5	55,6	21,2, 86,3
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	5	50,0	18,7, 81,3
		No improvement	5	50,0	18,7, 81,3
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33,3	7,5, 70,1
		No improvement	6	66,7	29,9, 92,5
	Pre-cycle 25 (N=4)	Categories of change [d]			
		Improvement	2	50,0	6,8, 93,2
		No improvement	2	50,0	6,8, 93,2
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=10)	Categories of change [d]			
		Improvement	6	60,0	26,2, 87,8
		No improvement	4	40,0	12,2, 73,8

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2.3.3 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrollment = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	1	11,1	0,3, 48,2
		No improvement	8	88,9	51,8, 99,7
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	4	44,4	13,7, 78,8
		No improvement	5	55,6	21,2, 86,3
	Pre-cycle 25 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=10)	Categories of change [d]			
		Improvement	5	50,0	18,7, 81,3
		No improvement	5	50,0	18,7, 81,3

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2.3.4 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrol. = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	2	18,2	2,3, 51,8
		No improvement	9	81,8	48,2, 97,7
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	4	44,4	13,7, 78,8
		No improvement	5	55,6	21,2, 86,3
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8
	Overall (N=11)	Categories of change [d]			
		Improvement	5	45,5	16,7, 76,6
		No improvement	6	54,5	23,4, 83,3

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2.3.4 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrol. = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7
	Pre-cycle 13 (N=8)	Categories of change [d]			
		Improvement	1	12,5	0,3, 52,7
		No improvement	7	87,5	47,3, 99,7
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Overall (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2.3.5 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrollment = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility - Raw Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	2	28,6	3,7, 71,0
		No improvement	5	71,4	29,0, 96,3
	Overall (N=10)	Categories of change [d]			
		Improvement	5	50,0	18,7, 81,3
		No improvement	5	50,0	18,7, 81,3

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

Table 2.5.2.3.5 PROMIS parent-report raw score categories of change over time - percentage of patients with Improvement by >= 4.8 points - PN status at enrollment = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=11) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Upper Extremity - Raw Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Overall (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/no improvement are defined using a threshold of 4.8. NC - not calculated.

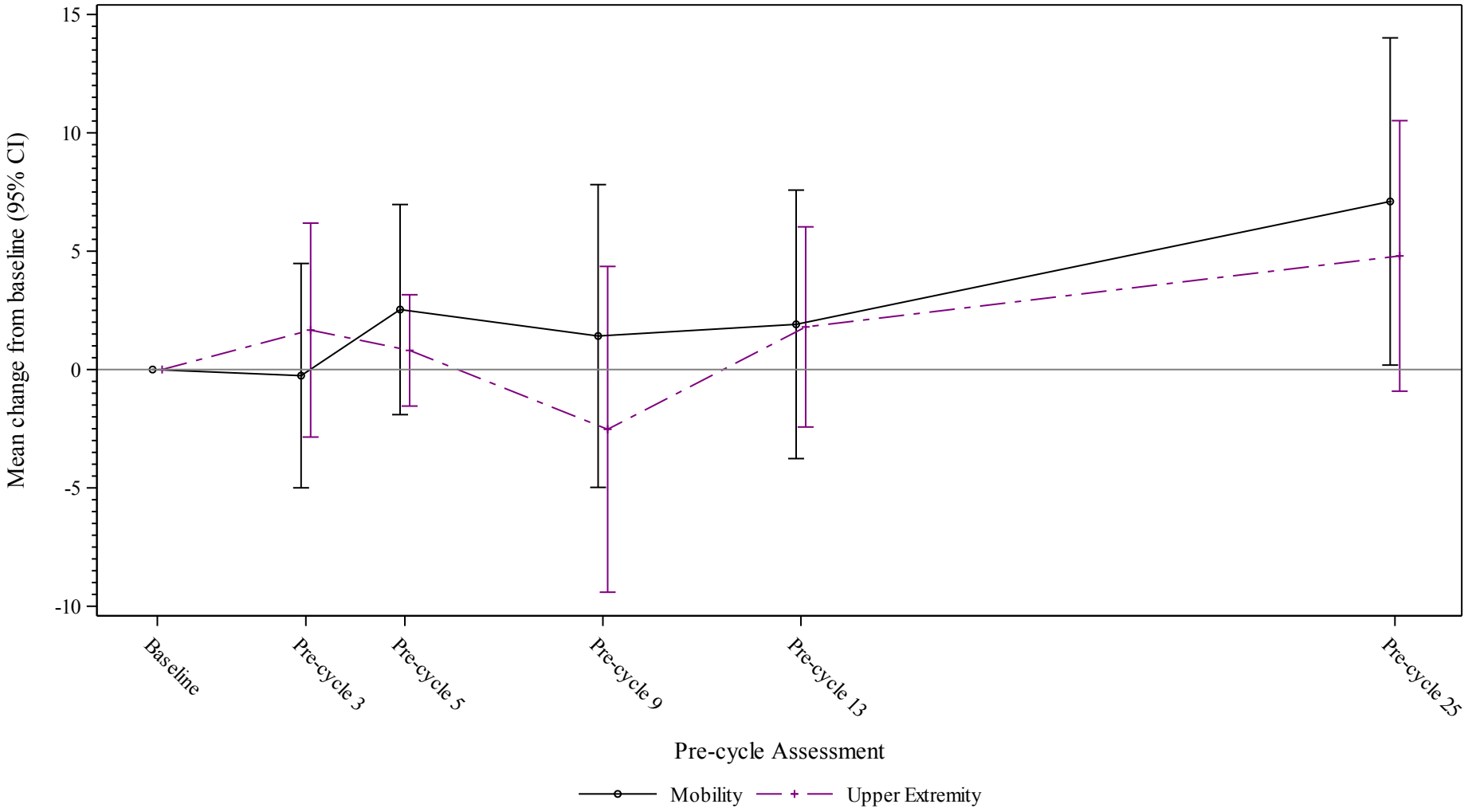
Table 2.5.3 PROMIS self-report transformed score categories of change - percentage of patients with Improvement
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=24) [a]			
			T-Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility	Overall (N=22)	Categories of change - literature-based [d]			
		Improvement	19	86,4	65,1, 97,1
		No improvement	3	13,6	2,9, 34,9
Upper Extremity	Overall (N=21)	Categories of change - literature-based [d]			
		Improvement	10	47,6	25,7, 70,2
		No improvement	11	52,4	29,8, 74,3

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed self-report measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions. exact method for binomial proportions.
[d] Improvement/No improvement are defined using thresholds reported in Thissen et al. 2016.
NC - not calculated.

Figure 2.5.3.1.1 Mean change from baseline of PROMIS self-report T-scores over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

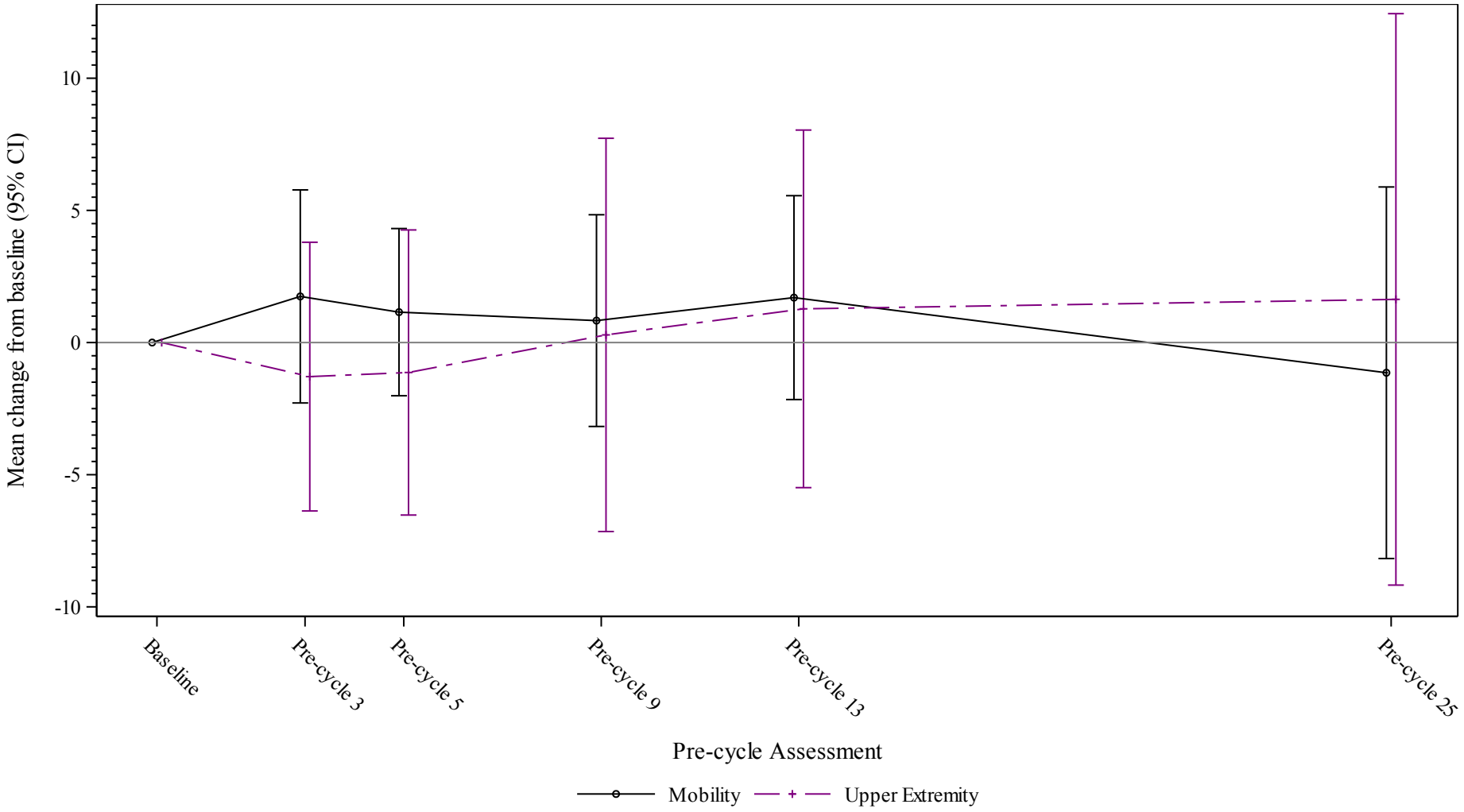
N = 14



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PROMIS.
CI = Confidence interval.

Figure 2.5.3.1.2 Mean change from baseline of PROMIS self-report T-scores over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

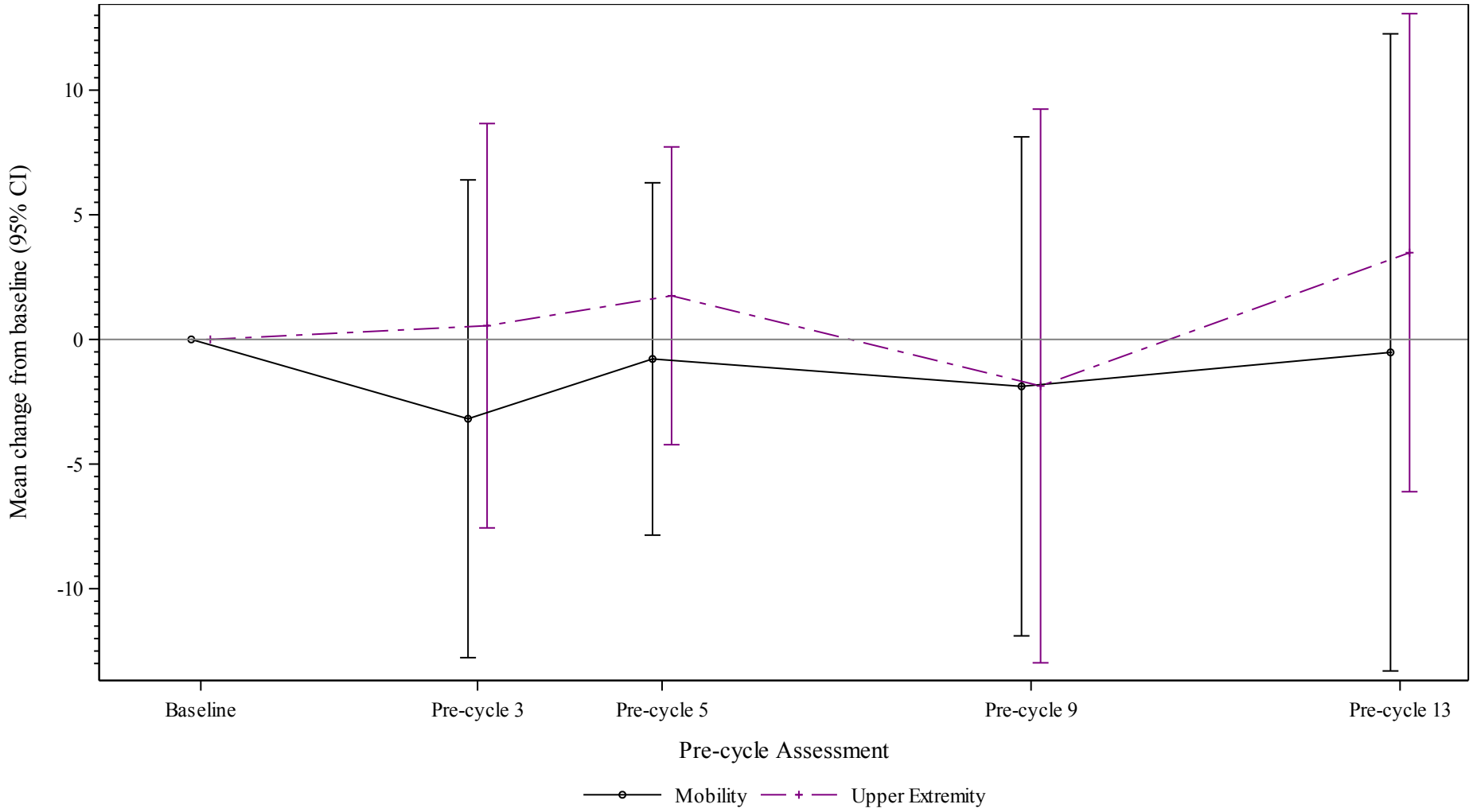
N = 10



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PROMIS.
CI = Confidence interval.

Figure 2.5.3.1.3 Mean change from baseline of PROMIS self-report T-scores over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

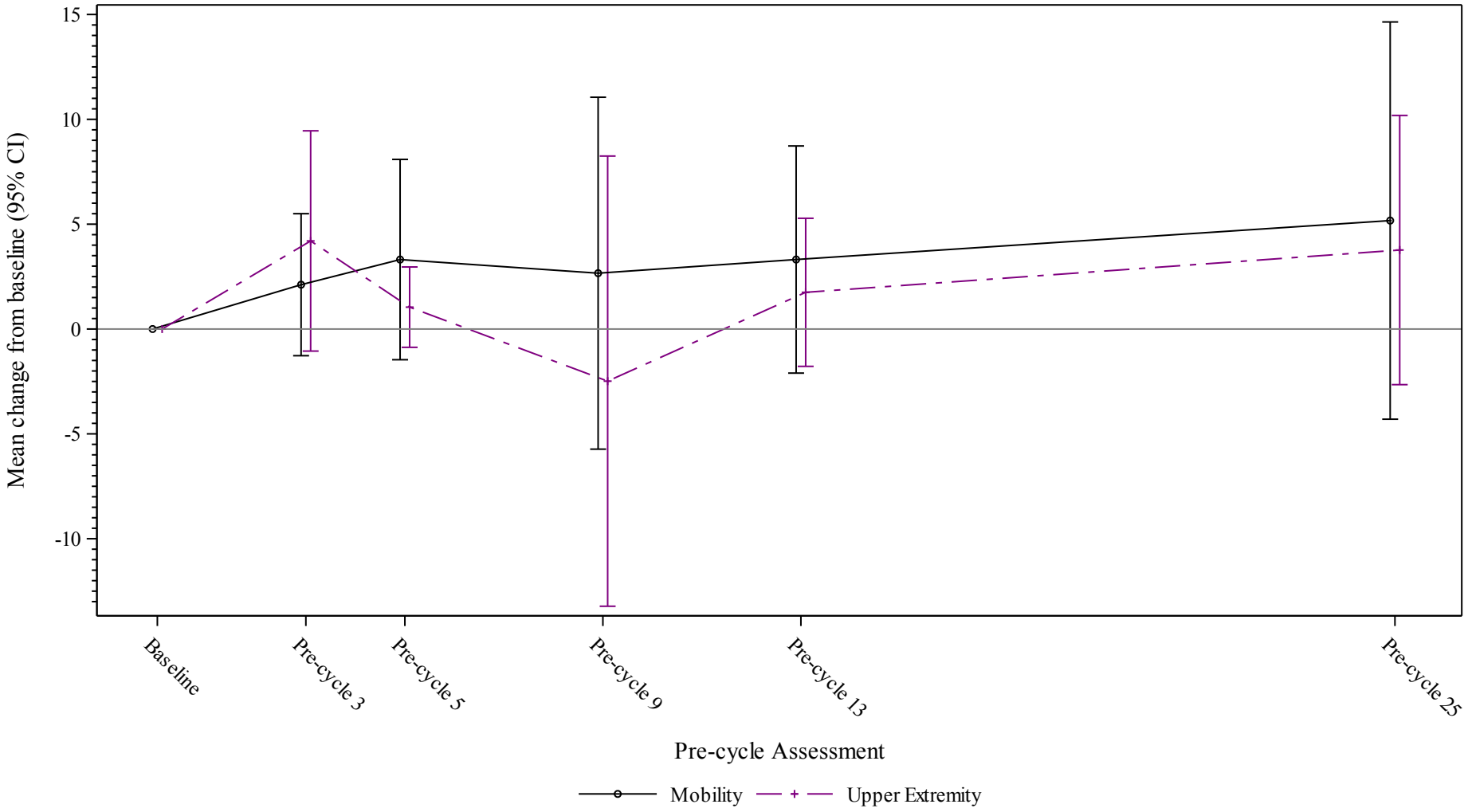
N = 6



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PROMIS.
CI = Confidence interval.

Figure 2.5.3.1.4 Mean change from baseline of PROMIS self-report T-scores over time - PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

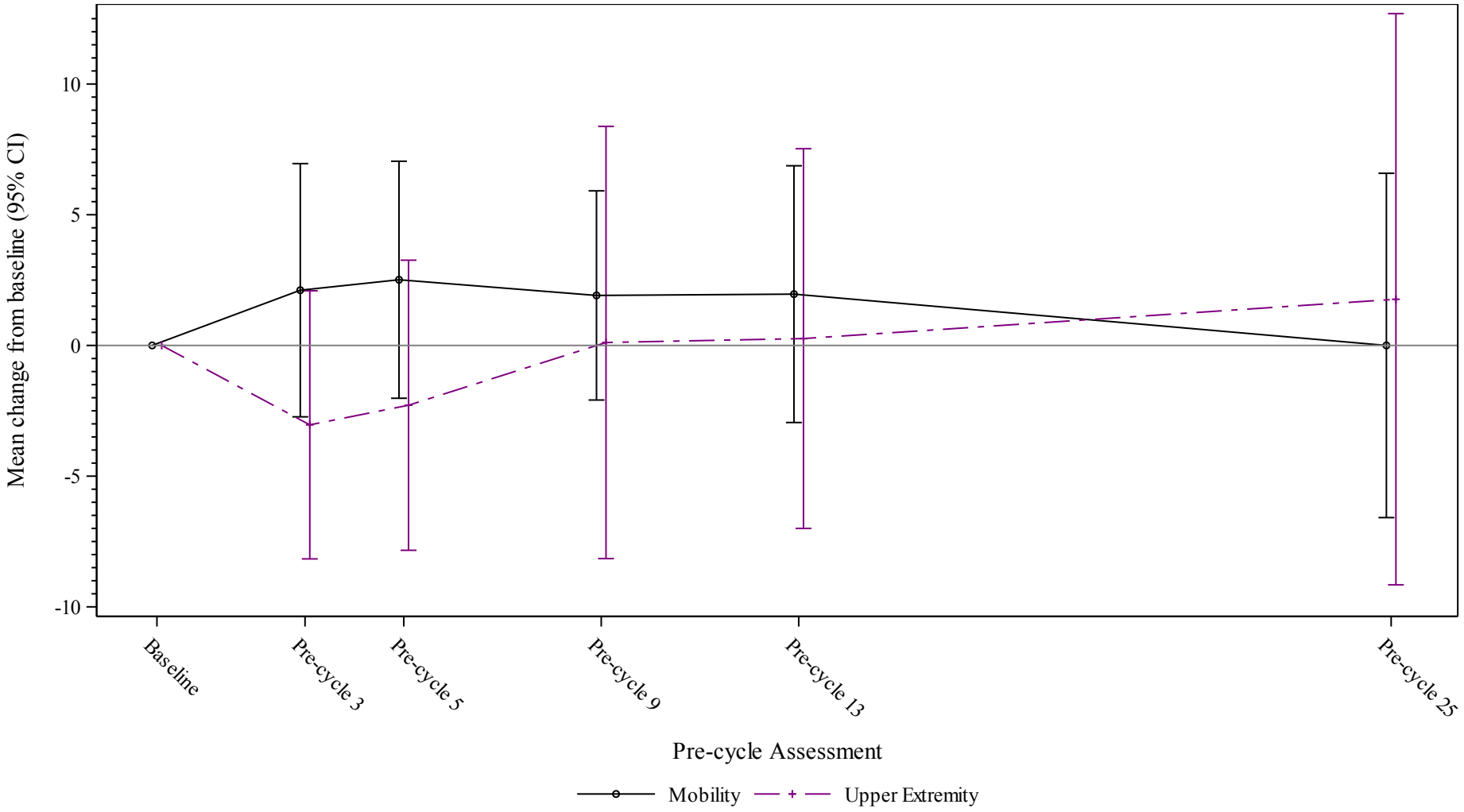
N = 8



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PROMIS.
CI = Confidence interval.

Figure 2.5.3.1.5 Mean change from baseline of PROMIS self-report T-scores over time - PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 10



Note: Children, ages 8 to 18 years at enrolment, completed self-report measures of the PROMIS.
CI = Confidence interval.

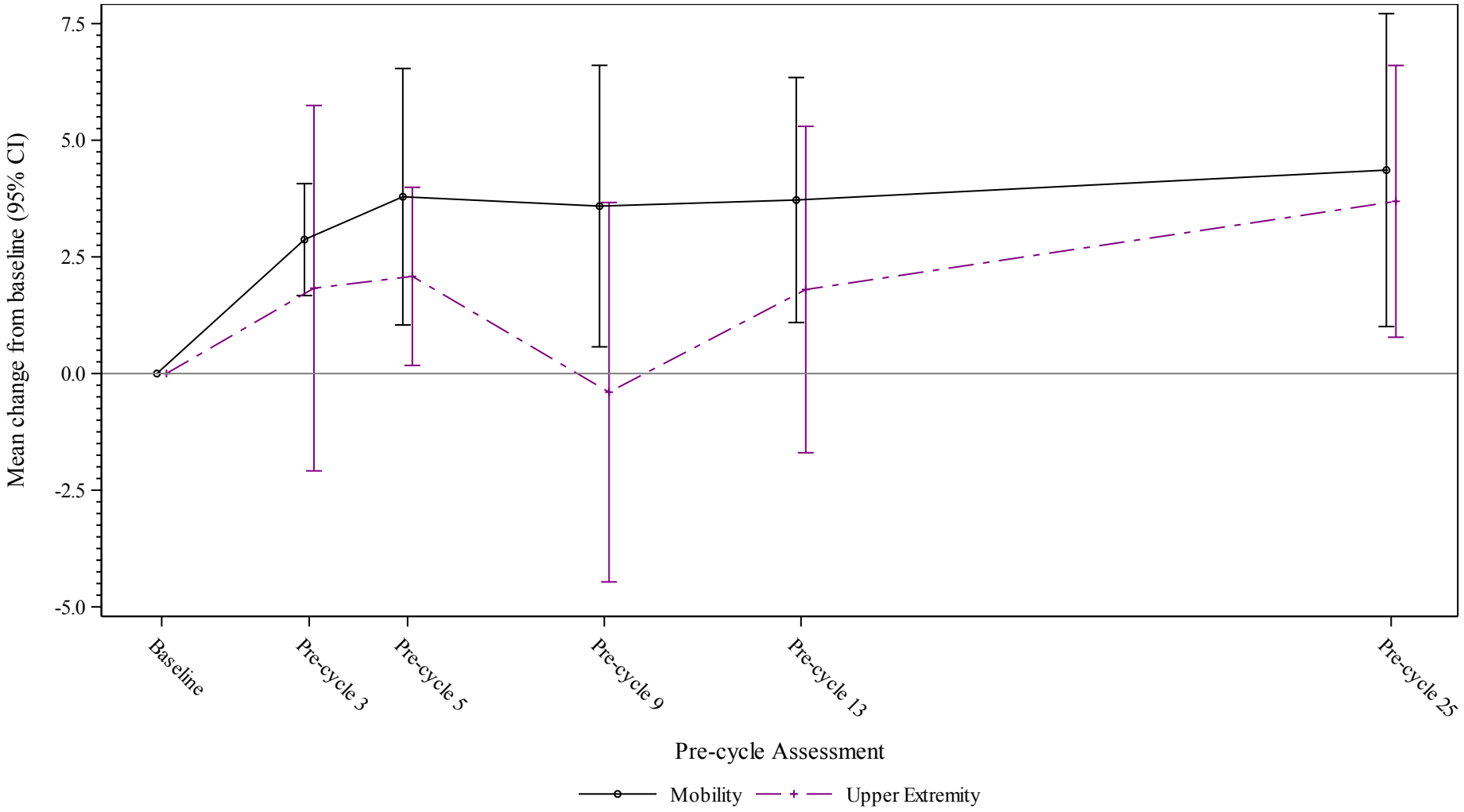
Table 2.5.4 PROMIS parent-report transformed score categories of change - percentage of patients with Improvement
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=33) [a]			
			T-Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Mobility	Overall (N=31)	Categories of change - literature-based [d]			
		Improvement	22	71,0	52,0, 85,8
		No improvement	9	29,0	14,2, 48,0
Upper Extremity	Overall (N=30)	Categories of change - literature-based [d]			
		Improvement	18	60,0	40,6, 77,3
		No improvement	12	40,0	22,7, 59,4

[a] Parents or legal guardians of children 5-18 years of age at enrolment with a motor PN-related morbidity completed the parent proxy measures of the PROMIS physical functioning questionnaire. [b] Percentages are based on the number of patients with a non-missing score at each analysis visit. [c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using thresholds reported in Thissen et al. 2016.
NC - not calculated.

Figure 2.5.4.1.1 Mean change from baseline of PROMIS parent-report T-scores over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

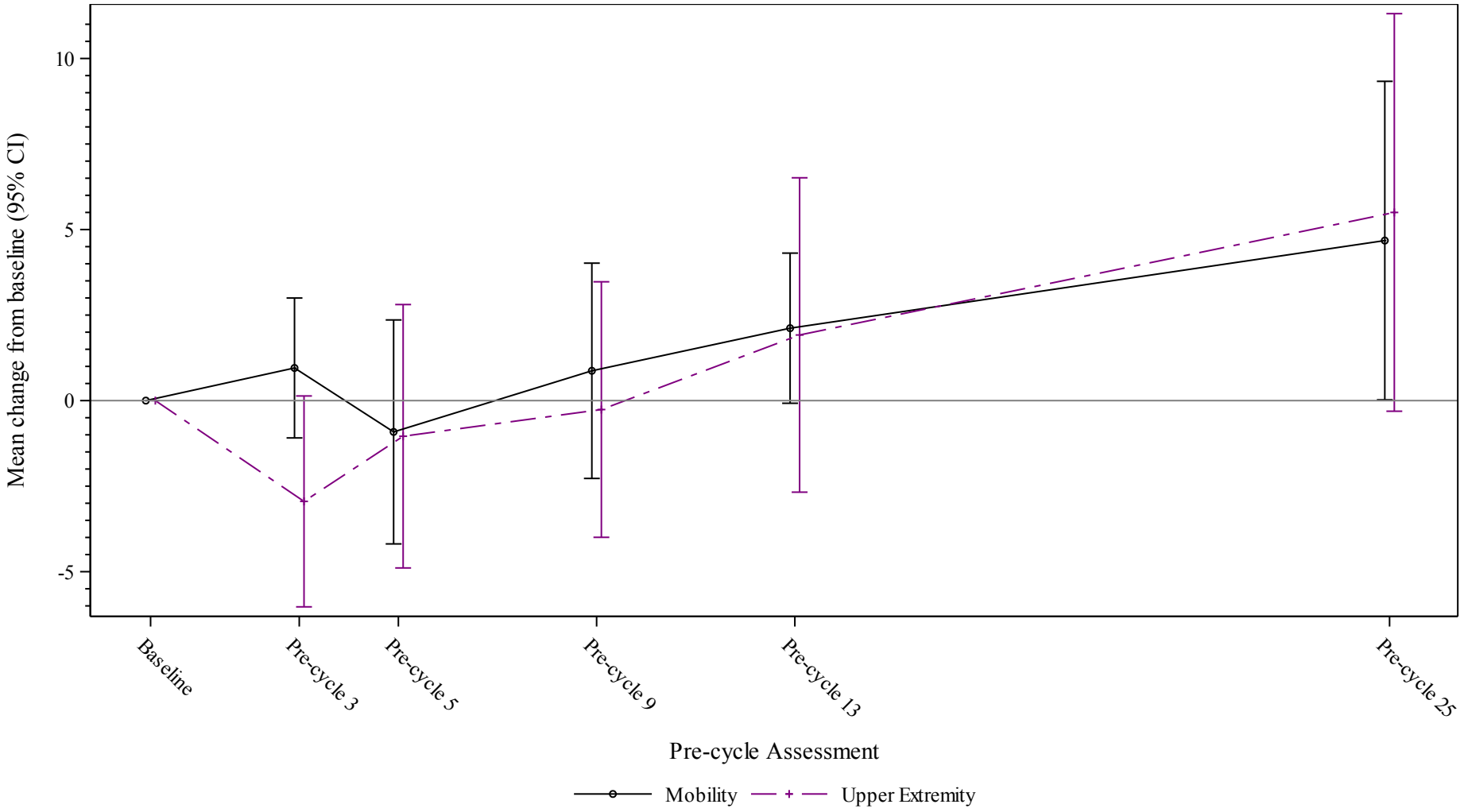
N = 19



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PROMIS.
CI = Confidence interval.

Figure 2.5.4.1.2 Mean change from baseline of PROMIS parent-report T-scores over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

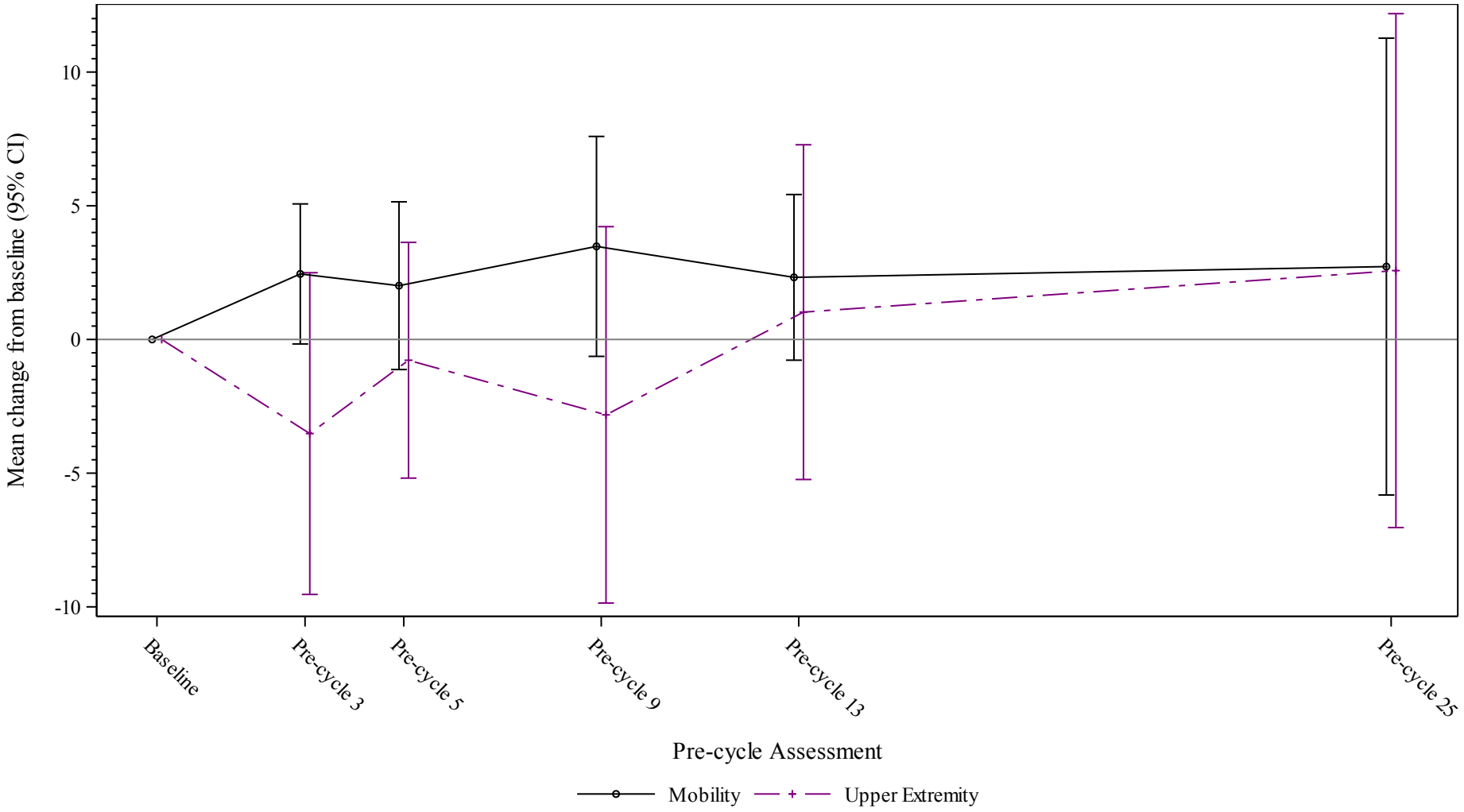
N = 14



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PROMIS.
CI = Confidence interval.

Figure 2.5.4.1.3 Mean change from baseline of PROMIS parent-report T-scores over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

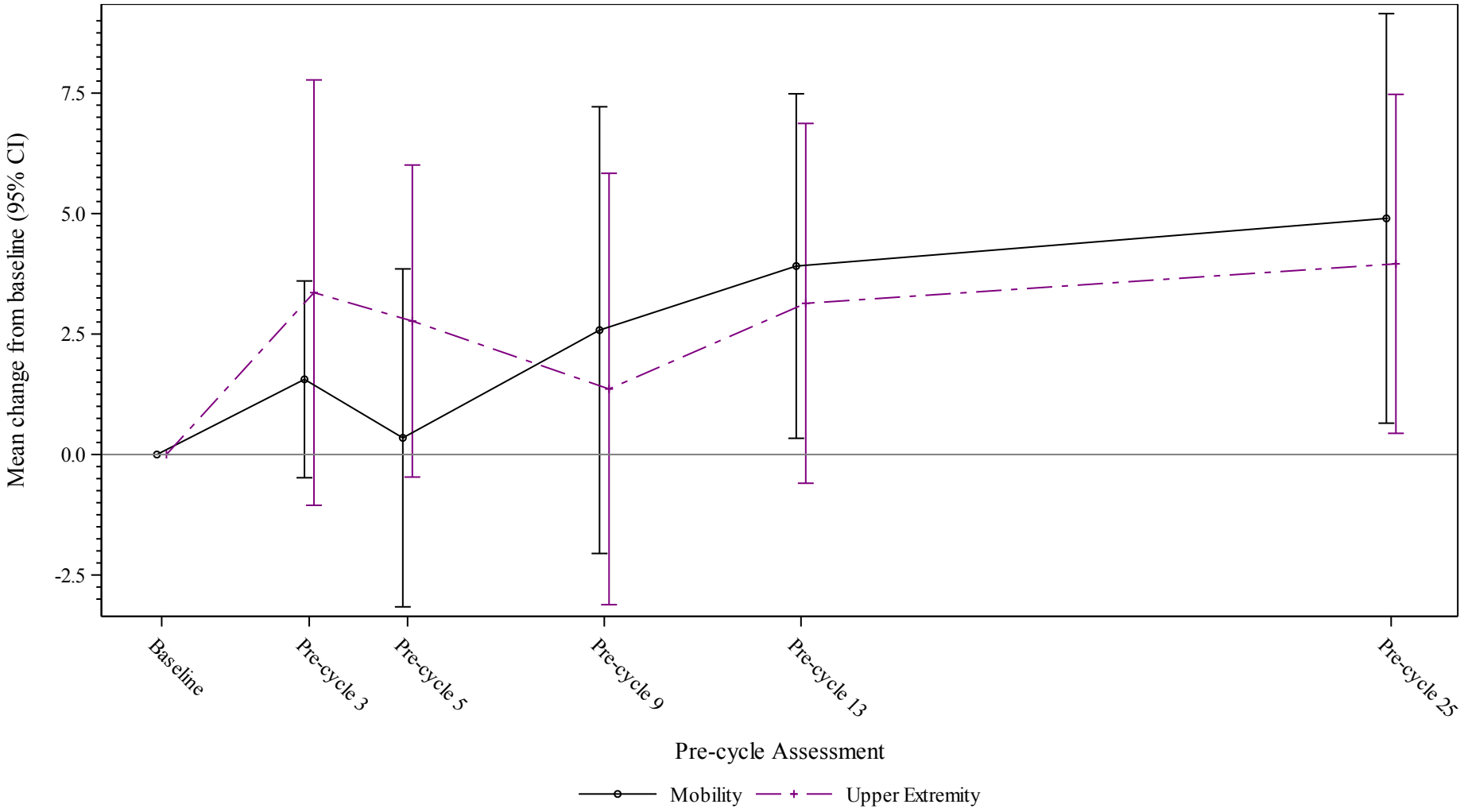
N = 11



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PROMIS.
CI = Confidence interval.

Figure 2.5.4.1.4 Mean change from baseline of PROMIS parent-report T-scores over time - PN status at enrollment = Non-progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

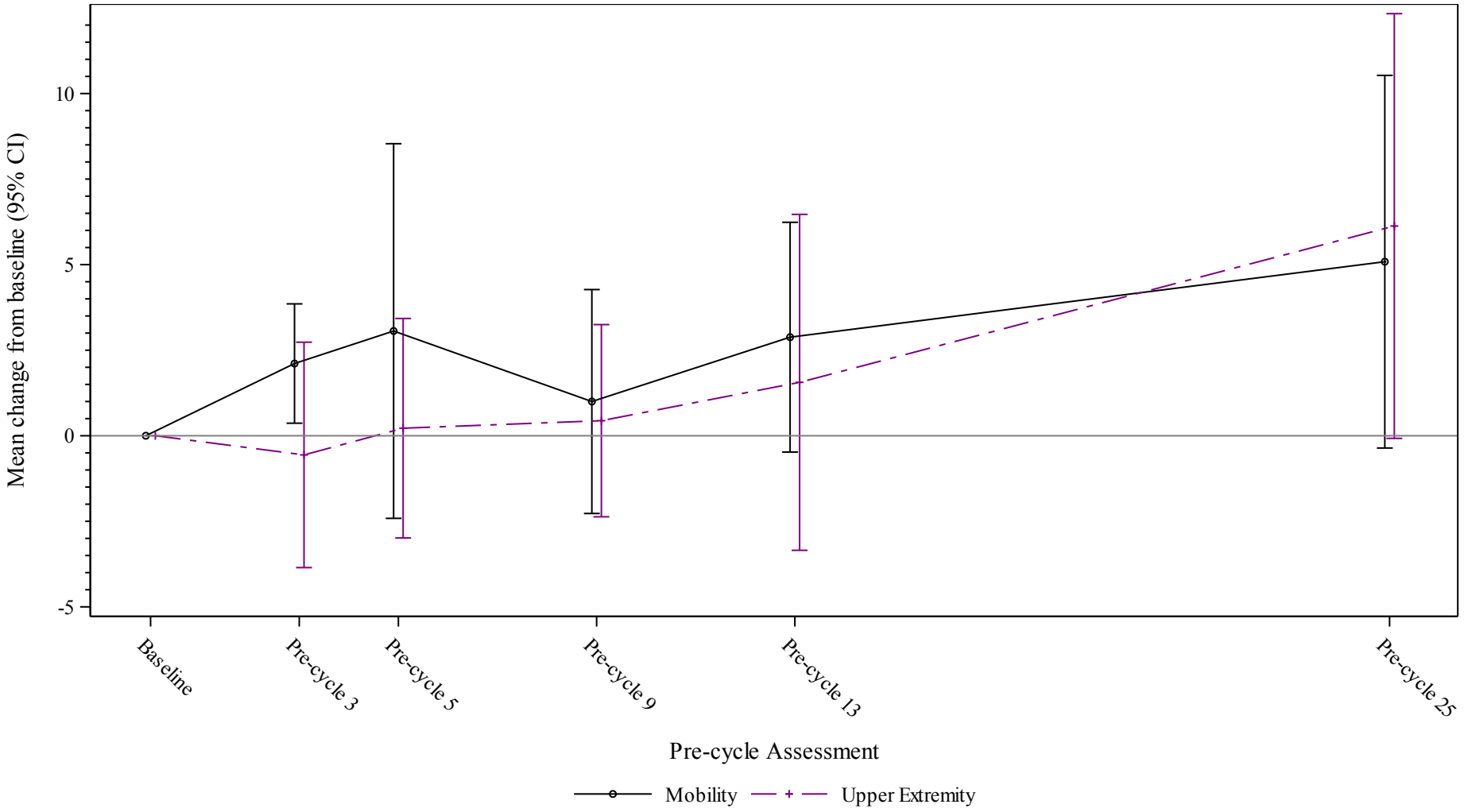
N = 11



Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PROMIS.
CI = Confidence interval.

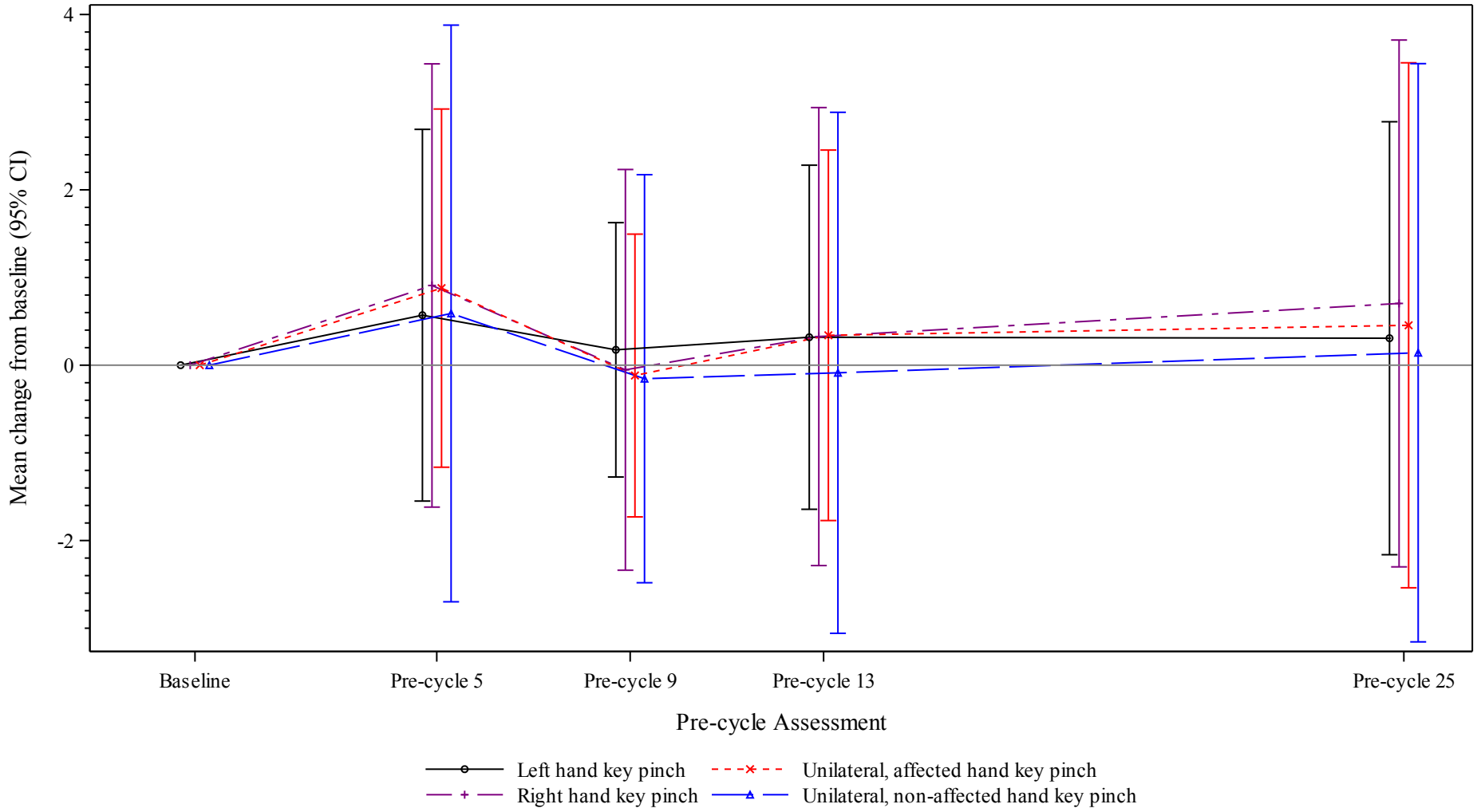
Figure 2.5.4.1.5 Mean change from baseline of PROMIS parent-report T-scores over time - PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 11



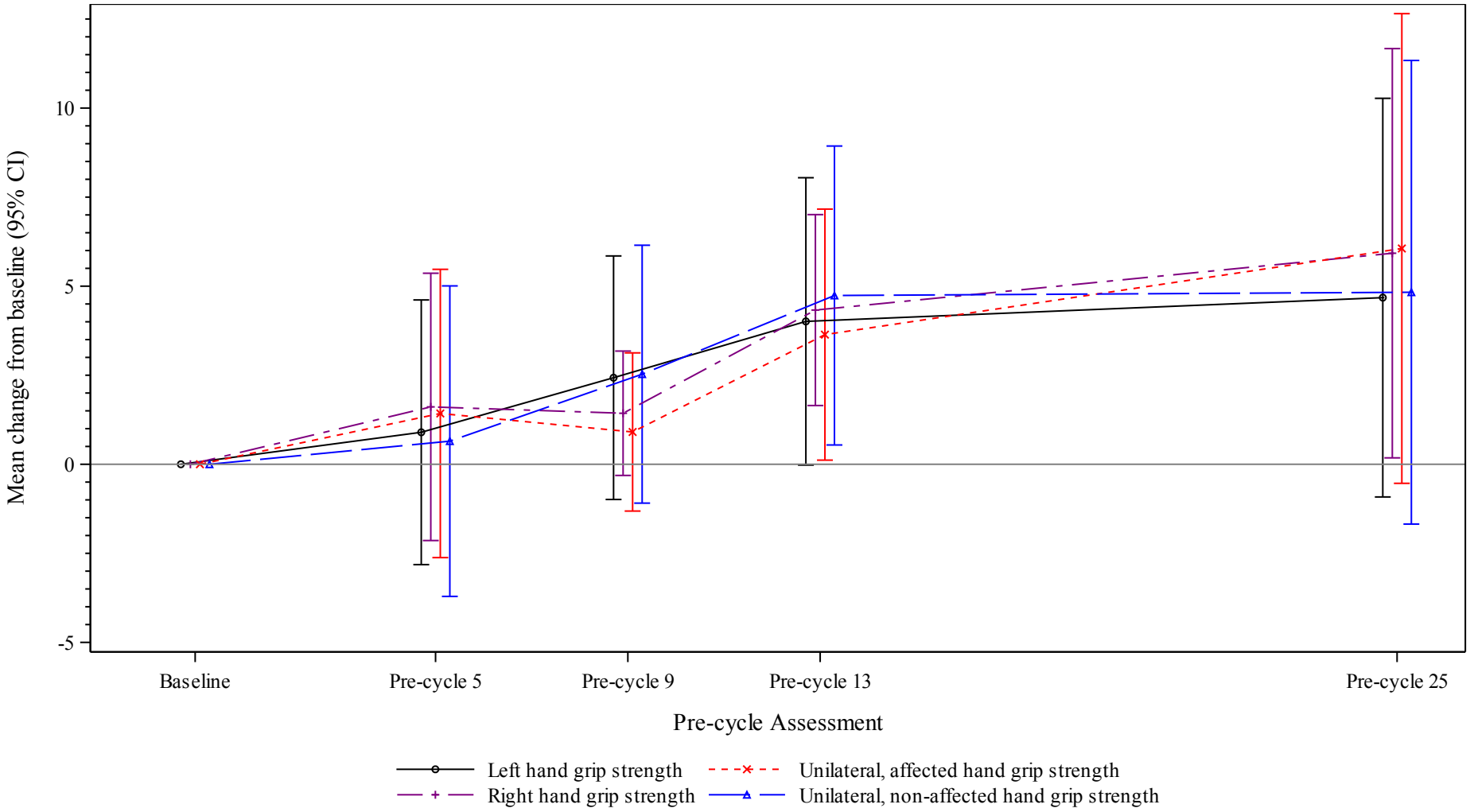
Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy PROMIS.
CI = Confidence interval.

Figure 2.6.1 Mean change from baseline of key pinch test scores
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 33



CI = Confidence interval.
Bilateral patients omitted owing to insufficient data.

Figure 2.6.2 Mean change from baseline of grip strength test scores
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 33



CI = Confidence interval.
Bilateral patients omitted owing to insufficient data.

Table 2.6.3.1.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=19) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Grooved Pegboard, dominant hand time (s)	Baseline (n=16)	93,05	36,008	88,69	41,0	164,7	15,8							
	Pre-cycle 5 (n=15)	82,92	41,125	78,72	37,0	209,4	21,1	15	-8,85	33,370	1,91	-96,7	44,8	21,1
	Pre-cycle 9 (n=14)	104,12	122,773	77,71	32,6	515,0	26,3	14	12,32	107,225	-13,61	-117,0	350,4	26,3
	Pre-cycle 13 (n=14)	109,52	79,098	88,63	29,7	367,0	26,3	14	16,69	67,778	-5,35	-61,3	202,4	26,3
	Pre-cycle 25 (n=8)	107,34	51,958	91,12	60,2	228,2	57,9	8	0,34	46,986	-15,16	-59,8	63,5	57,9
Grooved Pegboard, non-dominant hand time (s)	Baseline (n=15)	128,87	111,802	95,21	46,0	505,9	21,1							
	Pre-cycle 5 (n=14)	115,44	84,805	87,04	39,0	300,0	26,3	14	-14,38	74,183	-5,56	-205,9	152,4	26,3
	Pre-cycle 9 (n=14)	120,42	135,086	88,91	31,4	569,0	26,3	14	-9,40	49,677	-12,68	-98,9	92,2	26,3
	Pre-cycle 13 (n=13)	138,65	91,367	111,66	34,1	384,0	31,6	13	14,98	64,952	-1,82	-121,9	134,8	31,6
	Pre-cycle 25 (n=8)	171,21	173,400	106,69	65,9	584,6	57,9	8	22,88	65,230	13,94	-71,3	107,4	57,9
Grooved Pegboard, dominant hand z-score	Baseline (n=16)	3,15	3,692	1,95	0,0	12,4	15,8							
	Pre-cycle 5 (n=15)	1,85	3,511	0,70	-0,5	13,8	21,1	15	-1,21	3,279	-0,45	-10,7	4,3	21,1
	Pre-cycle 9 (n=14)	3,93	11,436	0,27	-0,6	43,2	26,3	14	0,66	10,176	-0,85	-13,0	33,7	26,3
	Pre-cycle 13 (n=14)	3,72	7,897	0,63	-0,9	28,9	26,3	14	0,43	7,265	-0,59	-12,2	19,5	26,3
	Pre-cycle 25 (n=8)	2,03	2,319	1,36	0,2	7,3	57,9	8	-2,47	4,197	-2,15	-12,2	1,1	57,9
Grooved Pegboard non-dominant hand z-score	Baseline (n=15)	4,92	9,644	2,41	-0,2	39,2	21,1							
	Pre-cycle 5 (n=14)	3,09	5,548	1,08	-0,6	20,7	26,3	14	-1,89	5,179	-1,01	-18,6	4,5	26,3
	Pre-cycle 9 (n=14)	4,57	11,860	0,72	-0,7	44,9	26,3	14	-0,41	2,820	-0,81	-3,7	5,7	26,3
	Pre-cycle 13 (n=13)	5,03	8,347	1,53	-0,5	28,2	31,6	13	-0,03	5,133	-0,62	-11,0	10,1	31,6
	Pre-cycle 25 (n=8)	4,37	8,155	1,85	-0,4	24,3	57,9	8	-2,34	5,272	-0,94	-15,0	2,0	57,9
Grooved Pegboard dominant hand # pegs dropped	Baseline (n=16)	0,75	0,856	1,00	0,0	3,0	15,8							
	Pre-cycle 5 (n=15)	1,07	1,033	1,00	0,0	3,0	21,1	15	0,27	1,335	0,00	-1,0	3,0	21,1
	Pre-cycle 9 (n=14)	1,29	2,894	0,00	0,0	11,0	26,3	14	0,50	3,156	0,00	-2,0	11,0	26,3
	Pre-cycle 13 (n=14)	0,79	1,718	0,00	0,0	6,0	26,3	14	0,00	1,881	0,00	-2,0	6,0	26,3
	Pre-cycle 25 (n=8)	1,13	0,991	1,50	0,0	2,0	57,9	8	0,13	0,991	0,00	-1,0	2,0	57,9
Grooved Pegboard non-dominant hand # pegs dropped	Baseline (n=15)	1,73	1,870	1,00	0,0	5,0	21,1							
	Pre-cycle 5 (n=14)	1,07	1,639	0,50	0,0	6,0	26,3	14	-0,79	1,311	-0,50	-3,0	1,0	26,3
	Pre-cycle 9 (n=14)	1,43	1,555	1,00	0,0	4,0	26,3	14	-0,43	1,869	-0,50	-3,0	3,0	26,3
	Pre-cycle 13 (n=13)	1,92	1,977	2,00	0,0	6,0	31,6	13	0,23	2,386	1,00	-5,0	5,0	31,6
	Pre-cycle 25 (n=8)	2,00	2,268	1,00	0,0	6,0	57,9	8	0,00	1,195	0,00	-2,0	2,0	57,9

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.1.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=19) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Left hand grip strength (pounds or Kg)	Baseline (n=6)	11,58	6,127	12,00	4,0	18,1	68,4							
	Pre-cycle 5 (n=13)	12,15	8,522	10,88	0,0	28,3	31,6	5	1,92	7,545	-2,00	-4,0	14,6	73,7
	Pre-cycle 9 (n=13)	15,11	9,822	12,24	0,7	33,0	31,6	5	3,91	7,154	3,30	-3,3	15,6	73,7
	Pre-cycle 13 (n=13)	15,53	8,863	14,21	1,0	30,7	31,6	5	4,99	8,089	3,33	-3,0	18,6	73,7
	Pre-cycle 25 (n=6)	15,75	10,575	19,00	0,8	28,0	68,4	4	6,36	11,242	3,00	-3,2	22,6	78,9
Right hand grip strength (pounds or Kg)	Baseline (n=6)	16,83	10,021	16,39	6,2	34,0	68,4							
	Pre-cycle 5 (n=13)	14,19	9,549	10,73	2,0	30,0	31,6	5	2,61	8,175	2,00	-4,3	15,8	73,7
	Pre-cycle 9 (n=12)	16,76	9,620	14,46	3,2	34,0	36,8	4	1,66	1,967	1,17	0,0	4,3	78,9
	Pre-cycle 13 (n=13)	18,34	10,240	14,67	3,9	36,7	31,6	5	4,76	5,402	4,00	0,0	13,8	73,7
	Pre-cycle 25 (n=6)	23,67	10,310	28,17	8,0	32,0	68,4	4	6,78	11,937	2,67	-2,0	23,8	78,9
Left hand Key-pinch strength (pounds or Kg)	Baseline (n=6)	4,99	2,890	4,80	1,3	10,0	68,4							
	Pre-cycle 5 (n=12)	4,46	2,319	4,00	1,2	9,0	36,8	5	-0,65	3,356	-0,17	-6,0	3,3	73,7
	Pre-cycle 9 (n=13)	5,18	3,402	4,50	1,0	14,0	31,6	5	-0,11	3,361	0,00	-5,5	3,3	73,7
	Pre-cycle 13 (n=13)	5,16	2,790	4,00	1,0	9,3	31,6	5	0,24	4,049	0,50	-6,0	5,1	73,7
	Pre-cycle 25 (n=6)	4,83	3,110	4,75	1,3	8,5	68,4	4	-0,34	5,087	0,92	-7,5	4,3	78,9
Right hand Key-pinch strength (pounds or Kg)	Baseline (n=6)	6,85	5,607	4,65	3,0	18,0	68,4							
	Pre-cycle 5 (n=12)	5,13	2,274	4,27	2,3	8,5	36,8	5	-0,86	5,062	0,00	-9,5	3,7	73,7
	Pre-cycle 9 (n=12)	5,92	4,100	4,75	2,3	17,0	36,8	4	-1,63	4,990	0,25	-9,0	2,0	78,9
	Pre-cycle 13 (n=13)	5,61	2,530	5,44	2,3	9,9	31,6	5	-0,58	5,223	0,50	-9,5	4,0	73,7
	Pre-cycle 25 (n=6)	7,07	2,461	7,55	2,7	9,5	68,4	4	0,22	6,293	2,33	-9,0	5,2	78,9
Leg length discrepancy (cm)	Baseline (n=11)	2,42	2,348	1,50	0,1	8,5	42,1							
	Pre-cycle 5 (n=10)	2,28	3,314	0,75	0,0	10,5	47,4	9	-0,20	1,364	0,00	-2,8	2,0	52,6
	Pre-cycle 9 (n=10)	2,04	2,385	1,00	0,0	6,0	47,4	8	-0,31	1,360	-0,50	-2,5	2,0	57,9
	Pre-cycle 13 (n=10)	2,32	1,979	1,50	0,1	5,5	47,4	10	-0,24	1,241	0,00	-3,0	1,1	47,4
	Pre-cycle 25 (n=6)	1,53	1,757	1,00	0,2	5,0	68,4	6	-1,33	1,538	-0,75	-3,5	0,0	68,4
	Pre-cycle 37 (n=1)	NC	NC	NC	2,0	2,0	94,7	0	NC	NC	NC	NC	NC	100,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.1.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Grooved Pegboard, dominant hand time (s)	Baseline (n=9)	83,59	32,535	80,19	41,0	151,8	35,7							
	Pre-cycle 5 (n=9)	95,37	50,490	68,00	47,3	166,8	35,7	9	11,77	28,741	3,00	-24,8	63,0	35,7
	Pre-cycle 9 (n=9)	77,88	33,819	70,33	33,9	152,9	35,7	9	-5,71	15,431	1,17	-27,2	12,0	35,7
	Pre-cycle 13 (n=8)	83,75	32,243	75,50	42,9	144,8	42,9	8	-0,27	12,909	1,35	-26,0	14,0	42,9
	Pre-cycle 25 (n=5)	71,17	26,342	72,00	30,4	100,7	64,3	5	-18,67	21,540	-13,00	-51,1	7,0	64,3
Grooved Pegboard, non-dominant hand time (s)	Baseline (n=9)	138,85	81,711	119,34	67,6	300,0	35,7							
	Pre-cycle 5 (n=9)	104,65	41,167	82,40	67,0	168,0	35,7	9	-34,20	74,489	-10,61	-217,6	28,4	35,7
	Pre-cycle 9 (n=9)	89,05	27,286	84,20	38,6	123,4	35,7	9	-49,80	65,813	-35,14	-178,4	5,9	35,7
	Pre-cycle 13 (n=8)	93,71	29,560	93,38	51,3	145,0	42,9	8	-24,99	40,108	-19,45	-111,0	23,0	42,9
	Pre-cycle 25 (n=5)	77,46	24,685	76,39	39,4	104,5	64,3	5	-38,42	36,624	-38,26	-95,0	4,0	64,3
Grooved Pegboard, dominant hand z-score	Baseline (n=9)	0,77	1,718	0,17	-1,0	4,3	35,7							
	Pre-cycle 5 (n=9)	1,14	2,126	0,19	-1,1	5,2	35,7	9	0,37	1,141	0,21	-1,0	2,8	35,7
	Pre-cycle 9 (n=9)	0,60	1,407	0,41	-0,8	3,7	35,7	9	-0,16	1,004	-0,06	-2,2	1,2	35,7
	Pre-cycle 13 (n=8)	0,74	1,374	0,40	-0,6	3,3	42,9	8	0,01	0,793	-0,07	-1,0	1,3	42,9
	Pre-cycle 25 (n=5)	0,14	0,518	0,37	-0,7	0,6	64,3	5	-1,10	1,992	-0,02	-3,9	0,7	64,3
Grooved Pegboard non-dominant hand z-score	Baseline (n=9)	2,94	4,181	1,10	-0,9	12,2	35,7							
	Pre-cycle 5 (n=9)	1,25	1,752	1,23	-0,7	4,7	35,7	9	-1,70	3,697	-0,35	-10,9	1,2	35,7
	Pre-cycle 9 (n=9)	0,88	1,841	0,41	-1,0	4,8	35,7	9	-2,06	3,346	-1,23	-9,4	0,5	35,7
	Pre-cycle 13 (n=8)	1,05	1,427	0,50	-0,3	3,7	42,9	8	-0,74	2,246	-0,63	-5,7	2,1	42,9
	Pre-cycle 25 (n=5)	0,59	1,403	0,04	-0,3	3,1	64,3	5	-1,04	0,904	-1,28	-1,8	0,4	64,3
Grooved Pegboard dominant hand # pegs dropped	Baseline (n=9)	1,89	2,369	0,00	0,0	6,0	35,7							
	Pre-cycle 5 (n=9)	1,78	4,265	0,00	0,0	13,0	35,7	9	-0,11	3,296	0,00	-4,0	7,0	35,7
	Pre-cycle 9 (n=9)	2,00	3,041	0,00	0,0	9,0	35,7	9	0,11	2,205	0,00	-4,0	3,0	35,7
	Pre-cycle 13 (n=8)	1,00	1,309	1,00	0,0	4,0	42,9	8	-0,63	1,506	0,00	-3,0	1,0	42,9
	Pre-cycle 25 (n=5)	0,60	0,894	0,00	0,0	2,0	64,3	5	-2,00	1,871	-3,00	-4,0	0,0	64,3
Grooved Pegboard non-dominant hand # pegs dropped	Baseline (n=9)	3,67	5,916	1,00	0,0	18,0	35,7							
	Pre-cycle 5 (n=9)	0,67	0,707	1,00	0,0	2,0	35,7	9	-3,00	5,385	-1,00	-16,0	1,0	35,7
	Pre-cycle 9 (n=9)	1,56	1,590	1,00	0,0	5,0	35,7	9	-2,11	6,294	0,00	-17,0	4,0	35,7
	Pre-cycle 13 (n=8)	1,13	1,126	1,00	0,0	3,0	42,9	8	-2,00	5,855	0,00	-16,0	2,0	42,9
	Pre-cycle 25 (n=5)	0,40	0,548	0,00	0,0	1,0	64,3	5	-4,20	7,259	-1,00	-17,0	0,0	64,3

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.1.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
(Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Left hand grip strength (pounds or Kg)	Baseline (n=7)	13,95	8,211	14,67	2,7	27,3	50,0							
	Pre-cycle 5 (n=9)	20,61	17,764	17,33	3,5	62,6	35,7	5	-0,12	1,066	0,00	-1,4	1,0	64,3
	Pre-cycle 9 (n=10)	17,90	8,528	17,80	2,0	29,3	28,6	6	1,19	2,606	0,68	-1,3	5,5	57,1
	Pre-cycle 13 (n=9)	19,87	9,520	18,00	3,2	35,0	35,7	5	3,04	1,928	3,00	0,5	5,8	64,3
	Pre-cycle 25 (n=8)	20,60	13,577	19,07	4,7	45,7	42,9	5	3,33	2,475	2,00	1,5	7,5	64,3
Right hand grip strength (pounds or Kg)	Baseline (n=7)	12,45	7,337	9,50	4,0	24,3	50,0							
	Pre-cycle 5 (n=10)	13,63	8,156	11,25	4,5	29,0	28,6	6	0,78	2,661	0,32	-2,0	4,7	57,1
	Pre-cycle 9 (n=10)	15,83	7,732	14,00	4,7	30,7	28,6	6	1,28	2,886	0,67	-2,5	6,4	57,1
	Pre-cycle 13 (n=9)	16,68	6,216	16,00	8,0	29,0	35,7	5	3,90	1,389	4,00	1,7	5,3	64,3
	Pre-cycle 25 (n=8)	16,78	7,008	17,17	8,3	29,0	42,9	5	5,24	1,873	4,70	3,0	7,8	64,3
Left hand Key-pinch strength (pounds or Kg)	Baseline (n=7)	4,60	2,026	4,50	2,2	8,0	50,0							
	Pre-cycle 5 (n=9)	7,33	2,706	7,00	4,0	12,0	35,7	5	1,79	2,180	1,33	0,0	5,5	64,3
	Pre-cycle 9 (n=10)	5,94	2,390	5,42	2,8	11,0	28,6	6	0,41	0,374	0,35	0,0	0,8	57,1
	Pre-cycle 13 (n=9)	5,88	2,023	5,90	2,0	9,0	35,7	5	0,39	0,727	0,27	-0,3	1,5	64,3
	Pre-cycle 25 (n=8)	6,24	2,807	5,72	3,0	12,0	42,9	5	0,83	0,690	0,67	0,2	2,0	64,3
Right hand Key-pinch strength (pounds or Kg)	Baseline (n=7)	4,37	2,116	3,42	2,5	8,0	50,0							
	Pre-cycle 5 (n=10)	6,85	2,170	7,00	4,0	10,0	28,6	6	2,38	1,443	1,70	1,0	4,5	57,1
	Pre-cycle 9 (n=10)	5,58	1,723	5,22	3,5	9,5	28,6	6	1,00	0,367	1,04	0,5	1,5	57,1
	Pre-cycle 13 (n=9)	5,83	1,331	5,44	4,0	8,5	35,7	5	1,23	0,821	0,90	0,5	2,5	64,3
	Pre-cycle 25 (n=8)	5,81	2,170	5,25	3,3	9,0	42,9	5	1,09	0,656	0,91	0,2	1,8	64,3
Leg length discrepancy (cm)	Baseline (n=12)	1,80	1,143	1,50	0,1	4,0	14,3							
	Pre-cycle 5 (n=11)	2,00	1,998	1,50	0,2	7,5	21,4	10	0,08	1,369	0,00	-1,6	3,5	28,6
	Pre-cycle 9 (n=11)	1,94	1,373	1,50	0,3	5,0	21,4	10	0,00	0,906	0,00	-1,5	1,5	28,6
	Pre-cycle 13 (n=9)	1,43	1,044	1,20	0,1	3,5	35,7	8	-0,21	0,669	-0,50	-1,0	1,0	42,9
	Pre-cycle 25 (n=8)	1,55	1,278	1,00	0,4	4,5	42,9	7	0,11	1,029	0,00	-1,2	2,0	50,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.1.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Grooved Pegboard, dominant hand time (s)	Baseline (n=8)	67,15	24,775	63,70	41,0	104,5	27,3							
	Pre-cycle 5 (n=8)	75,85	39,839	70,32	37,0	155,0	27,3	8	8,70	26,188	6,15	-29,8	54,0	27,3
	Pre-cycle 9 (n=8)	58,42	27,484	48,23	33,7	104,0	27,3	8	-8,73	28,566	-11,15	-48,9	47,0	27,3
	Pre-cycle 13 (n=8)	83,78	35,427	90,86	29,7	135,8	27,3	8	16,63	30,134	7,97	-21,3	65,5	27,3
	Pre-cycle 25 (n=3)	67,58	41,403	60,15	30,4	112,2	72,7	3	-4,32	43,443	-10,56	-44,3	41,9	72,7
Grooved Pegboard, non-dominant hand time (s)	Baseline (n=8)	103,08	56,534	83,46	46,0	224,0	27,3							
	Pre-cycle 5 (n=8)	103,33	86,045	77,56	39,0	298,1	27,3	8	0,25	68,234	-8,81	-78,0	152,4	27,3
	Pre-cycle 9 (n=8)	67,23	30,919	65,22	31,4	115,0	27,3	8	-35,85	38,371	-32,56	-109,0	11,0	27,3
	Pre-cycle 13 (n=8)	98,19	41,386	105,41	34,1	165,6	27,3	8	-4,89	56,497	-6,85	-111,0	70,4	27,3
	Pre-cycle 25 (n=3)	105,47	85,947	74,39	39,4	202,6	72,7	3	-0,72	95,100	-38,26	-71,3	107,4	72,7
Grooved Pegboard, dominant hand z-score	Baseline (n=8)	1,10	1,354	0,80	-0,7	3,6	27,3							
	Pre-cycle 5 (n=8)	1,09	1,736	0,49	-0,5	3,9	27,3	8	-0,01	1,726	0,20	-3,3	2,8	27,3
	Pre-cycle 9 (n=8)	0,04	0,545	0,06	-0,8	0,9	27,3	8	-1,06	1,338	-0,51	-3,3	0,4	27,3
	Pre-cycle 13 (n=8)	0,61	1,179	0,38	-0,9	2,7	27,3	8	-0,49	0,659	-0,35	-1,6	0,3	27,3
	Pre-cycle 25 (n=3)	0,84	1,595	0,80	-0,7	2,5	72,7	3	-0,71	1,829	-0,02	-2,8	0,7	72,7
Grooved Pegboard non-dominant hand z-score	Baseline (n=8)	2,35	2,024	2,22	-0,2	6,3	27,3							
	Pre-cycle 5 (n=8)	1,46	2,431	0,43	-0,6	6,9	27,3	8	-0,89	2,555	-1,03	-3,6	4,5	27,3
	Pre-cycle 9 (n=8)	0,23	0,879	0,25	-1,0	1,8	27,3	8	-2,12	1,813	-1,78	-5,6	0,1	27,3
	Pre-cycle 13 (n=8)	1,11	1,326	1,00	-0,5	3,1	27,3	8	-1,24	1,922	-0,68	-5,7	0,4	27,3
	Pre-cycle 25 (n=3)	1,97	2,108	2,29	-0,3	3,9	72,7	3	-0,21	0,452	-0,12	-0,7	0,2	72,7
Grooved Pegboard dominant hand # pegs dropped	Baseline (n=8)	0,38	0,518	0,00	0,0	1,0	27,3							
	Pre-cycle 5 (n=8)	1,38	1,188	1,00	0,0	3,0	27,3	8	1,00	1,512	0,50	-1,0	3,0	27,3
	Pre-cycle 9 (n=8)	2,25	3,732	1,00	0,0	11,0	27,3	8	1,88	3,871	0,50	-1,0	11,0	27,3
	Pre-cycle 13 (n=8)	0,88	2,100	0,00	0,0	6,0	27,3	8	0,50	2,330	0,00	-1,0	6,0	27,3
	Pre-cycle 25 (n=3)	0,67	1,155	0,00	0,0	2,0	72,7	3	0,33	1,528	0,00	-1,0	2,0	72,7
Grooved Pegboard non-dominant hand # pegs dropped	Baseline (n=8)	1,75	1,832	1,00	0,0	5,0	27,3							
	Pre-cycle 5 (n=8)	0,63	0,744	0,50	0,0	2,0	27,3	8	-1,13	1,458	-1,00	-3,0	1,0	27,3
	Pre-cycle 9 (n=8)	1,38	1,996	0,50	0,0	5,0	27,3	8	-0,38	2,066	-0,50	-3,0	4,0	27,3
	Pre-cycle 13 (n=8)	1,50	1,512	1,50	0,0	4,0	27,3	8	-0,25	2,375	0,50	-5,0	2,0	27,3
	Pre-cycle 25 (n=3)	1,67	2,887	0,00	0,0	5,0	72,7	3	-0,67	1,155	0,00	-2,0	0,0	72,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.1.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Left hand grip strength (pounds or Kg)	Baseline (n=2)	NC	NC	NC	2,7	10,0	81,8							
	Pre-cycle 5 (n=7)	11,21	6,413	10,00	3,5	20,3	36,4	2	NC	NC	NC	-2,0	0,8	81,8
	Pre-cycle 9 (n=8)	14,27	9,648	11,12	2,0	33,0	27,3	2	NC	NC	NC	-0,7	0,0	81,8
	Pre-cycle 13 (n=8)	15,06	8,425	13,77	3,2	30,7	27,3	2	NC	NC	NC	0,5	2,0	81,8
	Pre-cycle 25 (n=3)	5,89	1,835	5,00	4,7	8,0	72,7	1	NC	NC	NC	2,0	2,0	90,9
Right hand grip strength (pounds or Kg)	Baseline (n=2)	NC	NC	NC	4,0	8,0	81,8							
	Pre-cycle 5 (n=7)	11,83	5,038	10,73	5,0	19,1	36,4	2	NC	NC	NC	1,0	2,0	81,8
	Pre-cycle 9 (n=8)	14,37	7,135	13,76	4,7	25,0	27,3	2	NC	NC	NC	0,7	2,0	81,8
	Pre-cycle 13 (n=8)	15,56	7,240	13,76	8,0	30,7	27,3	2	NC	NC	NC	4,0	4,0	81,8
	Pre-cycle 25 (n=3)	8,44	0,510	8,33	8,0	9,0	72,7	1	NC	NC	NC	4,3	4,3	90,9
Left hand Key-pinch strength (pounds or Kg)	Baseline (n=2)	NC	NC	NC	2,3	3,5	81,8							
	Pre-cycle 5 (n=6)	5,11	2,306	4,04	3,0	9,0	45,5	2	NC	NC	NC	-0,5	1,7	81,8
	Pre-cycle 9 (n=8)	5,53	3,628	4,38	2,8	14,0	27,3	2	NC	NC	NC	0,0	0,5	81,8
	Pre-cycle 13 (n=8)	4,99	2,412	4,49	2,0	9,0	27,3	2	NC	NC	NC	-0,3	0,5	81,8
	Pre-cycle 25 (n=3)	3,11	0,840	3,00	2,3	4,0	72,7	1	NC	NC	NC	0,7	0,7	90,9
Right hand Key-pinch strength (pounds or Kg)	Baseline (n=2)	NC	NC	NC	3,0	3,1	81,8							
	Pre-cycle 5 (n=6)	5,09	1,623	4,76	3,0	7,0	45,5	2	NC	NC	NC	0,0	3,9	81,8
	Pre-cycle 9 (n=8)	6,06	4,533	4,75	2,8	17,0	27,3	2	NC	NC	NC	0,5	1,2	81,8
	Pre-cycle 13 (n=8)	5,03	1,736	4,72	2,8	7,3	27,3	2	NC	NC	NC	0,5	0,9	81,8
	Pre-cycle 25 (n=3)	3,39	0,750	3,33	2,7	4,2	72,7	1	NC	NC	NC	0,2	0,2	90,9
Leg length discrepancy (cm)	Baseline (n=8)	2,20	1,220	2,50	0,1	3,5	27,3							
	Pre-cycle 5 (n=8)	1,66	1,530	1,50	0,0	4,5	27,3	7	-0,47	1,201	0,00	-2,8	1,0	36,4
	Pre-cycle 9 (n=7)	2,01	1,853	1,50	0,1	5,5	36,4	6	0,03	1,194	0,00	-1,5	2,0	45,5
	Pre-cycle 13 (n=7)	2,34	1,480	2,60	0,1	4,5	36,4	7	0,19	0,790	0,00	-0,7	1,0	36,4
	Pre-cycle 25 (n=3)	1,90	2,287	1,00	0,2	4,5	72,7	3	-0,50	2,500	-0,50	-3,0	2,0	72,7
	Pre-cycle 37 (n=1)	NC	NC	NC	2,0	2,0	90,9	0	NC	NC	NC	NC	NC	100,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.1.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Grooved Pegboard, dominant hand time (s)	Baseline (n=7)	94,42	33,398	86,14	60,9	164,7	36,4							
	Pre-cycle 5 (n=7)	95,70	52,200	79,40	55,4	209,4	36,4	7	1,28	22,792	1,91	-24,8	44,8	36,4
	Pre-cycle 9 (n=6)	144,85	181,662	75,09	53,0	515,0	45,5	6	49,90	147,777	-6,02	-27,2	350,4	45,5
	Pre-cycle 13 (n=5)	136,50	129,143	85,27	67,5	367,0	54,5	5	35,71	93,568	-2,23	-15,8	202,4	54,5
	Pre-cycle 25 (n=3)	129,72	85,311	83,17	77,8	228,2	72,7	3	10,74	46,344	-8,06	-23,3	63,5	72,7
Grooved Pegboard, non-dominant hand time (s)	Baseline (n=6)	218,15	163,484	159,72	78,6	505,9	45,5							
	Pre-cycle 5 (n=6)	131,62	87,789	92,89	67,4	300,0	45,5	6	-86,53	98,662	-40,15	-217,6	-4,1	45,5
	Pre-cycle 9 (n=6)	179,15	191,455	103,64	84,2	569,0	45,5	6	-39,00	85,816	-12,68	-178,4	63,1	45,5
	Pre-cycle 13 (n=4)	160,99	149,033	93,48	73,0	384,0	63,6	4	-38,78	55,575	-13,80	-121,9	-5,6	63,6
	Pre-cycle 25 (n=3)	249,84	289,896	86,16	78,8	584,6	72,7	3	9,69	59,742	-23,46	-26,1	78,7	72,7
Grooved Pegboard, dominant hand z-score	Baseline (n=7)	1,97	3,547	0,23	-0,5	9,5	36,4							
	Pre-cycle 5 (n=7)	2,20	5,140	0,21	-0,5	13,8	36,4	7	0,22	1,985	0,11	-2,1	4,3	36,4
	Pre-cycle 9 (n=6)	7,65	17,419	0,87	-0,5	43,2	45,5	6	5,38	13,904	0,15	-2,0	33,7	45,5
	Pre-cycle 13 (n=5)	6,31	12,675	0,72	-0,1	28,9	54,5	5	3,77	8,811	0,49	-1,5	19,5	54,5
	Pre-cycle 25 (n=3)	2,89	3,867	1,13	0,2	7,3	72,7	3	-1,47	1,259	-2,16	-2,2	0,0	72,7
Grooved Pegboard non-dominant hand z-score	Baseline (n=6)	10,03	14,920	3,76	0,5	39,2	45,5							
	Pre-cycle 5 (n=6)	4,25	8,094	1,27	-0,3	20,7	45,5	6	-5,78	7,384	-2,01	-18,6	-0,2	45,5
	Pre-cycle 9 (n=6)	8,71	17,759	1,78	0,2	44,9	45,5	6	-1,31	4,936	-0,75	-9,4	5,7	45,5
	Pre-cycle 13 (n=4)	7,76	13,697	1,35	0,1	28,2	63,6	4	-3,24	5,174	-0,78	-11,0	-0,4	63,6
	Pre-cycle 25 (n=3)	8,49	13,672	1,41	-0,2	24,3	72,7	3	-5,93	7,866	-2,11	-15,0	-0,7	72,7
Grooved Pegboard dominant hand # pegs dropped	Baseline (n=7)	1,43	1,272	1,00	0,0	4,0	36,4							
	Pre-cycle 5 (n=7)	0,57	0,787	0,00	0,0	2,0	36,4	7	-0,86	1,069	-1,00	-3,0	0,0	36,4
	Pre-cycle 9 (n=6)	0,50	0,837	0,00	0,0	2,0	45,5	6	-1,00	0,632	-1,00	-2,0	0,0	45,5
	Pre-cycle 13 (n=5)	1,00	1,225	1,00	0,0	3,0	54,5	5	0,00	1,000	0,00	-1,0	1,0	54,5
	Pre-cycle 25 (n=3)	1,67	0,577	2,00	1,0	2,0	72,7	3	0,33	0,577	0,00	0,0	1,0	72,7
Grooved Pegboard non-dominant hand # pegs dropped	Baseline (n=6)	3,17	3,061	2,50	0,0	8,0	45,5							
	Pre-cycle 5 (n=6)	1,67	2,251	1,00	0,0	6,0	45,5	6	-1,50	2,881	-0,50	-7,0	1,0	45,5
	Pre-cycle 9 (n=6)	1,67	1,366	1,50	0,0	4,0	45,5	6	-1,50	3,082	-0,50	-7,0	1,0	45,5
	Pre-cycle 13 (n=4)	1,75	2,872	0,50	0,0	6,0	63,6	4	0,00	1,155	0,00	-1,0	1,0	63,6
	Pre-cycle 25 (n=3)	2,67	2,887	1,00	1,0	6,0	72,7	3	0,33	0,577	0,00	0,0	1,0	72,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.1.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Left hand grip strength (pounds or Kg)	Baseline (n=8)	12,85	7,861	11,75	4,0	27,3	27,3							
	Pre-cycle 5 (n=8)	15,39	7,992	16,67	0,0	26,3	27,3	7	1,65	6,127	0,00	-4,0	14,6	36,4
	Pre-cycle 9 (n=7)	16,45	9,308	18,00	0,7	29,3	36,4	7	2,80	6,229	2,03	-3,3	15,6	36,4
	Pre-cycle 13 (n=6)	17,83	10,319	19,67	1,0	30,7	45,5	6	4,80	7,231	3,35	-3,0	18,6	45,5
	Pre-cycle 25 (n=6)	18,14	11,106	19,00	0,8	31,0	45,5	6	5,11	8,949	2,85	-3,2	22,6	45,5
Right hand grip strength (pounds or Kg)	Baseline (n=8)	17,33	9,325	17,34	6,2	34,0	27,3							
	Pre-cycle 5 (n=9)	17,53	9,423	19,00	4,0	30,0	18,2	8	1,89	6,621	0,67	-4,3	15,8	27,3
	Pre-cycle 9 (n=6)	22,30	8,933	21,40	11,3	34,0	45,5	6	1,72	3,193	1,08	-2,5	6,4	45,5
	Pre-cycle 13 (n=6)	22,83	7,896	22,34	13,3	34,0	45,5	6	4,72	4,839	4,24	0,0	13,8	45,5
	Pre-cycle 25 (n=6)	24,72	7,463	27,67	13,7	32,0	45,5	6	6,61	9,303	5,52	-2,0	23,8	45,5
Left hand Key-pinch strength (pounds or Kg)	Baseline (n=8)	5,17	2,851	5,00	1,3	10,0	27,3							
	Pre-cycle 5 (n=8)	5,91	2,797	6,30	1,2	10,0	27,3	7	0,58	3,573	0,10	-6,0	5,5	36,4
	Pre-cycle 9 (n=7)	5,67	2,622	5,83	1,0	8,8	36,4	7	0,07	2,767	0,16	-5,5	3,3	36,4
	Pre-cycle 13 (n=6)	5,79	3,020	6,33	1,0	9,3	45,5	6	0,20	3,629	0,25	-6,0	5,1	45,5
	Pre-cycle 25 (n=6)	5,72	3,051	6,92	1,3	8,5	45,5	6	0,13	4,050	1,00	-7,5	4,3	45,5
Right hand Key-pinch strength (pounds or Kg)	Baseline (n=8)	6,61	4,884	4,75	2,6	18,0	27,3							
	Pre-cycle 5 (n=9)	6,67	2,456	8,00	2,5	9,0	18,2	8	0,58	4,319	1,59	-9,5	4,5	27,3
	Pre-cycle 9 (n=6)	6,94	2,157	7,08	4,0	9,5	45,5	6	-0,72	4,118	0,58	-9,0	2,0	45,5
	Pre-cycle 13 (n=6)	6,93	1,919	7,71	4,0	8,5	45,5	6	-0,37	4,699	0,58	-9,5	4,0	45,5
	Pre-cycle 25 (n=6)	7,86	1,468	8,17	6,2	9,5	45,5	6	0,56	4,911	1,92	-9,0	5,2	45,5
Leg length discrepancy (cm)	Baseline (n=8)	1,65	1,106	1,25	0,5	4,0	27,3							
	Pre-cycle 5 (n=7)	1,87	2,536	1,00	0,5	7,5	36,4	7	0,06	1,660	-0,50	-1,6	3,5	36,4
	Pre-cycle 9 (n=7)	1,57	1,644	1,00	0,0	5,0	36,4	7	-0,24	0,772	-0,50	-1,0	1,0	36,4
	Pre-cycle 13 (n=6)	1,20	0,245	1,10	1,0	1,5	45,5	6	-0,25	0,612	0,00	-1,0	0,5	45,5
	Pre-cycle 25 (n=6)	1,08	0,492	1,00	0,5	2,0	45,5	6	-0,37	0,653	-0,25	-1,2	0,5	45,5

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.1.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Grooved Pegboard, dominant hand time (s)	Baseline (n=10)	104,29	35,101	105,64	60,0	151,8	9,1							
	Pre-cycle 5 (n=9)	91,70	44,398	82,75	49,0	166,8	18,2	9	-11,70	43,086	-8,85	-96,7	63,0	18,2
	Pre-cycle 9 (n=9)	91,35	40,116	77,00	32,6	152,9	18,2	9	-12,05	52,478	-12,00	-117,0	84,0	18,2
	Pre-cycle 13 (n=9)	94,50	30,529	87,08	61,8	144,8	18,2	9	-8,90	41,993	-6,99	-61,3	84,0	18,2
	Pre-cycle 25 (n=7)	88,96	16,421	89,78	66,8	115,0	36,4	7	-15,70	38,421	-22,26	-59,8	55,0	36,4
Grooved Pegboard, non-dominant hand time (s)	Baseline (n=10)	104,92	40,024	101,01	60,0	188,0	9,1							
	Pre-cycle 5 (n=9)	104,62	41,748	86,00	51,7	168,0	18,2	9	0,89	19,873	1,19	-34,8	28,4	18,2
	Pre-cycle 9 (n=9)	97,18	41,656	84,20	32,6	164,0	18,2	9	-6,56	54,042	4,94	-102,0	92,2	18,2
	Pre-cycle 13 (n=9)	124,74	58,086	111,09	65,8	238,0	18,2	9	21,01	59,175	1,88	-43,0	134,8	18,2
	Pre-cycle 25 (n=7)	98,72	30,814	93,00	65,9	150,0	36,4	7	-5,14	59,193	-12,90	-95,0	90,0	36,4
Grooved Pegboard, dominant hand z-score	Baseline (n=10)	3,47	4,036	3,41	-1,0	12,4	9,1							
	Pre-cycle 5 (n=9)	1,55	1,853	1,61	-1,1	5,2	18,2	9	-1,81	3,707	-0,45	-10,7	1,2	18,2
	Pre-cycle 9 (n=9)	1,59	2,322	1,05	-0,7	5,7	18,2	9	-1,78	4,613	-0,72	-13,0	3,4	18,2
	Pre-cycle 13 (n=9)	2,39	3,809	1,15	-0,6	11,8	18,2	9	-0,98	6,103	-0,78	-12,2	11,3	18,2
	Pre-cycle 25 (n=7)	0,82	0,908	0,41	0,1	2,5	36,4	7	-2,67	4,585	-2,14	-12,2	1,1	36,4
Grooved Pegboard non-dominant hand z-score	Baseline (n=10)	2,13	2,319	1,46	-0,9	6,2	9,1							
	Pre-cycle 5 (n=9)	1,93	2,368	1,42	-0,7	6,7	18,2	9	0,01	1,058	0,10	-2,4	1,2	18,2
	Pre-cycle 9 (n=9)	1,98	3,201	0,41	-0,6	8,4	18,2	9	0,06	2,305	0,28	-3,7	4,2	18,2
	Pre-cycle 13 (n=9)	3,76	5,414	2,03	-0,4	15,1	18,2	9	1,84	4,539	0,35	-2,3	10,1	18,2
	Pre-cycle 25 (n=7)	0,94	1,367	0,32	-0,4	3,1	36,4	7	-0,78	1,456	-1,28	-1,8	2,0	36,4
Grooved Pegboard dominant hand # pegs dropped	Baseline (n=10)	1,60	2,221	0,00	0,0	6,0	9,1							
	Pre-cycle 5 (n=9)	1,89	4,226	0,00	0,0	13,0	18,2	9	0,11	3,100	0,00	-4,0	7,0	18,2
	Pre-cycle 9 (n=9)	1,67	3,041	0,00	0,0	9,0	18,2	9	-0,11	1,965	0,00	-4,0	3,0	18,2
	Pre-cycle 13 (n=9)	0,78	1,302	0,00	0,0	4,0	18,2	9	-1,00	1,225	0,00	-3,0	0,0	18,2
	Pre-cycle 25 (n=7)	0,71	0,951	0,00	0,0	2,0	36,4	7	-1,57	1,718	-1,00	-4,0	0,0	36,4
Grooved Pegboard non-dominant hand # pegs dropped	Baseline (n=10)	2,60	5,502	1,00	0,0	18,0	9,1							
	Pre-cycle 5 (n=9)	0,67	0,866	0,00	0,0	2,0	18,2	9	-2,22	5,239	-1,00	-16,0	1,0	18,2
	Pre-cycle 9 (n=9)	1,44	1,333	1,00	0,0	3,0	18,2	9	-1,44	6,064	0,00	-17,0	3,0	18,2
	Pre-cycle 13 (n=9)	1,67	1,500	2,00	0,0	5,0	18,2	9	-1,22	5,954	0,00	-16,0	5,0	18,2
	Pre-cycle 25 (n=7)	0,71	0,756	1,00	0,0	2,0	36,4	7	-2,86	6,414	-1,00	-17,0	2,0	36,4

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.1.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Left hand grip strength (pounds or Kg)	Baseline (n=3)	17,20	2,221	18,10	14,7	18,8	72,7							
	Pre-cycle 5 (n=7)	20,28	21,579	13,30	2,0	62,6	36,4	1	NC	NC	NC	-1,4	-1,4	90,9
	Pre-cycle 9 (n=8)	18,27	9,420	17,80	2,9	30,3	27,3	2	NC	NC	NC	2,3	5,5	81,8
	Pre-cycle 13 (n=8)	19,16	9,774	17,84	5,4	35,0	27,3	2	NC	NC	NC	3,0	5,8	81,8
	Pre-cycle 25 (n=5)	26,56	11,228	22,66	16,7	45,7	54,5	2	NC	NC	NC	2,0	7,5	81,8
Right hand grip strength (pounds or Kg)	Baseline (n=3)	12,48	4,969	10,67	8,7	18,1	72,7							
	Pre-cycle 5 (n=7)	11,47	10,344	8,30	2,0	29,8	36,4	1	NC	NC	NC	-0,4	-0,4	90,9
	Pre-cycle 9 (n=8)	13,83	8,543	12,67	3,2	31,3	27,3	2	NC	NC	NC	0,7	0,7	81,8
	Pre-cycle 13 (n=8)	15,88	9,873	16,00	3,9	36,7	27,3	2	NC	NC	NC	1,7	5,3	81,8
	Pre-cycle 25 (n=5)	20,52	7,482	20,26	11,7	32,0	54,5	2	NC	NC	NC	3,0	6,3	81,8
Left hand Key-pinch strength (pounds or Kg)	Baseline (n=3)	4,99	0,656	5,33	4,2	5,4	72,7							
	Pre-cycle 5 (n=7)	5,95	3,558	4,67	1,8	12,0	36,4	1	NC	NC	NC	0,4	0,4	90,9
	Pre-cycle 9 (n=8)	5,35	2,922	4,77	1,8	11,0	27,3	2	NC	NC	NC	0,1	0,8	81,8
	Pre-cycle 13 (n=8)	5,67	2,385	5,86	1,8	9,0	27,3	2	NC	NC	NC	0,3	1,5	81,8
	Pre-cycle 25 (n=5)	7,05	2,878	6,00	4,8	12,0	54,5	2	NC	NC	NC	0,6	0,7	81,8
Right hand Key-pinch strength (pounds or Kg)	Baseline (n=3)	4,24	2,264	3,42	2,5	6,8	72,7							
	Pre-cycle 5 (n=7)	5,65	2,713	4,98	2,3	10,0	36,4	1	NC	NC	NC	1,5	1,5	90,9
	Pre-cycle 9 (n=8)	4,59	1,896	4,50	2,3	8,0	27,3	2	NC	NC	NC	1,0	1,1	81,8
	Pre-cycle 13 (n=8)	5,45	2,347	5,22	2,3	9,9	27,3	2	NC	NC	NC	1,6	2,5	81,8
	Pre-cycle 25 (n=5)	6,32	2,046	6,35	4,3	9,0	54,5	2	NC	NC	NC	0,9	1,8	81,8
Leg length discrepancy (cm)	Baseline (n=7)	2,49	2,886	1,50	0,1	8,5	36,4							
	Pre-cycle 5 (n=6)	3,07	3,918	1,50	0,2	10,5	45,5	5	0,38	1,083	0,39	-1,0	2,0	54,5
	Pre-cycle 9 (n=7)	2,37	2,274	1,00	0,3	6,0	36,4	5	-0,20	1,563	-0,50	-2,5	1,5	54,5
	Pre-cycle 13 (n=6)	2,08	2,438	0,75	0,1	5,5	45,5	5	-0,78	1,469	-0,50	-3,0	1,1	54,5
	Pre-cycle 25 (n=5)	1,88	1,802	1,50	0,4	5,0	54,5	4	-0,88	1,797	-0,25	-3,5	0,5	63,6

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, affected hand time (s)	Baseline (n=8)	138,46	151,397	88,84	41,0	505,9						
	Pre-cycle 5 (n=8)	123,63	109,540	74,67	46,0	300,0	8	-14,84	99,364	-11,43	-205,9	152,4
	Pre-cycle 9 (n=7)	134,31	192,934	75,57	32,6	569,0	7	-10,90	50,207	-26,05	-60,0	63,1
	Pre-cycle 13 (n=8)	142,75	101,699	111,74	68,7	384,0	8	4,29	61,432	11,49	-121,9	70,4
	Pre-cycle 25 (n=5)	214,39	213,062	127,22	74,4	584,6	5	29,49	71,047	40,77	-71,3	107,4

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, non-affected hand time (s)	Baseline (n=9)	100,27	35,858	89,28	57,1	164,7						
	Pre-cycle 5 (n=9)	94,88	48,667	90,57	40,5	209,4	9	-5,39	39,513	4,43	-96,7	44,8
	Pre-cycle 9 (n=9)	114,73	152,165	84,21	32,6	515,0	9	14,46	131,636	-12,11	-117,0	350,4
	Pre-cycle 13 (n=9)	125,61	92,079	93,71	73,8	367,0	9	25,34	75,471	-1,82	-61,3	202,4
	Pre-cycle 25 (n=5)	113,82	66,643	89,78	60,2	228,2	5	-4,96	54,522	-26,12	-59,8	63,5

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, dominant hand time (s)	Baseline (n=7)	93,27	31,511	101,06	51,0	137,0						
	Pre-cycle 5 (n=6)	71,32	23,691	79,06	37,0	101,0	6	-18,79	14,074	-17,83	-36,0	1,9
	Pre-cycle 9 (n=6)	88,70	39,496	80,37	35,8	144,0	6	-1,40	42,693	-13,61	-33,8	84,0
	Pre-cycle 13 (n=5)	86,51	41,827	85,27	29,7	144,0	5	-6,25	51,585	-21,32	-43,1	84,0
	Pre-cycle 25 (n=3)	95,09	18,734	92,46	77,8	115,0	3	3,16	44,883	-22,26	-23,3	55,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, non-dominant hand time (s)	Baseline (n=7)	108,40	55,357	109,62	46,0	209,8						
	Pre-cycle 5 (n=6)	98,18	43,550	85,49	39,0	154,2	6	-9,02	28,207	-2,91	-55,7	26,0
	Pre-cycle 9 (n=6)	106,44	48,311	103,64	31,4	164,0	6	-0,76	62,154	-4,15	-98,9	92,2
	Pre-cycle 13 (n=5)	126,14	86,783	97,95	34,1	238,0	5	39,46	71,812	-11,67	-12,9	134,8
	Pre-cycle 25 (n=3)	100,68	43,903	86,16	65,9	150,0	3	17,88	62,675	-12,90	-23,5	90,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, affected hand z-score	Baseline (n=8)	6,45	13,312	2,23	0,2	39,2						
	Pre-cycle 5 (n=8)	3,73	7,232	0,61	-0,4	20,7	8	-2,72	6,809	-1,22	-18,6	4,5
	Pre-cycle 9 (n=7)	6,66	16,874	0,26	-0,6	44,9	7	-0,68	3,194	-1,77	-3,7	5,7
	Pre-cycle 13 (n=8)	4,68	9,582	1,07	0,2	28,2	8	-1,77	3,822	-0,44	-11,0	0,5
	Pre-cycle 25 (n=5)	6,39	10,077	2,29	0,2	24,3	5	-3,35	6,551	-0,12	-15,0	0,2

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-affected hand z-score	Baseline (n=9)	3,78	4,237	2,12	0,1	12,4						
	Pre-cycle 5 (n=9)	2,58	4,335	1,58	0,1	13,8	9	-1,20	4,156	-0,11	-10,7	4,3
	Pre-cycle 9 (n=9)	4,91	14,365	0,03	-0,6	43,2	9	1,13	12,843	-1,88	-13,0	33,7
	Pre-cycle 13 (n=9)	4,01	9,398	0,50	-0,1	28,9	9	0,23	8,170	-0,42	-12,2	19,5
	Pre-cycle 25 (n=5)	2,12	3,081	0,80	-0,2	7,3	5	-3,43	5,072	-2,16	-12,2	0,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, dominant hand z-score	Baseline (n=7)	2,85	2,673	3,37	0,0	6,8						
	Pre-cycle 5 (n=6)	1,00	1,398	0,72	-0,5	3,4	6	-1,59	1,494	-1,33	-3,5	0,1
	Pre-cycle 9 (n=6)	1,93	2,416	1,38	-0,5	5,7	6	-0,66	2,259	-0,85	-3,3	3,4
	Pre-cycle 13 (n=5)	3,34	4,974	1,85	-0,9	11,8	5	0,24	6,291	-1,52	-4,1	11,3
	Pre-cycle 25 (n=3)	1,75	0,719	1,59	1,1	2,5	3	-1,09	1,900	-2,14	-2,2	1,1

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-dominant hand z-score	Baseline (n=7)	2,67	2,375	3,52	-0,2	6,2						
	Pre-cycle 5 (n=6)	2,02	2,478	1,45	-0,6	6,7	6	-0,42	1,333	-0,11	-2,2	1,2
	Pre-cycle 9 (n=6)	2,78	3,272	1,76	-0,7	8,4	6	0,35	2,602	0,01	-3,2	4,2
	Pre-cycle 13 (n=5)	5,44	7,020	2,47	-0,5	15,1	5	3,32	5,691	-0,24	-1,2	10,1
	Pre-cycle 25 (n=3)	1,14	1,449	1,41	-0,4	2,4	3	-0,42	2,170	-1,17	-2,1	2,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard affected hand # pegs dropped	Baseline (n=8)	2,13	1,885	1,50	0,0	5,0						
	Pre-cycle 5 (n=8)	1,75	2,053	1,50	0,0	6,0	8	-0,38	1,847	-0,50	-3,0	3,0
	Pre-cycle 9 (n=7)	1,14	1,574	0,00	0,0	4,0	7	-1,14	1,345	-1,00	-3,0	1,0
	Pre-cycle 13 (n=8)	1,50	2,330	0,00	0,0	6,0	8	-0,63	2,066	-0,50	-5,0	2,0
	Pre-cycle 25 (n=5)	2,80	2,588	2,00	0,0	6,0	5	-0,20	1,304	0,00	-2,0	1,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-affected hand # pegs dropped	Baseline (n=9)	1,44	1,333	1,00	0,0	4,0						
	Pre-cycle 5 (n=9)	1,22	0,972	1,00	0,0	3,0	9	-0,22	1,641	0,00	-3,0	3,0
	Pre-cycle 9 (n=9)	2,11	3,408	1,00	0,0	11,0	9	0,67	4,093	0,00	-3,0	11,0
	Pre-cycle 13 (n=9)	1,56	2,007	1,00	0,0	6,0	9	0,11	2,472	-1,00	-2,0	6,0
	Pre-cycle 25 (n=5)	1,40	0,894	2,00	0,0	2,0	5	0,00	1,225	0,00	-1,0	2,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard dominant hand # pegs dropped	Baseline (n=7)	0,43	0,535	0,00	0,0	1,0						
	Pre-cycle 5 (n=6)	0,50	0,548	0,50	0,0	1,0	6	0,00	0,894	0,00	-1,0	1,0
	Pre-cycle 9 (n=6)	0,17	0,408	0,00	0,0	1,0	6	-0,33	0,816	-0,50	-1,0	1,0
	Pre-cycle 13 (n=5)	0,20	0,447	0,00	0,0	1,0	5	-0,20	0,447	0,00	-1,0	0,0
	Pre-cycle 25 (n=3)	0,33	0,577	0,00	0,0	1,0	3	0,00	0,000	0,00	0,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-dominant hand # pegs dropped	Baseline (n=7)	0,71	1,496	0,00	0,0	4,0						
	Pre-cycle 5 (n=6)	0,50	0,837	0,00	0,0	2,0	6	-0,33	1,033	0,00	-2,0	1,0
	Pre-cycle 9 (n=6)	1,67	1,862	1,50	0,0	4,0	6	0,83	1,722	0,00	-1,0	3,0
	Pre-cycle 13 (n=5)	1,80	1,924	1,00	0,0	5,0	5	1,60	2,191	1,00	-1,0	5,0
	Pre-cycle 25 (n=3)	1,00	1,000	1,00	0,0	2,0	3	0,67	1,155	0,00	0,0	2,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Affected hand grip strength (Kg)	Baseline (n=4)	8,55	4,398	8,10	4,0	14,0						
	Pre-cycle 5 (n=7)	10,71	7,153	10,00	0,0	22,0	4	1,95	9,281	-2,00	-4,0	15,8
	Pre-cycle 9 (n=7)	13,76	10,343	10,00	0,7	33,0	3	0,22	3,670	0,00	-3,3	4,0
	Pre-cycle 13 (n=8)	14,46	8,805	13,17	1,0	30,7	4	4,20	7,045	3,00	-3,0	13,8
	Pre-cycle 25 (n=4)	13,46	13,232	11,50	0,8	30,0	3	8,21	13,969	4,00	-3,2	23,8

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-affected hand grip strength (Kg)	Baseline (n=4)	15,52	12,925	11,34	5,4	34,0						
	Pre-cycle 5 (n=7)	15,99	7,941	14,00	7,3	30,0	4	2,07	8,849	-1,00	-4,3	14,6
	Pre-cycle 9 (n=8)	17,97	8,413	17,34	7,5	34,0	4	4,48	7,463	1,17	0,0	15,6
	Pre-cycle 13 (n=8)	20,08	8,694	17,50	10,3	34,0	4	5,98	8,575	2,67	0,0	18,6
	Pre-cycle 25 (n=4)	20,42	11,422	20,84	8,0	32,0	3	6,53	13,923	-1,00	-2,0	22,6

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Dominant hand grip strength (Kg)	Baseline (n=2)	NC	NC	NC	18,1	20,0						
	Pre-cycle 5 (n=6)	14,36	10,919	13,37	2,0	29,8	1	NC	NC	NC	3,6	3,6
	Pre-cycle 9 (n=5)	16,54	11,244	13,91	3,2	31,3	1	NC	NC	NC	4,3	4,3
	Pre-cycle 13 (n=5)	17,55	13,257	14,51	3,9	36,7	1	NC	NC	NC	4,7	4,7
	Pre-cycle 25 (n=2)	NC	NC	NC	26,3	32,0	1	NC	NC	NC	6,3	6,3

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-dominant hand grip strength (Kg)	Baseline (n=2)	NC	NC	NC	18,0	18,1						
	Pre-cycle 5 (n=6)	11,57	10,856	7,44	2,0	28,3	1	NC	NC	NC	3,0	3,0
	Pre-cycle 9 (n=5)	14,95	10,918	12,24	2,9	30,3	1	NC	NC	NC	3,3	3,3
	Pre-cycle 13 (n=5)	15,25	9,122	14,21	5,4	27,3	1	NC	NC	NC	3,3	3,3
	Pre-cycle 25 (n=2)	NC	NC	NC	20,0	22,7	1	NC	NC	NC	2,0	2,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Affected hand Key-pinch strength (Kg)	Baseline (n=4)	4,78	3,698	3,90	1,3	10,0						
	Pre-cycle 5 (n=6)	4,49	2,558	3,88	1,2	8,0	4	-0,74	3,990	-0,34	-6,0	3,7
	Pre-cycle 9 (n=7)	5,01	4,160	3,75	1,0	14,0	3	-1,94	3,085	-0,33	-5,5	0,0
	Pre-cycle 13 (n=8)	4,78	2,566	4,00	1,0	8,3	4	-0,47	4,126	0,09	-6,0	4,0
	Pre-cycle 25 (n=4)	3,92	3,759	2,42	1,3	9,5	3	-0,77	6,385	0,00	-7,5	5,2

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-affected hand Key-pinch strength (Kg)	Baseline (n=4)	7,30	7,153	4,10	3,0	18,0						
	Pre-cycle 5 (n=6)	6,00	2,627	5,75	3,0	9,0	4	-1,55	5,524	0,00	-9,5	3,3
	Pre-cycle 9 (n=8)	6,66	4,667	4,75	2,8	17,0	4	-1,30	5,335	0,25	-9,0	3,3
	Pre-cycle 13 (n=8)	6,02	2,750	5,67	2,8	9,3	4	-0,99	6,113	0,25	-9,5	5,1
	Pre-cycle 25 (n=4)	6,58	2,887	7,33	2,7	9,0	3	-0,84	7,143	2,17	-9,0	4,3

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Dominant hand Key-pinch strength (Kg)	Baseline (n=2)	NC	NC	NC	5,0	6,8						
	Pre-cycle 5 (n=6)	4,68	2,084	4,27	2,3	7,8	1	NC	NC	NC	1,5	1,5
	Pre-cycle 9 (n=5)	5,05	2,585	5,44	2,3	8,0	1	NC	NC	NC	2,0	2,0
	Pre-cycle 13 (n=5)	5,66	3,000	5,44	2,3	9,9	1	NC	NC	NC	2,2	2,2
	Pre-cycle 25 (n=2)	NC	NC	NC	7,5	7,6	1	NC	NC	NC	2,5	2,5

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.1 Motor function secondary outcome scores and change from baseline over time - Gender = Male
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=19) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-dominant hand Key-pinch strength (Kg)	Baseline (n=2)	NC	NC	NC	5,4	5,5						
	Pre-cycle 5 (n=6)	4,02	1,834	3,79	1,8	6,6	1	NC	NC	NC	0,1	0,1
	Pre-cycle 9 (n=5)	4,95	2,700	5,44	1,8	7,5	1	NC	NC	NC	2,0	2,0
	Pre-cycle 13 (n=5)	5,06	2,715	4,98	1,8	8,0	1	NC	NC	NC	2,0	2,0
	Pre-cycle 25 (n=2)	NC	NC	NC	7,0	7,3	1	NC	NC	NC	1,8	1,8

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, affected hand time (s)	Baseline (n=8)	108,66	42,794	90,60	67,6	188,0						
	Pre-cycle 5 (n=8)	109,37	48,985	97,62	55,4	168,0	8	0,71	25,131	-6,28	-24,8	54,0
	Pre-cycle 9 (n=8)	89,45	37,041	85,10	38,6	152,9	8	-19,20	37,408	0,09	-102,0	5,9
	Pre-cycle 13 (n=7)	101,39	37,401	111,09	51,3	145,0	7	-11,34	18,703	-6,99	-43,0	14,0
	Pre-cycle 25 (n=4)	84,41	30,397	96,86	39,4	104,5	4	-51,05	31,976	-44,66	-95,0	-19,9

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, non-affected hand time (s)	Baseline (n=8)	124,72	90,598	95,76	41,0	300,0						
	Pre-cycle 5 (n=8)	98,65	45,947	83,03	47,3	162,0	8	-26,07	86,930	-0,94	-217,6	63,0
	Pre-cycle 9 (n=8)	79,35	28,098	72,17	33,9	121,6	8	-45,37	65,230	-23,88	-178,4	9,5
	Pre-cycle 13 (n=7)	77,00	23,021	73,00	42,9	113,0	7	-22,67	41,089	-5,43	-111,0	6,6
	Pre-cycle 25 (n=4)	64,89	24,301	71,58	30,4	86,0	4	-23,06	14,835	-19,37	-43,0	-10,6

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, dominant hand time (s)	Baseline (n=1)	NC	NC	NC	65,0	65,0						
	Pre-cycle 5 (n=1)	NC	NC	NC	68,0	68,0	1	NC	NC	NC	3,0	3,0
	Pre-cycle 9 (n=1)	NC	NC	NC	77,0	77,0	1	NC	NC	NC	12,0	12,0
	Pre-cycle 13 (n=1)	NC	NC	NC	78,0	78,0	1	NC	NC	NC	13,0	13,0
	Pre-cycle 25 (n=1)	NC	NC	NC	72,0	72,0	1	NC	NC	NC	7,0	7,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, non-dominant hand time (s)	Baseline (n=1)	NC	NC	NC	70,0	70,0						
	Pre-cycle 5 (n=1)	NC	NC	NC	68,0	68,0	1	NC	NC	NC	-2,0	-2,0
	Pre-cycle 9 (n=1)	NC	NC	NC	75,0	75,0	1	NC	NC	NC	5,0	5,0
	Pre-cycle 13 (n=1)	NC	NC	NC	93,0	93,0	1	NC	NC	NC	23,0	23,0
	Pre-cycle 25 (n=1)	NC	NC	NC	74,0	74,0	1	NC	NC	NC	4,0	4,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, affected hand z-score	Baseline (n=8)	1,67	1,954	1,09	-0,9	4,9						
	Pre-cycle 5 (n=8)	1,79	2,398	0,76	-0,7	5,2	8	0,12	1,239	-0,27	-1,0	2,8
	Pre-cycle 9 (n=8)	1,22	2,070	0,84	-1,0	4,8	8	-0,45	0,908	-0,32	-2,1	0,5
	Pre-cycle 13 (n=7)	1,34	1,700	0,65	-0,3	3,7	7	-0,42	0,655	-0,50	-1,2	0,6
	Pre-cycle 25 (n=4)	0,80	1,536	0,21	-0,3	3,1	4	-2,05	1,344	-1,79	-3,9	-0,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-affected hand z-score	Baseline (n=8)	2,52	4,579	0,64	-1,0	12,2						
	Pre-cycle 5 (n=8)	0,90	1,409	1,28	-1,1	2,7	8	-1,62	4,052	-0,05	-10,9	1,2
	Pre-cycle 9 (n=8)	0,26	1,161	0,12	-0,8	2,8	8	-2,25	3,516	-0,98	-9,4	0,9
	Pre-cycle 13 (n=7)	0,25	0,903	0,14	-0,6	2,0	7	-0,89	2,194	-0,52	-5,7	0,6
	Pre-cycle 25 (n=4)	-0,11	0,480	-0,06	-0,7	0,4	4	-0,88	1,249	-0,65	-2,5	0,2

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, dominant hand z-score	Baseline (n=1)	NC	NC	NC	-0,1	-0,1						
	Pre-cycle 5 (n=1)	NC	NC	NC	0,2	0,2	1	NC	NC	NC	0,3	0,3
	Pre-cycle 9 (n=1)	NC	NC	NC	1,1	1,1	1	NC	NC	NC	1,2	1,2
	Pre-cycle 13 (n=1)	NC	NC	NC	1,2	1,2	1	NC	NC	NC	1,3	1,3
	Pre-cycle 25 (n=1)	NC	NC	NC	0,6	0,6	1	NC	NC	NC	0,7	0,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-dominant hand z-score	Baseline (n=1)	NC	NC	NC	-0,1	-0,1						
	Pre-cycle 5 (n=1)	NC	NC	NC	-0,2	-0,2	1	NC	NC	NC	-0,2	-0,2
	Pre-cycle 9 (n=1)	NC	NC	NC	0,4	0,4	1	NC	NC	NC	0,5	0,5
	Pre-cycle 13 (n=1)	NC	NC	NC	2,0	2,0	1	NC	NC	NC	2,1	2,1
	Pre-cycle 25 (n=1)	NC	NC	NC	0,3	0,3	1	NC	NC	NC	0,4	0,4

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard affected hand # pegs dropped	Baseline (n=8)	4,00	6,071	2,00	0,0	18,0						
	Pre-cycle 5 (n=8)	2,50	4,309	1,00	0,0	13,0	8	-1,50	6,612	-0,50	-16,0	7,0
	Pre-cycle 9 (n=8)	2,38	2,925	1,50	0,0	9,0	8	-1,63	6,457	0,00	-17,0	3,0
	Pre-cycle 13 (n=7)	1,14	1,464	1,00	0,0	4,0	7	-2,86	5,984	-1,00	-16,0	1,0
	Pre-cycle 25 (n=4)	0,75	0,957	0,50	0,0	2,0	4	-6,00	7,528	-3,50	-17,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-affected hand # pegs dropped	Baseline (n=8)	2,13	2,800	1,00	0,0	8,0						
	Pre-cycle 5 (n=8)	0,25	0,463	0,00	0,0	1,0	8	-1,88	2,588	-0,50	-7,0	0,0
	Pre-cycle 9 (n=8)	1,50	2,000	0,50	0,0	5,0	8	-0,63	3,378	0,00	-7,0	4,0
	Pre-cycle 13 (n=7)	1,00	1,000	1,00	0,0	3,0	7	-0,29	1,704	0,00	-3,0	2,0
	Pre-cycle 25 (n=4)	0,50	0,577	0,50	0,0	1,0	4	-1,50	1,732	-1,50	-3,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard dominant hand # pegs dropped	Baseline (n=1)	NC	NC	NC	0,0	0,0						
	Pre-cycle 5 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	0,0	0,0
	Pre-cycle 9 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	0,0	0,0
	Pre-cycle 13 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	0,0	0,0
	Pre-cycle 25 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	0,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-dominant hand # pegs dropped	Baseline (n=1)	NC	NC	NC	1,0	1,0						
	Pre-cycle 5 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	-1,0	-1,0
	Pre-cycle 9 (n=1)	NC	NC	NC	1,0	1,0	1	NC	NC	NC	0,0	0,0
	Pre-cycle 13 (n=1)	NC	NC	NC	2,0	2,0	1	NC	NC	NC	1,0	1,0
	Pre-cycle 25 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	-1,0	-1,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Affected hand grip strength (Kg)	Baseline (n=7)	11,74	6,998	9,50	2,7	24,3						
	Pre-cycle 5 (n=9)	12,39	8,170	10,00	3,5	29,0	6	1,08	2,354	0,40	-1,7	4,7
	Pre-cycle 9 (n=9)	14,85	8,481	14,00	2,0	30,7	6	1,25	2,746	0,66	-1,3	6,4
	Pre-cycle 13 (n=8)	15,72	7,569	16,00	3,2	29,0	5	3,19	2,061	3,80	0,5	5,3
	Pre-cycle 25 (n=7)	15,62	8,307	17,00	4,7	29,0	5	4,77	2,386	4,70	2,0	7,8

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-affected hand grip strength (Kg)	Baseline (n=7)	14,66	8,284	14,67	4,0	27,3						
	Pre-cycle 5 (n=8)	15,76	8,583	16,15	5,0	27,0	5	-0,48	1,397	-1,05	-2,0	1,0
	Pre-cycle 9 (n=9)	18,40	8,447	18,50	4,7	29,3	6	1,23	2,754	1,35	-2,5	5,5
	Pre-cycle 13 (n=8)	20,80	9,048	19,20	8,0	35,0	5	3,74	1,294	3,37	2,5	5,8
	Pre-cycle 25 (n=7)	21,14	13,905	16,67	8,3	45,7	5	3,81	2,372	3,70	1,5	7,5

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Dominant hand grip strength (Kg)	Pre-cycle 5 (n=1)	NC	NC	NC	21,6	21,6	0	NC	NC	NC	NC	NC
	Pre-cycle 9 (n=1)	NC	NC	NC	19,5	19,5	0	NC	NC	NC	NC	NC
	Pre-cycle 13 (n=1)	NC	NC	NC	19,5	19,5	0	NC	NC	NC	NC	NC
	Pre-cycle 25 (n=1)	NC	NC	NC	20,3	20,3	0	NC	NC	NC	NC	NC

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-dominant hand grip strength (Kg)	Pre-cycle 5 (n=1)	NC	NC	NC	62,6	62,6	0	NC	NC	NC	NC	NC
	Pre-cycle 9 (n=1)	NC	NC	NC	18,6	18,6	0	NC	NC	NC	NC	NC
	Pre-cycle 13 (n=1)	NC	NC	NC	17,2	17,2	0	NC	NC	NC	NC	NC
	Pre-cycle 25 (n=1)	NC	NC	NC	21,5	21,5	0	NC	NC	NC	NC	NC

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Affected hand Key-pinch strength (Kg)	Baseline (n=7)	4,14	2,095	3,42	2,3	8,0						
	Pre-cycle 5 (n=9)	6,59	2,363	7,00	4,0	10,0	6	1,96	1,273	1,60	1,0	4,5
	Pre-cycle 9 (n=9)	5,28	1,919	5,00	2,8	9,5	6	0,80	0,486	0,77	0,2	1,5
	Pre-cycle 13 (n=8)	5,63	1,891	5,58	2,0	8,5	5	0,99	1,077	0,67	-0,3	2,5
	Pre-cycle 25 (n=7)	5,67	2,409	4,33	3,0	9,0	5	1,19	0,522	0,91	0,7	1,8

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-affected hand Key-pinch strength (Kg)	Baseline (n=7)	4,83	1,987	4,50	2,2	8,0						
	Pre-cycle 5 (n=8)	8,21	2,211	8,09	4,7	12,0	5	2,30	2,342	1,67	0,0	5,5
	Pre-cycle 9 (n=9)	6,41	2,287	6,17	4,3	11,0	6	0,61	0,473	0,75	0,0	1,2
	Pre-cycle 13 (n=8)	6,22	1,685	6,20	4,0	9,0	5	0,63	0,633	0,67	-0,2	1,5
	Pre-cycle 25 (n=7)	6,43	2,930	6,00	3,3	12,0	5	0,73	0,742	0,60	0,2	2,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Dominant hand Key-pinch strength (Kg)	Pre-cycle 5 (n=1)	NC	NC	NC	5,0	5,0	0	NC	NC	NC	NC	NC
	Pre-cycle 9 (n=1)	NC	NC	NC	5,4	5,4	0	NC	NC	NC	NC	NC
	Pre-cycle 13 (n=1)	NC	NC	NC	5,4	5,4	0	NC	NC	NC	NC	NC
	Pre-cycle 25 (n=1)	NC	NC	NC	6,4	6,4	0	NC	NC	NC	NC	NC

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.2 Motor function secondary outcome scores and change from baseline over time - Gender = Female
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=14) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-dominant hand Key-pinch strength (Kg)	Pre-cycle 5 (n=1)	NC	NC	NC	4,5	4,5	0	NC	NC	NC	NC	NC
	Pre-cycle 9 (n=1)	NC	NC	NC	4,5	4,5	0	NC	NC	NC	NC	NC
	Pre-cycle 13 (n=1)	NC	NC	NC	5,2	5,2	0	NC	NC	NC	NC	NC
	Pre-cycle 25 (n=1)	NC	NC	NC	5,4	5,4	0	NC	NC	NC	NC	NC

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, affected hand time (s)	Baseline (n=7)	86,11	32,697	77,64	41,0	145,7						
	Pre-cycle 5 (n=7)	109,13	90,948	73,33	46,0	298,1	7	23,02	66,543	1,94	-46,8	152,4
	Pre-cycle 9 (n=7)	68,73	25,880	75,57	38,6	104,0	7	-17,37	37,628	-26,05	-60,0	47,0
	Pre-cycle 13 (n=7)	103,38	37,897	111,82	51,3	165,6	7	17,27	40,547	14,00	-33,9	70,4
	Pre-cycle 25 (n=3)	105,47	85,947	74,39	39,4	202,6	3	-0,72	95,100	-38,26	-71,3	107,4

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, non-affected hand time (s)	Baseline (n=7)	94,58	60,677	76,00	41,0	224,0						
	Pre-cycle 5 (n=7)	84,80	36,899	88,08	40,5	146,0	7	-9,79	33,677	5,93	-78,0	18,0
	Pre-cycle 9 (n=7)	65,26	32,322	55,52	33,7	115,0	7	-29,32	40,499	-23,44	-109,0	11,0
	Pre-cycle 13 (n=7)	95,47	28,227	96,44	42,9	135,8	7	0,89	55,603	1,94	-111,0	65,5
	Pre-cycle 25 (n=3)	67,58	41,403	60,15	30,4	112,2	3	-4,32	43,443	-10,56	-44,3	41,9

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, dominant hand time (s)	Baseline (n=1)	NC	NC	NC	51,0	51,0						
	Pre-cycle 5 (n=1)	NC	NC	NC	37,0	37,0	1	NC	NC	NC	-14,0	-14,0
	Pre-cycle 9 (n=1)	NC	NC	NC	35,8	35,8	1	NC	NC	NC	-15,2	-15,2
	Pre-cycle 13 (n=1)	NC	NC	NC	29,7	29,7	1	NC	NC	NC	-21,3	-21,3

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, non-dominant hand time (s)	Baseline (n=1)	NC	NC	NC	46,0	46,0						
	Pre-cycle 5 (n=1)	NC	NC	NC	39,0	39,0	1	NC	NC	NC	-7,0	-7,0
	Pre-cycle 9 (n=1)	NC	NC	NC	31,4	31,4	1	NC	NC	NC	-14,6	-14,6
	Pre-cycle 13 (n=1)	NC	NC	NC	34,1	34,1	1	NC	NC	NC	-11,9	-11,9

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values						Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, affected hand z-score	Baseline (n=7)	1,50	1,271	1,08	0,3	3,7						
	Pre-cycle 5 (n=7)	1,71	2,681	0,51	-0,4	6,9	7	0,21	2,628	-0,35	-3,2	4,5
	Pre-cycle 9 (n=7)	0,25	0,599	0,26	-1,0	0,9	7	-1,25	1,285	-1,40	-3,5	0,4
	Pre-cycle 13 (n=7)	1,13	1,326	0,65	-0,3	3,1	7	-0,37	0,396	-0,43	-0,8	0,4
	Pre-cycle 25 (n=3)	1,97	2,108	2,29	-0,3	3,9	3	-0,21	0,452	-0,12	-0,7	0,2

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values						Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-affected hand z-score	Baseline (n=7)	2,46	2,142	2,12	-0,7	6,3						
	Pre-cycle 5 (n=7)	1,35	1,425	1,58	-0,5	3,3	7	-1,11	1,918	-0,11	-3,6	1,1
	Pre-cycle 9 (n=7)	0,19	0,877	-0,10	-0,8	1,8	7	-2,27	1,966	-2,60	-5,6	0,1
	Pre-cycle 13 (n=7)	1,03	1,066	0,68	-0,4	2,7	7	-1,43	2,077	-0,92	-5,7	0,3
	Pre-cycle 25 (n=3)	0,84	1,595	0,80	-0,7	2,5	3	-0,71	1,829	-0,02	-2,8	0,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values					Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max	
Grooved Pegboard, dominant hand z-score	Baseline (n=1)	NC	NC	NC	0,1	0,1							
	Pre-cycle 5 (n=1)	NC	NC	NC	-0,5	-0,5	1	NC	NC	NC	-0,6	-0,6	
	Pre-cycle 9 (n=1)	NC	NC	NC	-0,3	-0,3	1	NC	NC	NC	-0,4	-0,4	
	Pre-cycle 13 (n=1)	NC	NC	NC	-0,9	-0,9	1	NC	NC	NC	-1,0	-1,0	

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-dominant hand z-score	Baseline (n=1)	NC	NC	NC	-0,2	-0,2						
	Pre-cycle 5 (n=1)	NC	NC	NC	-0,6	-0,6	1	NC	NC	NC	-0,3	-0,3
	Pre-cycle 9 (n=1)	NC	NC	NC	-0,7	-0,7	1	NC	NC	NC	-0,4	-0,4
	Pre-cycle 13 (n=1)	NC	NC	NC	-0,5	-0,5	1	NC	NC	NC	-0,2	-0,2

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard affected hand # pegs dropped	Baseline (n=7)	1,29	1,799	1,00	0,0	5,0						
	Pre-cycle 5 (n=7)	1,29	1,113	1,00	0,0	3,0	7	0,00	2,160	0,00	-3,0	3,0
	Pre-cycle 9 (n=7)	1,29	1,704	0,00	0,0	4,0	7	0,00	1,633	0,00	-2,0	3,0
	Pre-cycle 13 (n=7)	0,71	1,496	0,00	0,0	4,0	7	-0,57	2,225	0,00	-5,0	2,0
	Pre-cycle 25 (n=3)	1,67	2,887	0,00	0,0	5,0	3	-0,67	1,155	0,00	-2,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-affected hand # pegs dropped	Baseline (n=7)	1,00	1,414	1,00	0,0	4,0						
	Pre-cycle 5 (n=7)	0,86	1,069	1,00	0,0	3,0	7	-0,14	1,864	0,00	-3,0	3,0
	Pre-cycle 9 (n=7)	2,86	3,976	1,00	0,0	11,0	7	1,86	4,525	0,00	-3,0	11,0
	Pre-cycle 13 (n=7)	1,86	2,193	2,00	0,0	6,0	7	0,86	2,610	0,00	-2,0	6,0
	Pre-cycle 25 (n=3)	0,67	1,155	0,00	0,0	2,0	3	0,33	1,528	0,00	-1,0	2,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard dominant hand # pegs dropped	Baseline (n=1)	NC	NC	NC	1,0	1,0						
	Pre-cycle 5 (n=1)	NC	NC	NC	1,0	1,0	1	NC	NC	NC	0,0	0,0
	Pre-cycle 9 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	-1,0	-1,0
	Pre-cycle 13 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	-1,0	-1,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-dominant hand # pegs dropped	Baseline (n=1)	NC	NC	NC	0,0	0,0						
	Pre-cycle 5 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	0,0	0,0
	Pre-cycle 9 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	0,0	0,0
	Pre-cycle 13 (n=1)	NC	NC	NC	1,0	1,0	1	NC	NC	NC	1,0	1,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Affected hand grip strength (Kg)	Baseline (n=2)	NC	NC	NC	2,7	10,0						
	Pre-cycle 5 (n=6)	10,59	6,077	9,00	3,5	19,1	2	NC	NC	NC	-2,0	0,8
	Pre-cycle 9 (n=7)	14,94	10,849	10,00	2,0	33,0	2	NC	NC	NC	-0,7	0,0
	Pre-cycle 13 (n=7)	14,45	9,061	13,00	3,2	30,7	2	NC	NC	NC	0,5	2,0
	Pre-cycle 25 (n=3)	5,89	1,835	5,00	4,7	8,0	1	NC	NC	NC	2,0	2,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-affected hand grip strength (Kg)	Baseline (n=2)	NC	NC	NC	4,0	8,0						
	Pre-cycle 5 (n=6)	12,68	6,347	12,00	5,0	20,3	2	NC	NC	NC	1,0	2,0
	Pre-cycle 9 (n=7)	14,06	7,000	13,60	4,7	23,0	2	NC	NC	NC	0,7	2,0
	Pre-cycle 13 (n=7)	16,43	7,705	14,67	8,0	30,7	2	NC	NC	NC	4,0	4,0
	Pre-cycle 25 (n=3)	8,44	0,510	8,33	8,0	9,0	1	NC	NC	NC	4,3	4,3

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values					Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max	
Dominant hand grip strength (Kg)	Pre-cycle 5 (n=1)	NC	NC	NC	10,7	10,7	0	NC	NC	NC	NC	NC	
	Pre-cycle 9 (n=1)	NC	NC	NC	13,9	13,9	0	NC	NC	NC	NC	NC	
	Pre-cycle 13 (n=1)	NC	NC	NC	14,5	14,5	0	NC	NC	NC	NC	NC	

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values					Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max	
Non-dominant hand grip strength (Kg)	Pre-cycle 5 (n=1)	NC	NC	NC	10,9	10,9	0	NC	NC	NC	NC	NC	
	Pre-cycle 9 (n=1)	NC	NC	NC	12,2	12,2	0	NC	NC	NC	NC	NC	
	Pre-cycle 13 (n=1)	NC	NC	NC	14,2	14,2	0	NC	NC	NC	NC	NC	

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Affected hand Key-pinch strength (Kg)	Baseline (n=2)	NC	NC	NC	2,3	3,5						
	Pre-cycle 5 (n=5)	4,55	1,544	4,00	3,0	7,0	2	NC	NC	NC	-0,5	1,7
	Pre-cycle 9 (n=7)	5,47	3,906	3,75	2,8	14,0	2	NC	NC	NC	0,0	0,5
	Pre-cycle 13 (n=7)	4,77	2,218	4,00	2,0	7,7	2	NC	NC	NC	-0,3	0,5
	Pre-cycle 25 (n=3)	3,11	0,840	3,00	2,3	4,0	1	NC	NC	NC	0,7	0,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-affected hand Key-pinch strength (Kg)	Baseline (n=2)	NC	NC	NC	3,0	3,1						
	Pre-cycle 5 (n=5)	5,96	2,431	6,80	3,0	9,0	2	NC	NC	NC	0,0	3,9
	Pre-cycle 9 (n=7)	6,21	4,888	4,50	2,8	17,0	2	NC	NC	NC	0,5	1,2
	Pre-cycle 13 (n=7)	5,19	2,292	4,00	2,8	9,0	2	NC	NC	NC	0,5	0,9
	Pre-cycle 25 (n=3)	3,39	0,750	3,33	2,7	4,2	1	NC	NC	NC	0,2	0,2

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Dominant hand Key-pinch strength (Kg)	Pre-cycle 5 (n=1)	NC	NC	NC	4,5	4,5	0	NC	NC	NC	NC	NC
	Pre-cycle 9 (n=1)	NC	NC	NC	5,4	5,4	0	NC	NC	NC	NC	NC
	Pre-cycle 13 (n=1)	NC	NC	NC	5,4	5,4	0	NC	NC	NC	NC	NC

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.3 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values					Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max	
Non-dominant hand Key-pinch strength (Kg)	Pre-cycle 5 (n=1)	NC	NC	NC	4,1	4,1	0	NC	NC	NC	NC	NC	
	Pre-cycle 9 (n=1)	NC	NC	NC	5,4	5,4	0	NC	NC	NC	NC	NC	
	Pre-cycle 13 (n=1)	NC	NC	NC	5,0	5,0	0	NC	NC	NC	NC	NC	

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, affected hand time (s)	Baseline (n=4)	188,99	211,351	85,71	78,6	505,9						
	Pre-cycle 5 (n=4)	129,58	114,850	81,43	55,4	300,0	4	-59,41	98,376	-18,00	-205,9	4,3
	Pre-cycle 9 (n=3)	235,41	289,320	84,19	53,0	569,0	3	13,84	45,694	5,57	-27,2	63,1
	Pre-cycle 13 (n=3)	182,00	175,120	89,00	73,0	384,0	3	-43,25	68,134	-5,62	-121,9	-2,2
	Pre-cycle 25 (n=2)	NC	NC	NC	83,2	584,6	2	NC	NC	NC	-8,1	78,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, non-affected hand time (s)	Baseline (n=5)	143,32	95,581	104,93	60,9	300,0						
	Pre-cycle 5 (n=5)	108,82	58,131	90,57	60,9	209,4	5	-34,50	104,210	-0,01	-217,6	44,8
	Pre-cycle 9 (n=5)	176,79	189,993	92,82	70,3	515,0	5	33,47	193,141	-1,93	-178,4	350,4
	Pre-cycle 13 (n=4)	149,31	145,408	81,39	67,5	367,0	4	45,16	105,258	-2,89	-15,9	202,4
	Pre-cycle 25 (n=2)	NC	NC	NC	78,8	228,2	2	NC	NC	NC	-26,1	63,5

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, dominant hand time (s)	Baseline (n=2)	NC	NC	NC	76,8	101,1						
	Pre-cycle 5 (n=2)	NC	NC	NC	78,7	79,4	2	NC	NC	NC	-21,7	1,9
	Pre-cycle 9 (n=2)	NC	NC	NC	66,7	79,8	2	NC	NC	NC	-21,2	-10,1
	Pre-cycle 13 (n=1)	NC	NC	NC	85,3	85,3	1	NC	NC	NC	-15,8	-15,8
	Pre-cycle 25 (n=1)	NC	NC	NC	77,8	77,8	1	NC	NC	NC	-23,3	-23,3

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, non-dominant hand time (s)	Baseline (n=2)	NC	NC	NC	109,6	209,8						
	Pre-cycle 5 (n=2)	NC	NC	NC	85,0	154,2	2	NC	NC	NC	-55,7	-24,7
	Pre-cycle 9 (n=2)	NC	NC	NC	96,4	110,9	2	NC	NC	NC	-98,9	-13,2
	Pre-cycle 13 (n=1)	NC	NC	NC	98,0	98,0	1	NC	NC	NC	-11,7	-11,7
	Pre-cycle 25 (n=1)	NC	NC	NC	86,2	86,2	1	NC	NC	NC	-23,5	-23,5

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, affected hand z-score	Baseline (n=4)	10,32	19,275	0,92	0,2	39,2						
	Pre-cycle 5 (n=4)	5,21	10,316	0,22	-0,3	20,7	4	-5,11	8,974	-1,01	-18,6	0,1
	Pre-cycle 9 (n=3)	15,86	25,155	1,45	1,2	44,9	3	2,18	3,035	0,50	0,4	5,7
	Pre-cycle 13 (n=3)	9,73	16,032	0,72	0,2	28,2	3	-3,67	6,361	-0,50	-11,0	0,5
	Pre-cycle 25 (n=2)	NC	NC	NC	0,2	24,3	2	NC	NC	NC	-15,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-affected hand z-score	Baseline (n=5)	4,35	5,993	0,52	-0,5	12,2						
	Pre-cycle 5 (n=5)	3,02	6,052	0,37	-0,5	13,8	5	-1,33	5,684	0,00	-10,9	4,3
	Pre-cycle 9 (n=5)	9,32	18,955	0,41	0,0	43,2	5	4,97	16,586	-0,06	-9,4	33,7
	Pre-cycle 13 (n=4)	7,27	14,450	0,12	-0,1	28,9	4	4,87	9,739	0,22	-0,4	19,5
	Pre-cycle 25 (n=2)	NC	NC	NC	-0,2	7,3	2	NC	NC	NC	-2,2	-0,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, dominant hand z-score	Baseline (n=2)	NC	NC	NC	0,0	3,4						
	Pre-cycle 5 (n=2)	NC	NC	NC	0,2	1,3	2	NC	NC	NC	-2,1	0,1
	Pre-cycle 9 (n=2)	NC	NC	NC	-0,5	1,3	2	NC	NC	NC	-2,0	-0,6
	Pre-cycle 13 (n=1)	NC	NC	NC	1,9	1,9	1	NC	NC	NC	-1,5	-1,5
	Pre-cycle 25 (n=1)	NC	NC	NC	1,1	1,1	1	NC	NC	NC	-2,2	-2,2

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-dominant hand z-score	Baseline (n=2)	NC	NC	NC	3,5	4,0						
	Pre-cycle 5 (n=2)	NC	NC	NC	1,3	2,2	2	NC	NC	NC	-2,2	-1,8
	Pre-cycle 9 (n=2)	NC	NC	NC	0,8	2,3	2	NC	NC	NC	-3,2	-1,2
	Pre-cycle 13 (n=1)	NC	NC	NC	2,5	2,5	1	NC	NC	NC	-1,1	-1,1
	Pre-cycle 25 (n=1)	NC	NC	NC	1,4	1,4	1	NC	NC	NC	-2,1	-2,1

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard affected hand # pegs dropped	Baseline (n=4)	2,50	2,380	2,50	0,0	5,0						
	Pre-cycle 5 (n=4)	1,75	2,872	0,50	0,0	6,0	4	-0,75	1,708	-0,50	-3,0	1,0
	Pre-cycle 9 (n=3)	1,67	0,577	2,00	1,0	2,0	3	-1,33	2,082	-2,00	-3,0	1,0
	Pre-cycle 13 (n=3)	2,33	3,215	1,00	0,0	6,0	3	0,33	1,155	1,00	-1,0	1,0
	Pre-cycle 25 (n=2)	NC	NC	NC	2,0	6,0	2	NC	NC	NC	1,0	1,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-affected hand # pegs dropped	Baseline (n=5)	2,40	3,209	1,00	0,0	8,0						
	Pre-cycle 5 (n=5)	1,00	0,707	1,00	0,0	2,0	5	-1,40	3,130	0,00	-7,0	0,0
	Pre-cycle 9 (n=5)	0,80	0,837	1,00	0,0	2,0	5	-1,60	3,130	-1,00	-7,0	1,0
	Pre-cycle 13 (n=4)	1,00	1,414	0,50	0,0	3,0	4	0,00	1,155	0,00	-1,0	1,0
	Pre-cycle 25 (n=2)	NC	NC	NC	1,0	2,0	2	NC	NC	NC	0,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard dominant hand # pegs dropped	Baseline (n=2)	NC	NC	NC	1,0	1,0						
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	0,0	2	NC	NC	NC	-1,0	-1,0
	Pre-cycle 9 (n=2)	NC	NC	NC	0,0	0,0	2	NC	NC	NC	-1,0	-1,0
	Pre-cycle 13 (n=1)	NC	NC	NC	1,0	1,0	1	NC	NC	NC	0,0	0,0
	Pre-cycle 25 (n=1)	NC	NC	NC	1,0	1,0	1	NC	NC	NC	0,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-dominant hand # pegs dropped	Baseline (n=2)	NC	NC	NC	1,0	4,0						
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	2,0	2	NC	NC	NC	-2,0	-1,0
	Pre-cycle 9 (n=2)	NC	NC	NC	0,0	4,0	2	NC	NC	NC	-1,0	0,0
	Pre-cycle 13 (n=1)	NC	NC	NC	0,0	0,0	1	NC	NC	NC	-1,0	-1,0
	Pre-cycle 25 (n=1)	NC	NC	NC	1,0	1,0	1	NC	NC	NC	0,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Affected hand grip strength (Kg)	Baseline (n=7)	12,05	7,031	9,50	4,0	24,3						
	Pre-cycle 5 (n=7)	14,31	9,541	12,50	0,0	29,0	7	2,26	6,680	0,00	-4,0	15,8
	Pre-cycle 9 (n=5)	15,33	10,884	16,00	0,7	30,7	5	1,51	3,918	1,83	-3,3	6,4
	Pre-cycle 13 (n=5)	16,26	10,259	18,00	1,0	29,0	5	4,66	5,987	4,00	-3,0	13,8
	Pre-cycle 25 (n=5)	19,03	11,779	18,00	0,8	30,0	5	7,43	9,996	4,70	-3,2	23,8

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-affected hand grip strength (Kg)	Baseline (n=7)	17,02	10,812	14,67	5,4	34,0						
	Pre-cycle 5 (n=6)	19,35	8,016	19,50	10,3	30,0	6	0,70	7,087	-1,53	-4,3	14,6
	Pre-cycle 9 (n=6)	21,11	9,259	19,75	8,8	34,0	6	2,47	6,600	0,17	-2,5	15,6
	Pre-cycle 13 (n=5)	23,33	9,358	24,00	12,0	34,0	5	5,16	7,619	2,50	0,0	18,6
	Pre-cycle 25 (n=5)	23,13	10,012	28,00	11,0	32,0	5	4,96	10,108	1,50	-2,0	22,6

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Dominant hand grip strength (Kg)	Baseline (n=1)	NC	NC	NC	20,0	20,0						
	Pre-cycle 5 (n=2)	NC	NC	NC	16,0	23,6	1	NC	NC	NC	3,6	3,6
	Pre-cycle 9 (n=1)	NC	NC	NC	24,3	24,3	1	NC	NC	NC	4,3	4,3
	Pre-cycle 13 (n=1)	NC	NC	NC	24,7	24,7	1	NC	NC	NC	4,7	4,7
	Pre-cycle 25 (n=1)	NC	NC	NC	26,3	26,3	1	NC	NC	NC	6,3	6,3

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-dominant hand grip strength (Kg)	Baseline (n=1)	NC	NC	NC	18,0	18,0						
	Pre-cycle 5 (n=2)	NC	NC	NC	4,0	21,0	1	NC	NC	NC	3,0	3,0
	Pre-cycle 9 (n=1)	NC	NC	NC	21,3	21,3	1	NC	NC	NC	3,3	3,3
	Pre-cycle 13 (n=1)	NC	NC	NC	21,3	21,3	1	NC	NC	NC	3,3	3,3
	Pre-cycle 25 (n=1)	NC	NC	NC	20,0	20,0	1	NC	NC	NC	2,0	2,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Affected hand Key-pinch strength (Kg)	Baseline (n=7)	5,20	3,004	4,50	1,3	10,0						
	Pre-cycle 5 (n=7)	6,07	2,977	7,00	1,2	9,0	7	0,87	3,426	1,33	-6,0	4,5
	Pre-cycle 9 (n=5)	5,17	3,043	5,00	1,0	9,5	5	-0,73	2,747	0,16	-5,5	1,5
	Pre-cycle 13 (n=5)	5,38	3,127	5,17	1,0	8,5	5	-0,24	3,609	0,50	-6,0	4,0
	Pre-cycle 25 (n=5)	5,67	3,667	6,17	1,3	9,5	5	0,04	4,657	0,83	-7,5	5,2

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-affected hand Key-pinch strength (Kg)	Baseline (n=7)	6,77	5,298	4,50	2,2	18,0						
	Pre-cycle 5 (n=6)	7,70	1,999	8,09	4,0	10,0	6	0,16	5,177	0,84	-9,5	5,5
	Pre-cycle 9 (n=6)	6,83	2,131	7,33	4,0	9,0	6	-0,70	4,244	0,33	-9,0	3,3
	Pre-cycle 13 (n=5)	6,95	2,255	7,83	4,0	9,3	5	-0,79	5,317	0,00	-9,5	5,1
	Pre-cycle 25 (n=5)	7,67	1,258	8,17	6,2	9,0	5	-0,07	5,201	2,00	-9,0	4,3

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Dominant hand Key-pinch strength (Kg)	Baseline (n=1)	NC	NC	NC	5,0	5,0						
	Pre-cycle 5 (n=2)	NC	NC	NC	4,0	6,5	1	NC	NC	NC	1,5	1,5
	Pre-cycle 9 (n=1)	NC	NC	NC	7,0	7,0	1	NC	NC	NC	2,0	2,0
	Pre-cycle 13 (n=1)	NC	NC	NC	7,2	7,2	1	NC	NC	NC	2,2	2,2
	Pre-cycle 25 (n=1)	NC	NC	NC	7,5	7,5	1	NC	NC	NC	2,5	2,5

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.4 Motor function secondary outcome scores and change from baseline over time - PN status at enrol. = Non-progressive by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-dominant hand Key-pinch strength (Kg)	Baseline (n=1)	NC	NC	NC	5,5	5,5						
	Pre-cycle 5 (n=2)	NC	NC	NC	2,5	5,6	1	NC	NC	NC	0,1	0,1
	Pre-cycle 9 (n=1)	NC	NC	NC	7,5	7,5	1	NC	NC	NC	2,0	2,0
	Pre-cycle 13 (n=1)	NC	NC	NC	7,5	7,5	1	NC	NC	NC	2,0	2,0
	Pre-cycle 25 (n=1)	NC	NC	NC	7,3	7,3	1	NC	NC	NC	1,8	1,8

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, affected hand time (s)	Baseline (n=5)	123,65	48,619	124,40	67,6	188,0						
	Pre-cycle 5 (n=5)	116,35	53,242	122,46	51,7	168,0	5	-7,30	20,012	-1,94	-34,8	15,1
	Pre-cycle 9 (n=5)	93,68	46,356	86,00	32,6	152,9	5	-29,97	47,048	-1,00	-102,0	5,9
	Pre-cycle 13 (n=5)	116,41	31,119	111,66	69,5	145,0	5	-7,24	24,758	-6,99	-43,0	25,2
	Pre-cycle 25 (n=4)	106,37	14,707	102,62	93,0	127,2	4	-31,29	57,076	-35,47	-95,0	40,8

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, non-affected hand time (s)	Baseline (n=5)	104,29	32,844	99,00	61,0	149,6						
	Pre-cycle 5 (n=5)	101,09	50,689	83,66	52,8	162,0	5	-3,20	59,511	-1,86	-96,7	63,0
	Pre-cycle 9 (n=5)	65,31	19,510	69,76	32,6	84,2	5	-38,98	46,066	-25,00	-117,0	5,0
	Pre-cycle 13 (n=5)	80,78	13,084	87,08	61,8	93,8	5	-23,52	24,273	-25,58	-61,3	0,8
	Pre-cycle 25 (n=4)	79,74	10,319	81,20	66,8	89,8	4	-35,37	20,391	-34,35	-59,8	-13,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, dominant hand time (s)	Baseline (n=5)	97,80	33,674	112,28	60,0	137,0						
	Pre-cycle 5 (n=4)	75,20	22,056	75,38	49,0	101,0	4	-18,99	18,306	-21,48	-36,0	3,0
	Pre-cycle 9 (n=4)	106,72	33,037	102,95	77,0	144,0	4	12,54	51,174	0,00	-33,8	84,0
	Pre-cycle 13 (n=4)	98,91	32,785	90,00	71,6	144,0	4	4,72	58,353	-11,00	-43,1	84,0
	Pre-cycle 25 (n=3)	93,15	21,508	92,46	72,0	115,0	3	13,24	38,996	7,00	-22,3	55,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, non-dominant hand time (s)	Baseline (n=5)	92,67	33,334	78,77	60,0	139,0						
	Pre-cycle 5 (n=4)	94,74	34,331	82,98	68,0	145,0	4	7,80	12,568	3,60	-2,0	26,0
	Pre-cycle 9 (n=4)	118,73	45,856	117,96	75,0	164,0	4	31,78	41,364	15,00	4,9	92,2
	Pre-cycle 13 (n=4)	147,91	81,783	143,90	65,8	238,0	4	60,97	67,820	61,00	-12,9	134,8
	Pre-cycle 25 (n=3)	96,62	46,404	74,00	65,9	150,0	3	27,03	55,176	4,00	-12,9	90,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, affected hand z-score	Baseline (n=5)	2,63	2,294	3,11	-0,9	4,9						
	Pre-cycle 5 (n=5)	2,27	2,544	1,42	-0,7	5,2	5	-0,37	1,228	-0,18	-2,4	0,9
	Pre-cycle 9 (n=5)	1,41	2,625	-0,25	-0,6	4,8	5	-1,22	1,644	-0,54	-3,7	0,3
	Pre-cycle 13 (n=5)	1,93	1,684	2,17	-0,3	3,7	5	-0,71	1,173	-0,96	-2,3	0,6
	Pre-cycle 25 (n=4)	1,19	1,359	0,83	0,0	3,1	4	-2,33	1,057	-1,81	-3,9	-1,8

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-affected hand z-score	Baseline (n=5)	3,04	5,371	1,10	-1,0	12,4						
	Pre-cycle 5 (n=5)	1,17	1,295	1,65	-1,1	2,3	5	-1,87	5,020	-0,10	-10,7	1,2
	Pre-cycle 9 (n=5)	-0,33	0,444	-0,55	-0,7	0,4	5	-3,37	5,438	-1,23	-13,0	0,3
	Pre-cycle 13 (n=5)	0,31	1,030	0,22	-0,6	2,0	5	-2,73	5,298	-0,78	-12,2	0,6
	Pre-cycle 25 (n=4)	0,12	0,246	0,13	-0,2	0,4	4	-3,92	5,616	-1,88	-12,2	0,2

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values						Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard, dominant hand z-score	Baseline (n=5)	3,27	2,961	4,45	-0,1	6,8						
	Pre-cycle 5 (n=4)	1,30	1,545	0,90	0,0	3,4	4	-1,67	1,870	-1,76	-3,5	0,3
	Pre-cycle 9 (n=4)	3,01	2,176	2,67	1,1	5,7	4	0,04	2,877	0,00	-3,3	3,4
	Pre-cycle 13 (n=4)	4,23	5,172	2,31	0,5	11,8	4	1,25	7,083	-1,06	-4,1	11,3
	Pre-cycle 25 (n=3)	1,57	0,985	1,59	0,6	2,5	3	-0,12	1,760	0,67	-2,1	1,1

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-dominant hand z-score	Baseline (n=5)	2,27	2,719	0,75	-0,1	6,2						
	Pre-cycle 5 (n=4)	2,23	3,079	1,22	-0,2	6,7	4	0,41	0,593	0,32	-0,2	1,2
	Pre-cycle 9 (n=4)	3,66	3,661	2,90	0,4	8,4	4	1,84	1,785	1,36	0,4	4,2
	Pre-cycle 13 (n=4)	6,81	7,246	6,28	-0,4	15,1	4	4,99	5,421	5,50	-1,2	10,1
	Pre-cycle 25 (n=3)	0,78	1,484	0,32	-0,4	2,4	3	0,41	1,600	0,37	-1,2	2,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard affected hand # pegs dropped	Baseline (n=5)	6,00	6,964	3,00	1,0	18,0						
	Pre-cycle 5 (n=5)	3,60	5,320	2,00	0,0	13,0	5	-2,40	8,385	-1,00	-16,0	7,0
	Pre-cycle 9 (n=5)	2,60	3,782	1,00	0,0	9,0	5	-3,40	7,829	-1,00	-17,0	3,0
	Pre-cycle 13 (n=5)	1,60	1,673	2,00	0,0	4,0	5	-4,40	6,580	-2,00	-16,0	0,0
	Pre-cycle 25 (n=4)	1,00	0,816	1,00	0,0	2,0	4	-6,25	7,274	-3,50	-17,0	-1,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-affected hand # pegs dropped	Baseline (n=5)	2,20	1,643	3,00	0,0	4,0						
	Pre-cycle 5 (n=5)	0,40	0,894	0,00	0,0	2,0	5	-1,80	1,643	-1,00	-4,0	0,0
	Pre-cycle 9 (n=5)	1,40	1,673	1,00	0,0	4,0	5	-0,80	2,168	0,00	-4,0	1,0
	Pre-cycle 13 (n=5)	0,80	0,447	1,00	0,0	1,0	5	-1,40	1,342	-2,00	-3,0	0,0
	Pre-cycle 25 (n=4)	1,00	0,816	1,00	0,0	2,0	4	-1,75	1,500	-2,00	-3,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard dominant hand # pegs dropped	Baseline (n=5)	0,00	0,000	0,00	0,0	0,0						
	Pre-cycle 5 (n=4)	0,50	0,577	0,50	0,0	1,0	4	0,50	0,577	0,50	0,0	1,0
	Pre-cycle 9 (n=4)	0,25	0,500	0,00	0,0	1,0	4	0,25	0,500	0,00	0,0	1,0
	Pre-cycle 13 (n=4)	0,00	0,000	0,00	0,0	0,0	4	0,00	0,000	0,00	0,0	0,0
	Pre-cycle 25 (n=3)	0,00	0,000	0,00	0,0	0,0	3	0,00	0,000	0,00	0,0	0,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]									
		Absolute values					Change from baseline				
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Grooved Pegboard non-dominant hand # pegs dropped	Baseline (n=5)	0,20	0,447	0,00	0,0	1,0						
	Pre-cycle 5 (n=4)	0,25	0,500	0,00	0,0	1,0	4	0,00	0,816	0,00	-1,0	1,0
	Pre-cycle 9 (n=4)	1,75	1,500	2,00	0,0	3,0	4	1,50	1,732	1,50	0,0	3,0
	Pre-cycle 13 (n=4)	2,50	1,732	2,00	1,0	5,0	4	2,25	1,893	1,50	1,0	5,0
	Pre-cycle 25 (n=3)	0,67	1,155	0,00	0,0	2,0	3	0,33	1,528	0,00	-1,0	2,0

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Affected hand grip strength (Kg)	Baseline (n=2)	NC	NC	NC	8,7	10,7						
	Pre-cycle 5 (n=3)	7,60	2,816	8,30	4,5	10,0	1	NC	NC	NC	-0,4	-0,4
	Pre-cycle 9 (n=4)	12,17	2,271	12,67	9,3	14,0	2	NC	NC	NC	0,7	0,7
	Pre-cycle 13 (n=4)	14,75	2,964	16,00	10,3	16,7	2	NC	NC	NC	1,7	5,3
	Pre-cycle 25 (n=3)	16,78	5,004	17,00	11,7	21,7	2	NC	NC	NC	3,0	6,3

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-affected hand grip strength (Kg)	Baseline (n=2)	NC	NC	NC	14,7	18,8						
	Pre-cycle 5 (n=3)	15,27	10,884	13,30	5,5	27,0	1	NC	NC	NC	-1,4	-1,4
	Pre-cycle 9 (n=4)	21,08	6,833	20,67	14,0	29,0	2	NC	NC	NC	2,3	5,5
	Pre-cycle 13 (n=4)	23,84	8,112	21,34	17,7	35,0	2	NC	NC	NC	3,0	5,8
	Pre-cycle 25 (n=3)	29,56	14,767	26,33	16,7	45,7	2	NC	NC	NC	2,0	7,5

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Dominant hand grip strength (Kg)	Baseline (n=1)	NC	NC	NC	18,1	18,1						
	Pre-cycle 5 (n=4)	14,37	13,510	12,86	2,0	29,8	0	NC	NC	NC	NC	NC
	Pre-cycle 9 (n=4)	16,00	12,195	14,75	3,2	31,3	0	NC	NC	NC	NC	NC
	Pre-cycle 13 (n=4)	17,02	14,672	13,75	3,9	36,7	0	NC	NC	NC	NC	NC
	Pre-cycle 25 (n=2)	NC	NC	NC	20,3	32,0	0	NC	NC	NC	NC	NC

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-dominant hand grip strength (Kg)	Baseline (n=1)	NC	NC	NC	18,1	18,1						
	Pre-cycle 5 (n=4)	24,03	28,433	15,77	2,0	62,6	0	NC	NC	NC	NC	NC
	Pre-cycle 9 (n=4)	14,95	12,143	13,30	2,9	30,3	0	NC	NC	NC	NC	NC
	Pre-cycle 13 (n=4)	14,49	9,940	12,62	5,4	27,3	0	NC	NC	NC	NC	NC
	Pre-cycle 25 (n=2)	NC	NC	NC	21,5	22,7	0	NC	NC	NC	NC	NC

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Affected hand Key-pinch strength (Kg)	Baseline (n=2)	NC	NC	NC	2,5	3,4						
	Pre-cycle 5 (n=3)	7,00	3,000	7,00	4,0	10,0	1	NC	NC	NC	1,5	1,5
	Pre-cycle 9 (n=4)	4,63	1,031	4,50	3,5	6,0	2	NC	NC	NC	1,0	1,1
	Pre-cycle 13 (n=4)	5,75	0,957	5,50	5,0	7,0	2	NC	NC	NC	1,6	2,5
	Pre-cycle 25 (n=3)	5,89	2,696	4,33	4,3	9,0	2	NC	NC	NC	0,9	1,8

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown
by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Unilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-affected hand Key-pinch strength (Kg)	Baseline (n=2)	NC	NC	NC	4,2	5,3						
	Pre-cycle 5 (n=3)	8,56	3,685	9,00	4,7	12,0	1	NC	NC	NC	0,4	0,4
	Pre-cycle 9 (n=4)	6,62	3,014	5,58	4,3	11,0	2	NC	NC	NC	0,1	0,8
	Pre-cycle 13 (n=4)	6,71	1,843	6,67	4,5	9,0	2	NC	NC	NC	0,3	1,5
	Pre-cycle 25 (n=3)	7,61	3,847	6,00	4,8	12,0	2	NC	NC	NC	0,6	0,7

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Dominant hand Key-pinch strength (Kg)	Baseline (n=1)	NC	NC	NC	6,8	6,8						
	Pre-cycle 5 (n=4)	4,51	2,441	3,99	2,3	7,8	0	NC	NC	NC	NC	NC
	Pre-cycle 9 (n=4)	4,56	2,706	3,97	2,3	8,0	0	NC	NC	NC	NC	NC
	Pre-cycle 13 (n=4)	5,28	3,324	4,47	2,3	9,9	0	NC	NC	NC	NC	NC
	Pre-cycle 25 (n=2)	NC	NC	NC	6,4	7,6	0	NC	NC	NC	NC	NC

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Table 2.6.3.2.5 Motor function secondary outcome scores and change from baseline over time - PN status at enrollment = Unknown by PN-affected laterality (Full analysis set with a motor PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

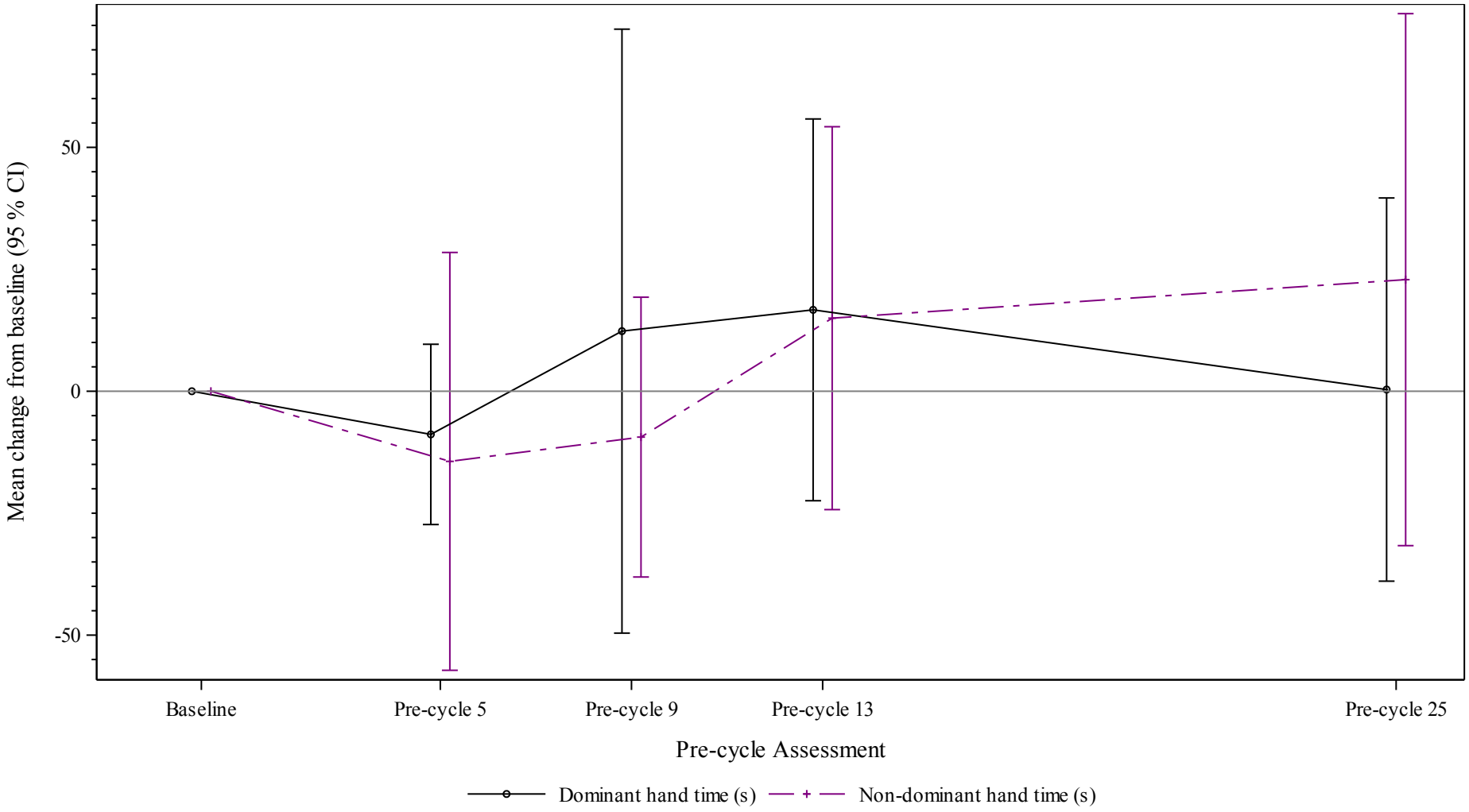
Bilateral patients

		Selumetinib 25 mg/m² BID (N=11) [a]										
		Absolute values					Change from baseline					
Motor function test score	Time point	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Non-dominant hand Key-pinch strength (Kg)	Baseline (n=1)	NC	NC	NC	5,4	5,4						
	Pre-cycle 5 (n=4)	4,12	2,019	4,02	1,8	6,6	0	NC	NC	NC	NC	NC
	Pre-cycle 9 (n=4)	4,08	2,556	3,52	1,8	7,5	0	NC	NC	NC	NC	NC
	Pre-cycle 13 (n=4)	4,51	2,727	4,11	1,8	8,0	0	NC	NC	NC	NC	NC
	Pre-cycle 25 (n=2)	NC	NC	NC	5,4	7,0	0	NC	NC	NC	NC	NC

[a] Patients with a motor PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation

Figure 2.6.3.3.1 Mean change from baseline of Grooved pegboard test scores - Gender = Male
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

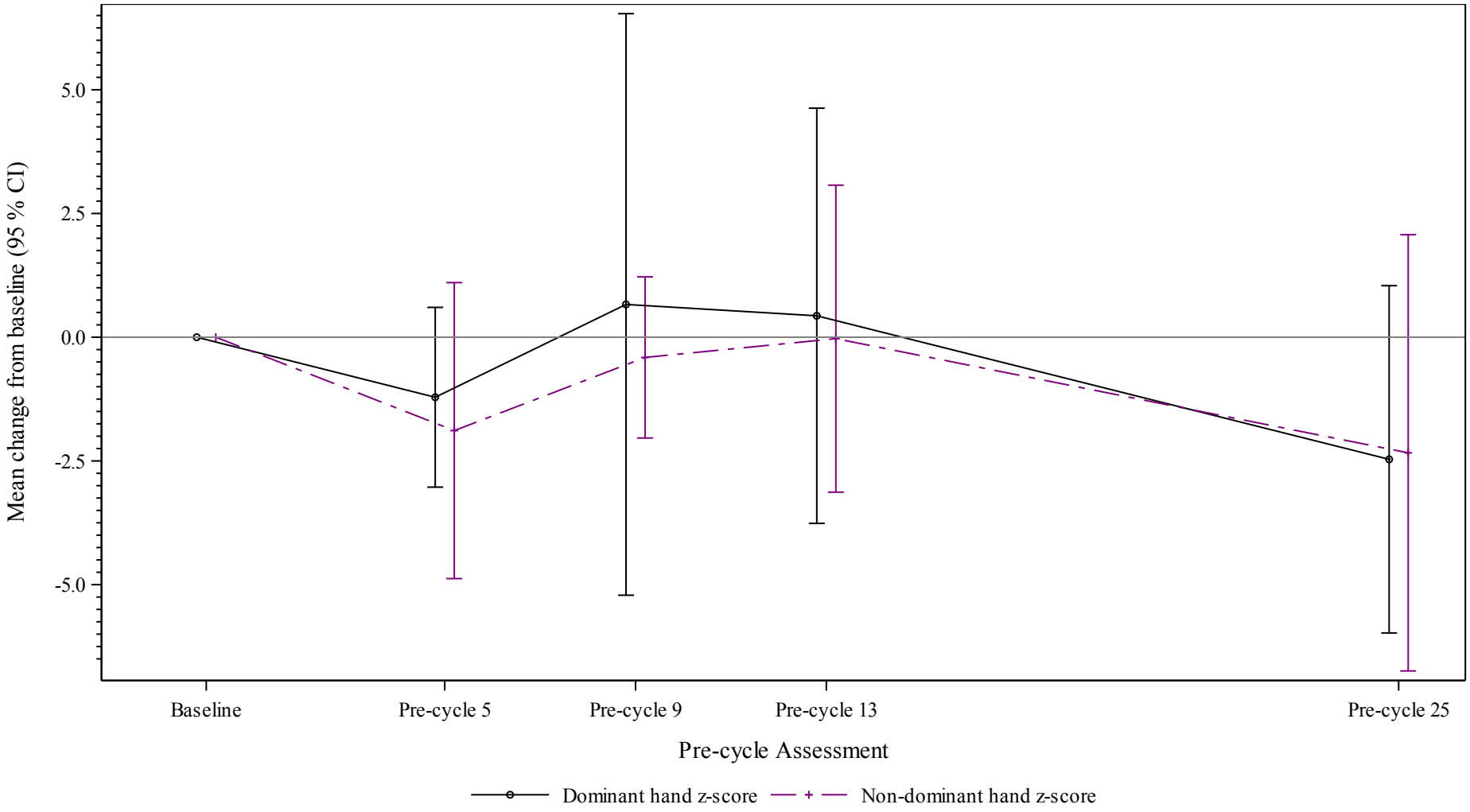
N = 18



CI = Confidence interval.

Figure 2.6.3.3.1 Mean change from baseline of Grooved pegboard test scores - Gender = Male
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

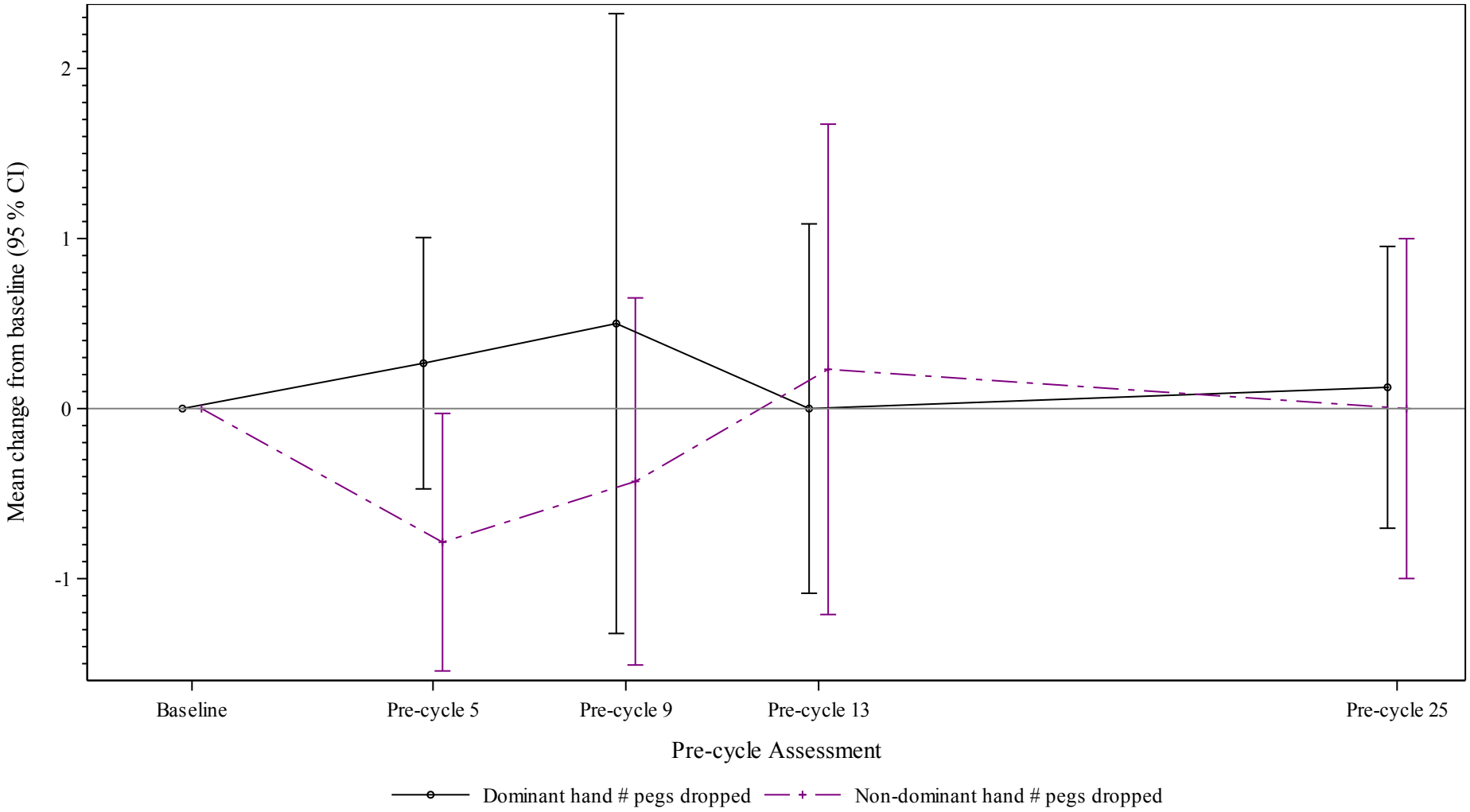
N = 18



CI = Confidence interval.

Figure 2.6.3.3.1 Mean change from baseline of Grooved pegboard test scores - Gender = Male
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

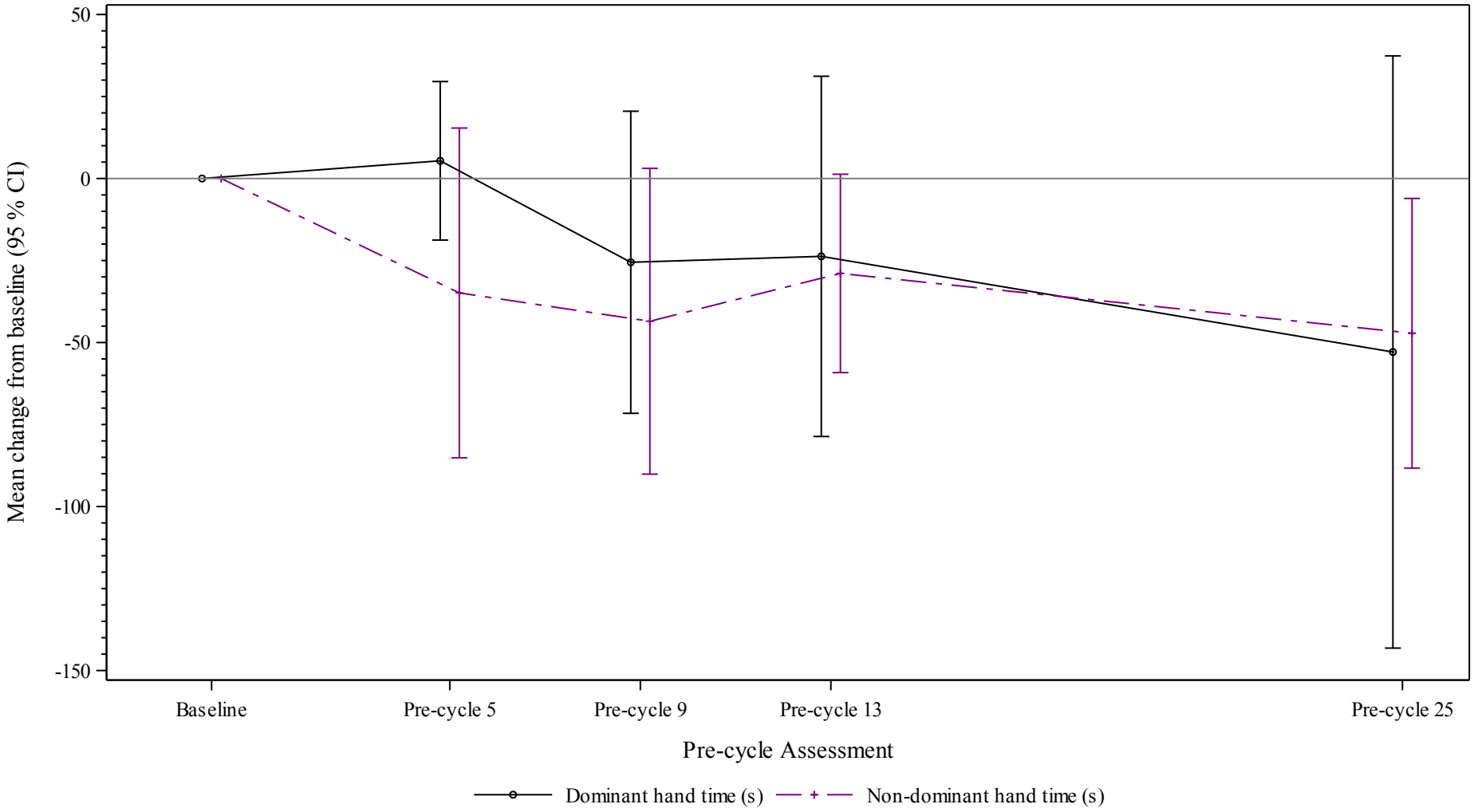
N = 18



CI = Confidence interval.

Figure 2.6.3.3.2 Mean change from baseline of Grooved pegboard test scores - Gender = Female
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

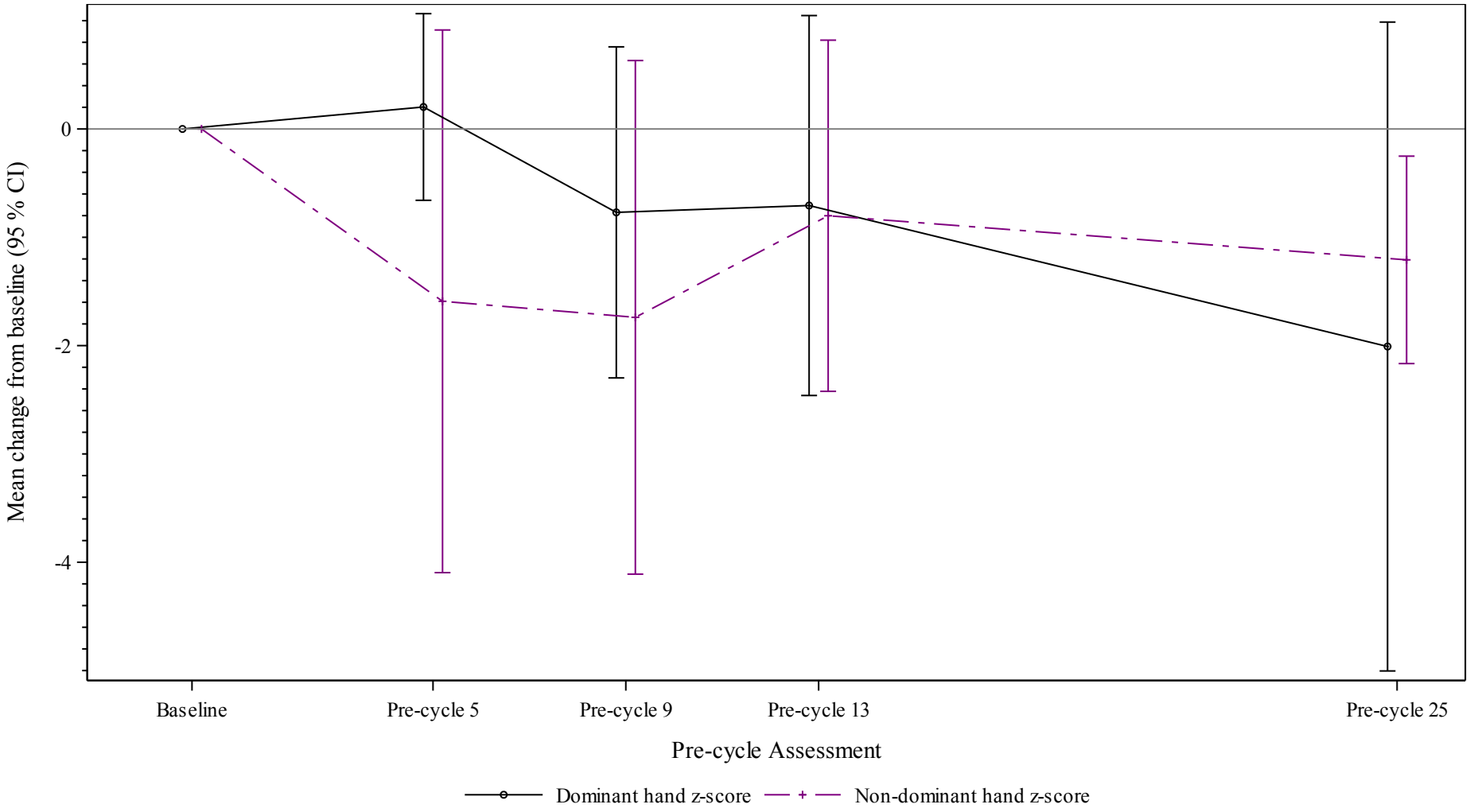
N = 10



CI = Confidence interval.

Figure 2.6.3.3.2 Mean change from baseline of Grooved pegboard test scores - Gender = Female
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

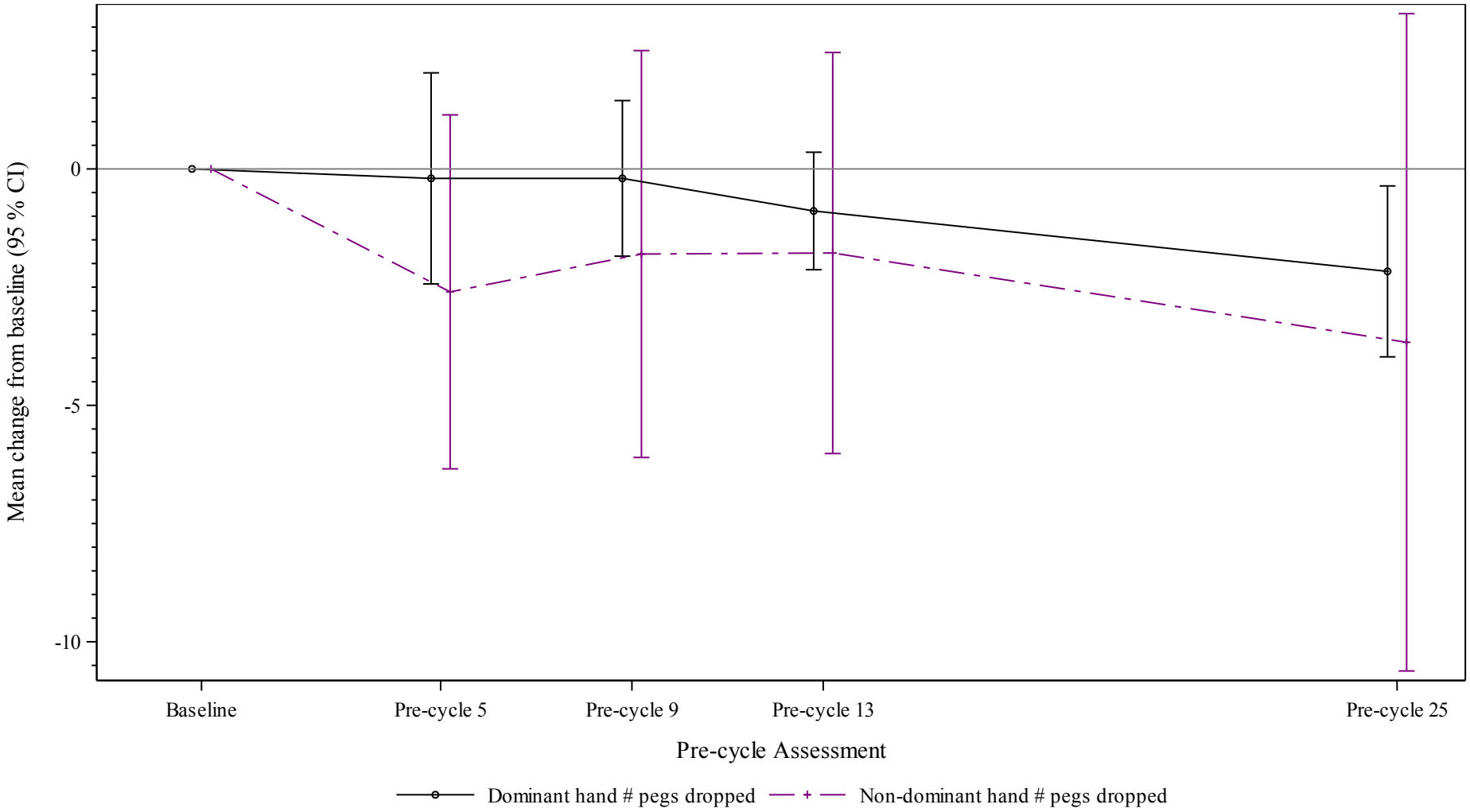
N = 10



CI = Confidence interval.

Figure 2.6.3.3.2 Mean change from baseline of Grooved pegboard test scores - Gender = Female
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

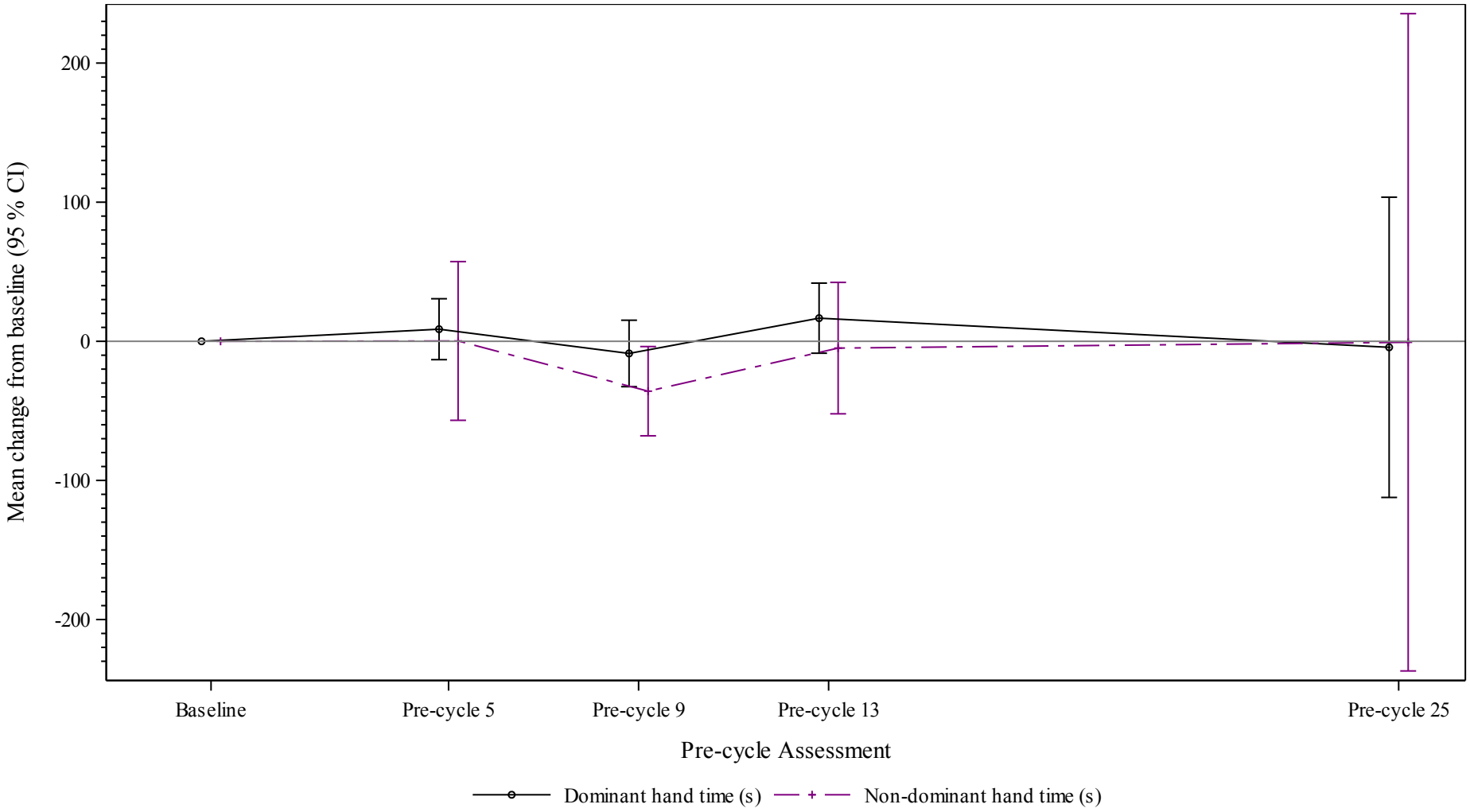
N = 10



CI = Confidence interval.

Figure 2.6.3.3.3 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

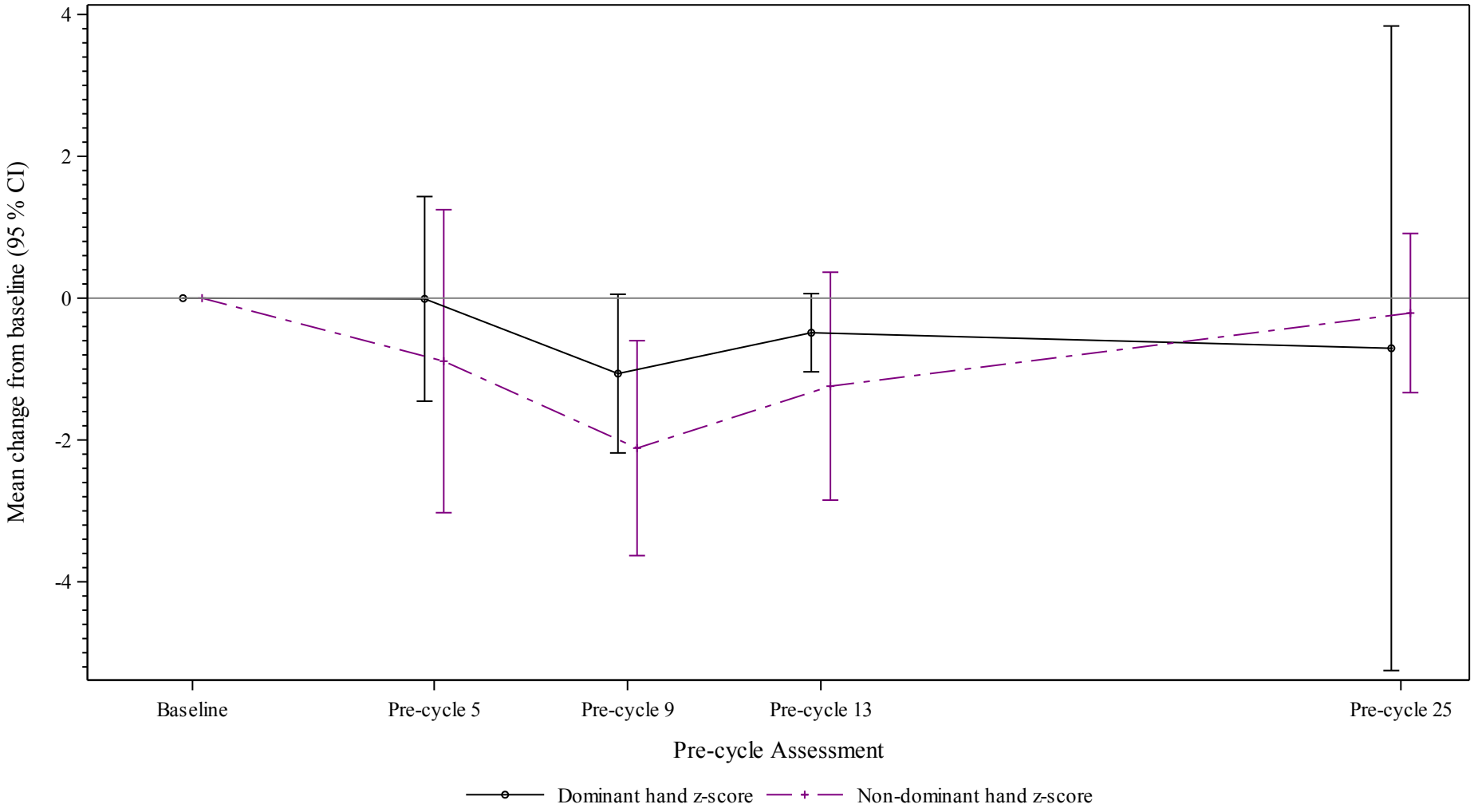
N = 8



CI = Confidence interval.

Figure 2.6.3.3.3 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

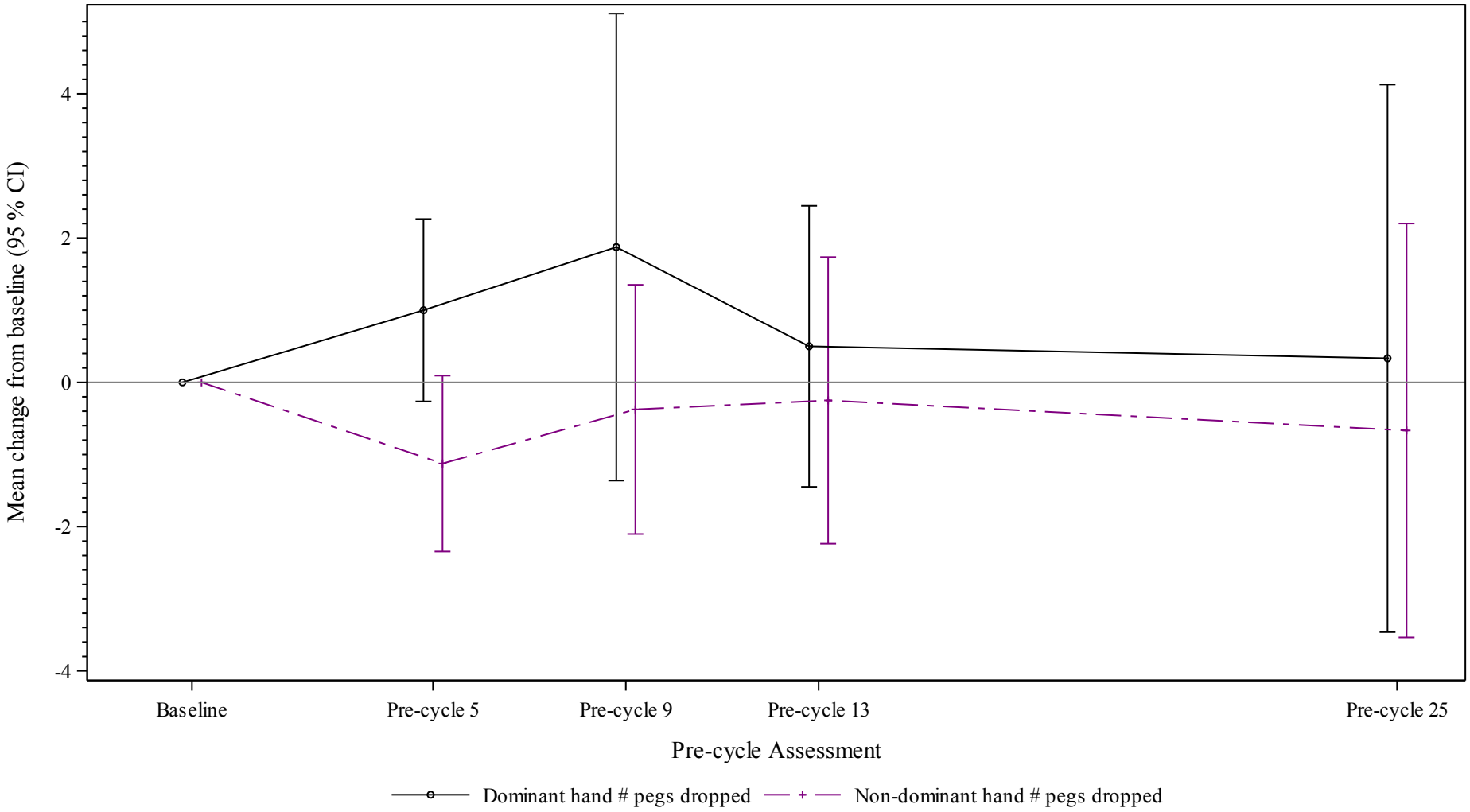
N = 8



CI = Confidence interval.

Figure 2.6.3.3.3 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

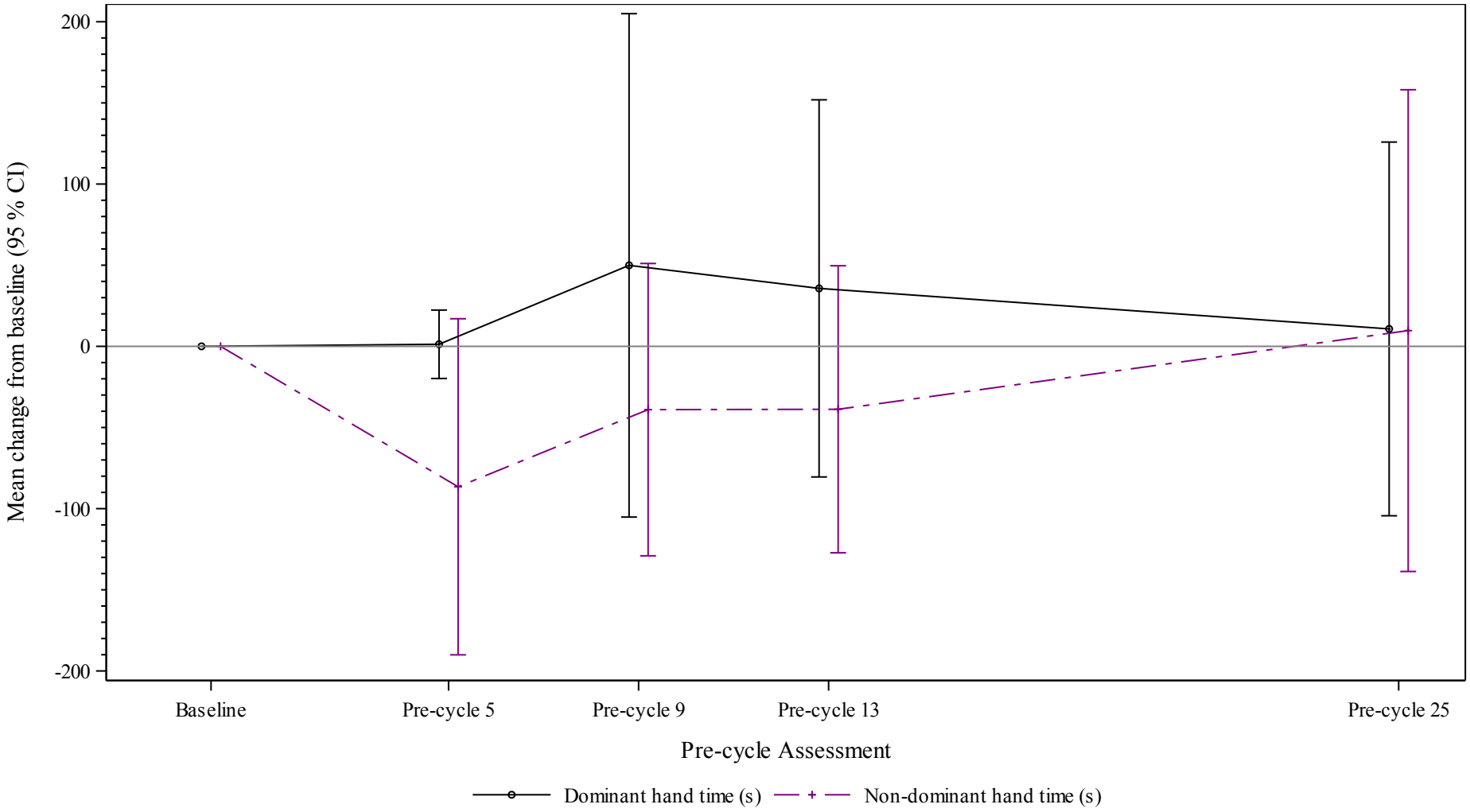
N = 8



CI = Confidence interval.

Figure 2.6.3.3.4 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Non-progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

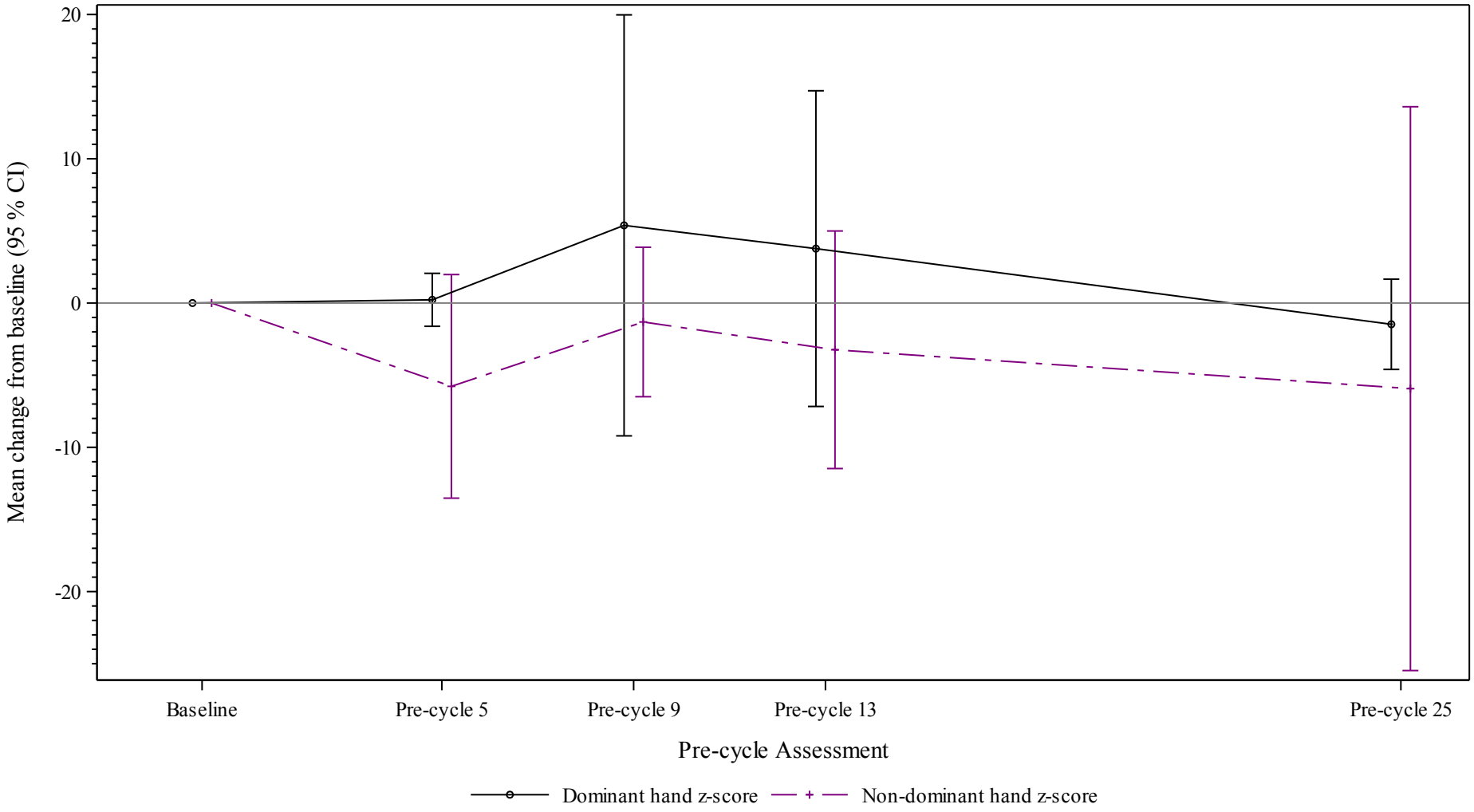
N = 8



CI = Confidence interval.

Figure 2.6.3.3.4 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Non-progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

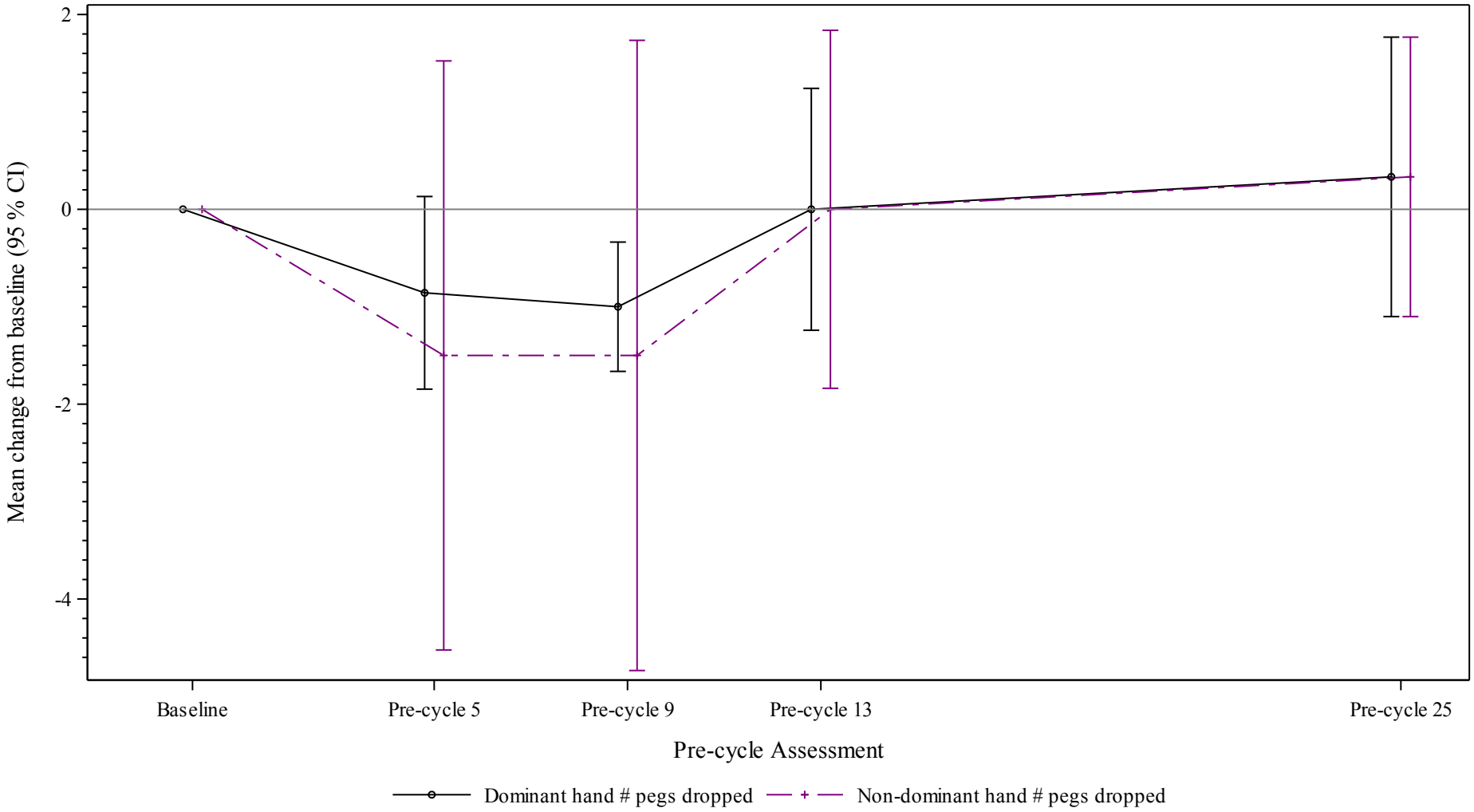
N = 8



CI = Confidence interval.

Figure 2.6.3.3.4 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Non-progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

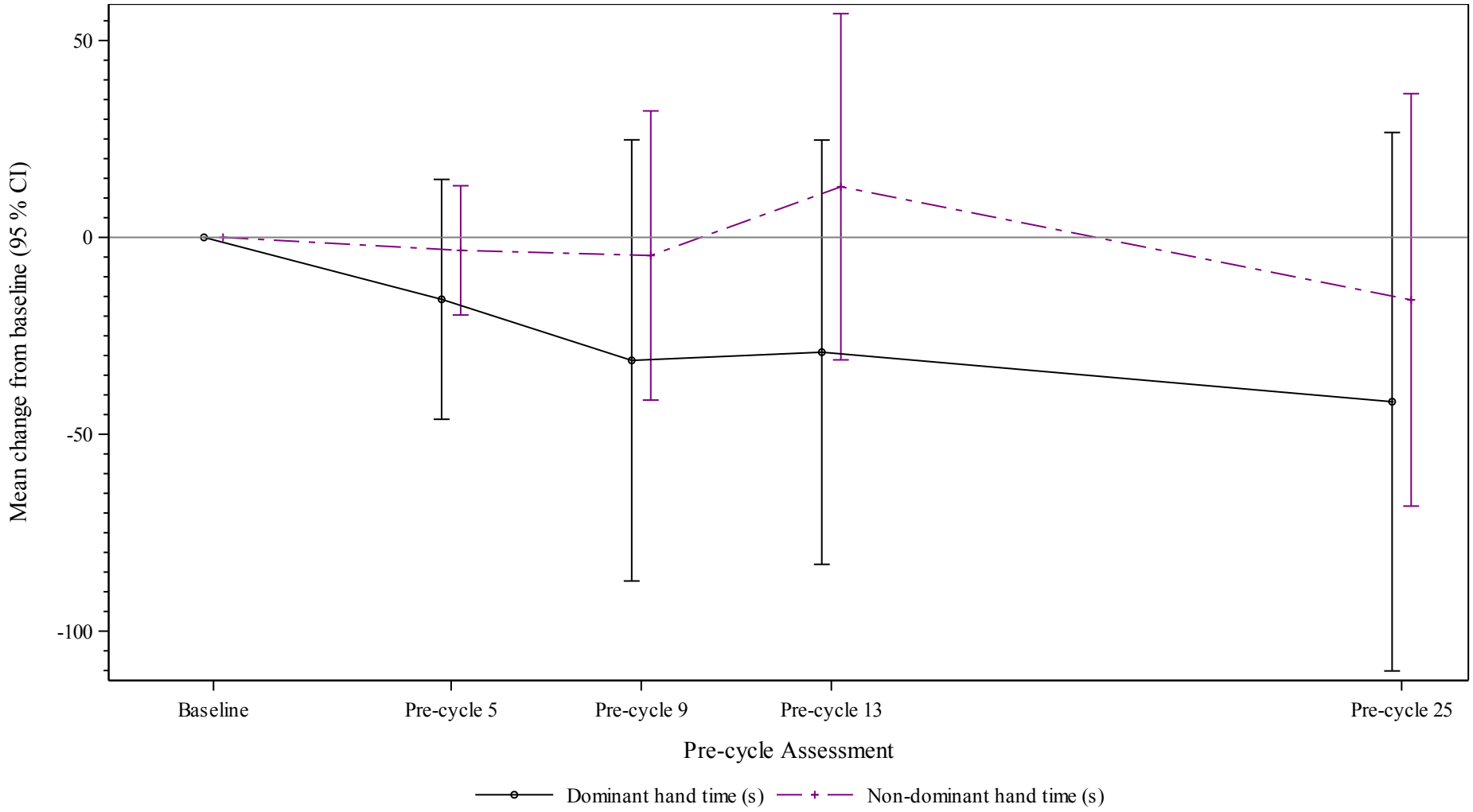
N = 8



CI = Confidence interval.

Figure 2.6.3.3.5 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Unknown
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

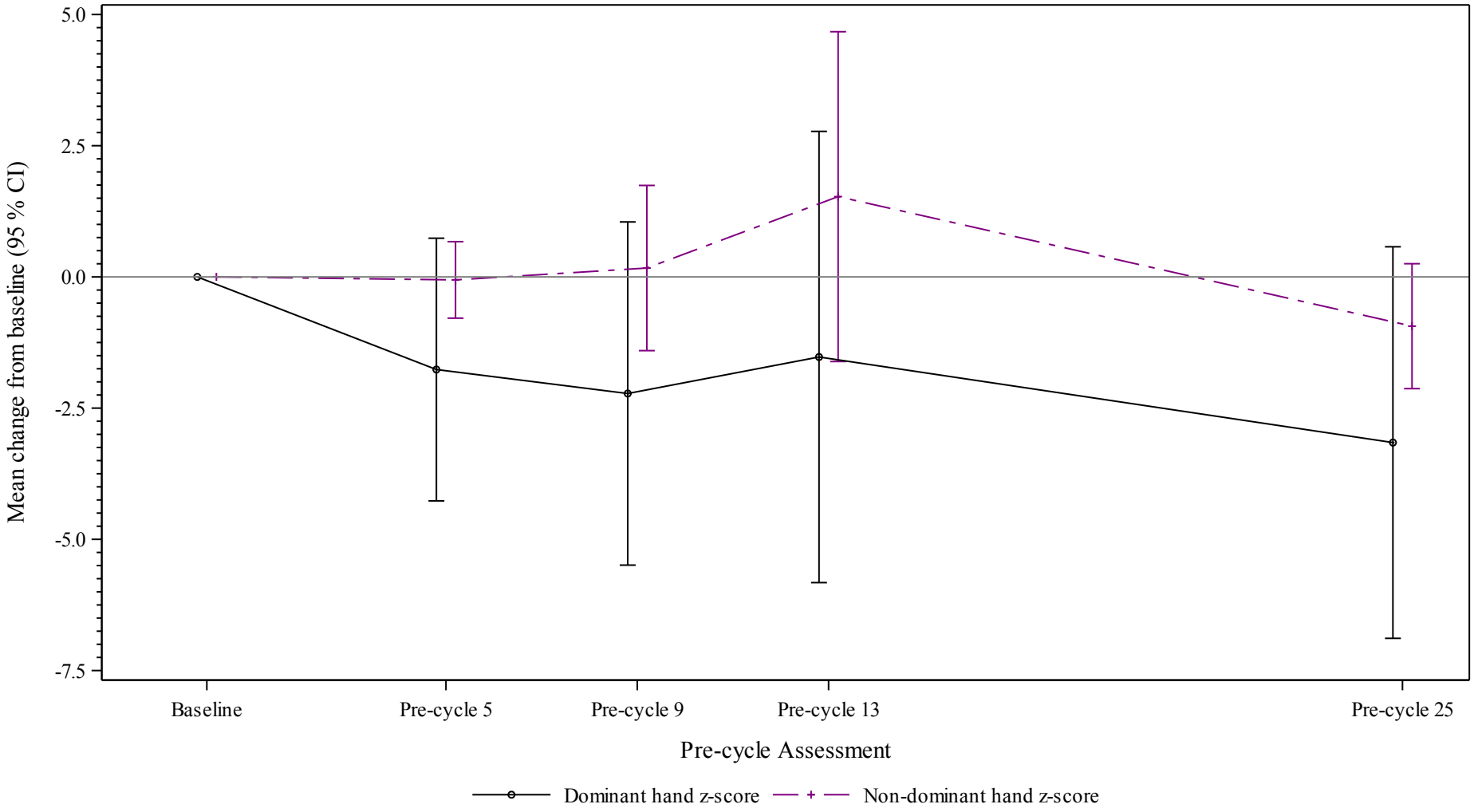
N = 12



CI = Confidence interval.

Figure 2.6.3.3.5 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Unknown
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

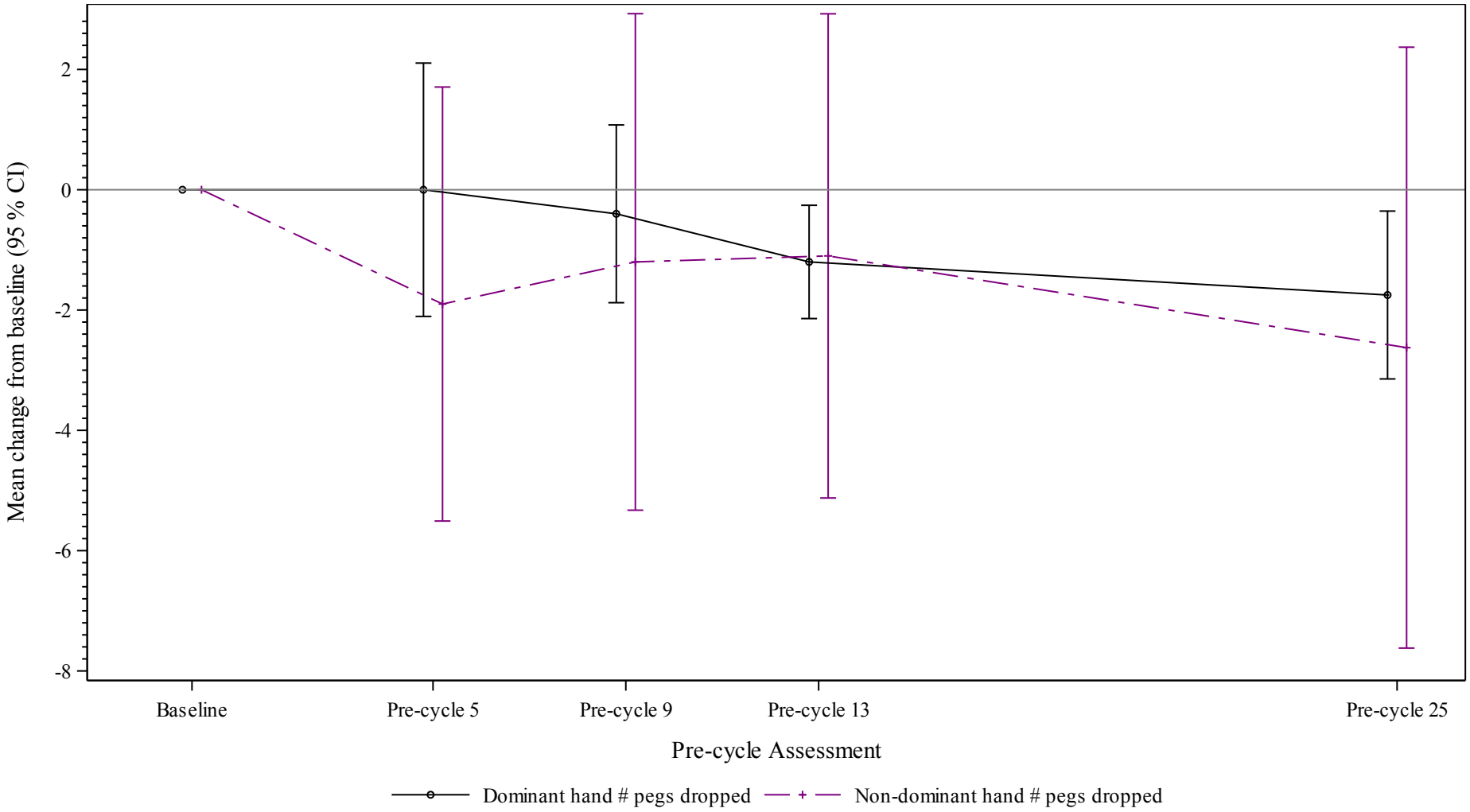
N = 12



CI = Confidence interval.

Figure 2.6.3.3.5 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Unknown
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb) Phase II Stratum 1, Data cut-off: 29th June 2018

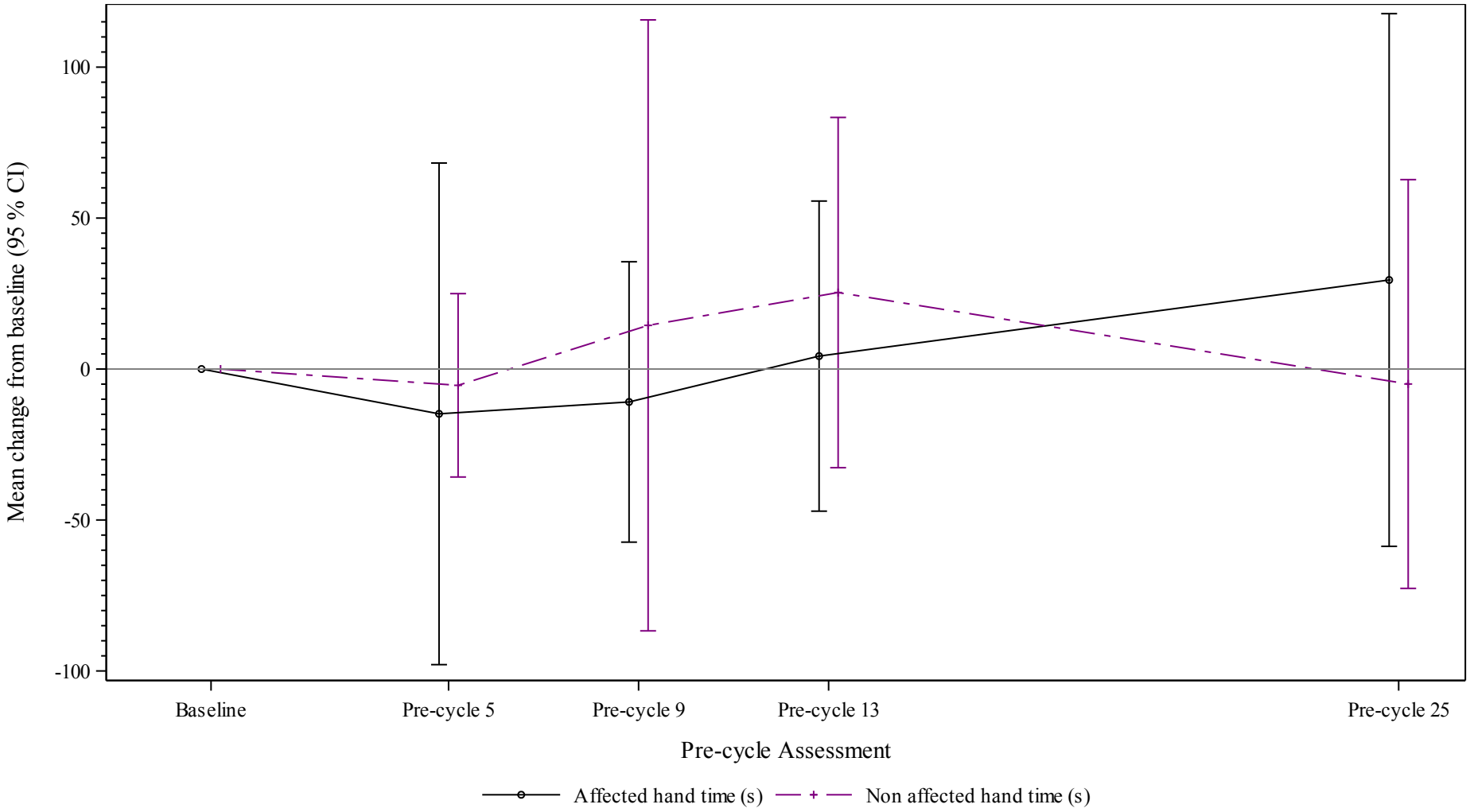
N = 12



CI = Confidence interval.

Figure 2.6.3.4.1 Mean change from baseline of Grooved pegboard test scores - Gender = Male
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 18

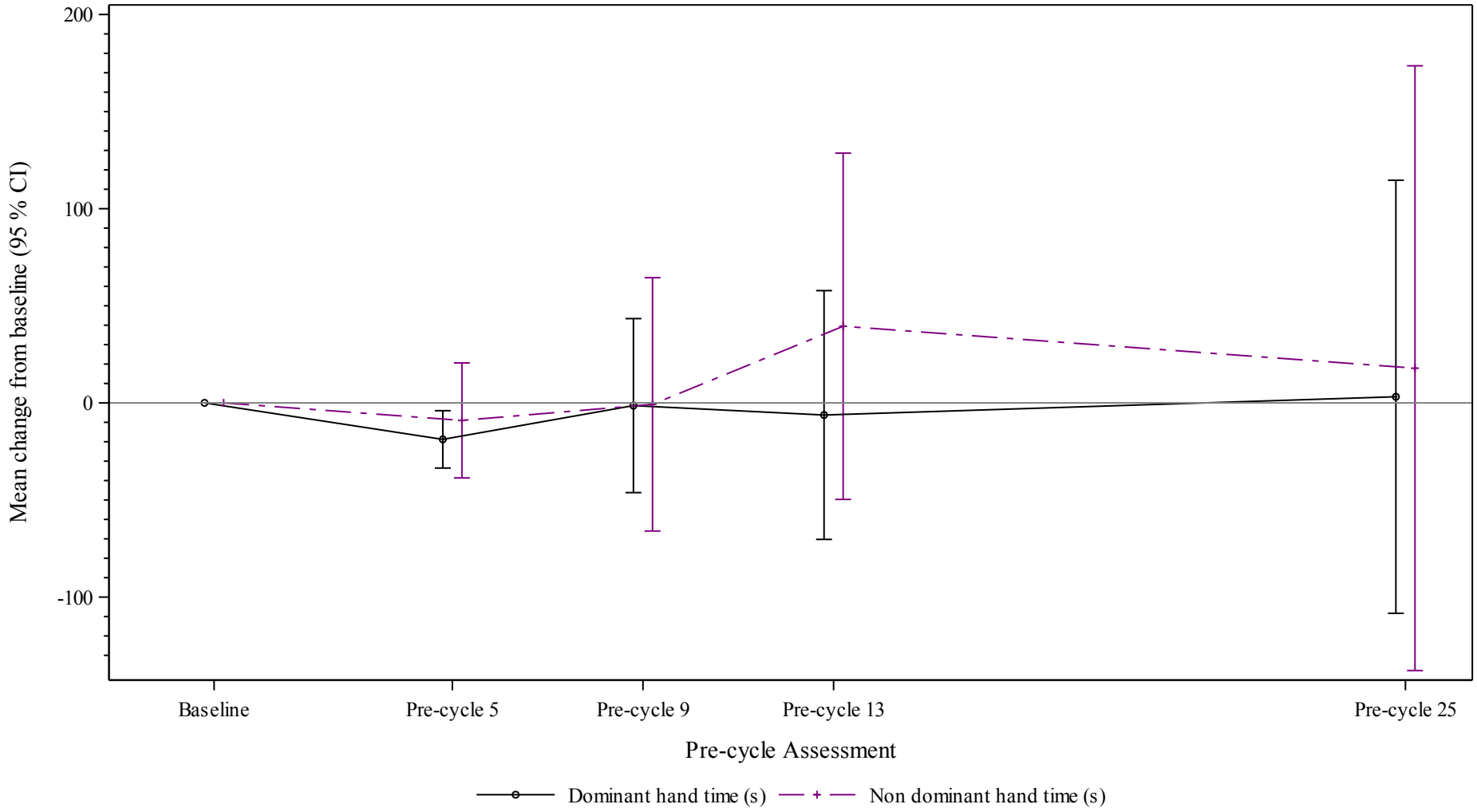
Unilateral Patients - time to complete Grooved pegboard test (s) (n=9)



CI = Confidence interval.

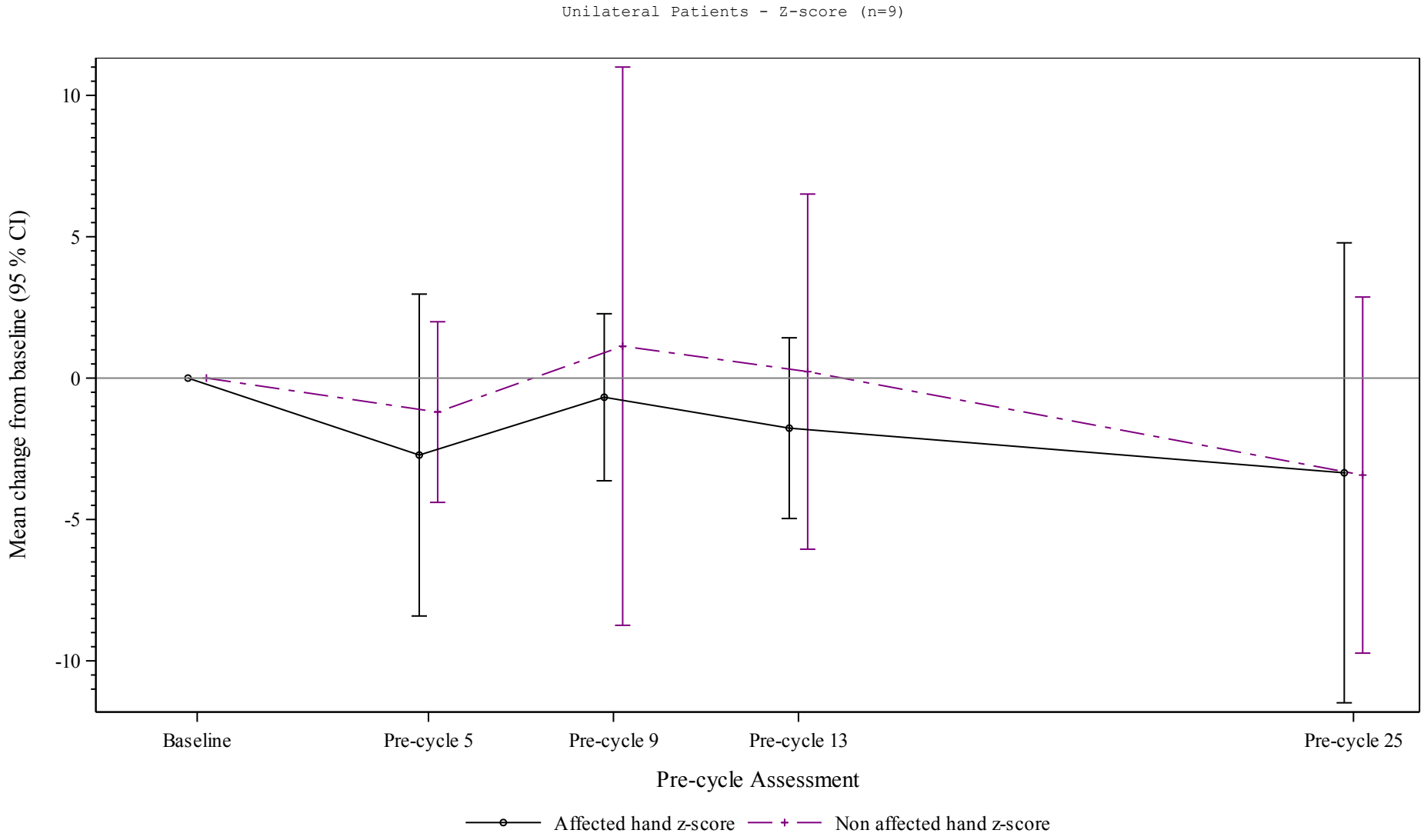
Figure 2.6.3.4.1 Mean change from baseline of Grooved pegboard test scores - Gender = Male
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 18

Bilateral Patients - time to complete Grooved pegboard test (s) (n=7)



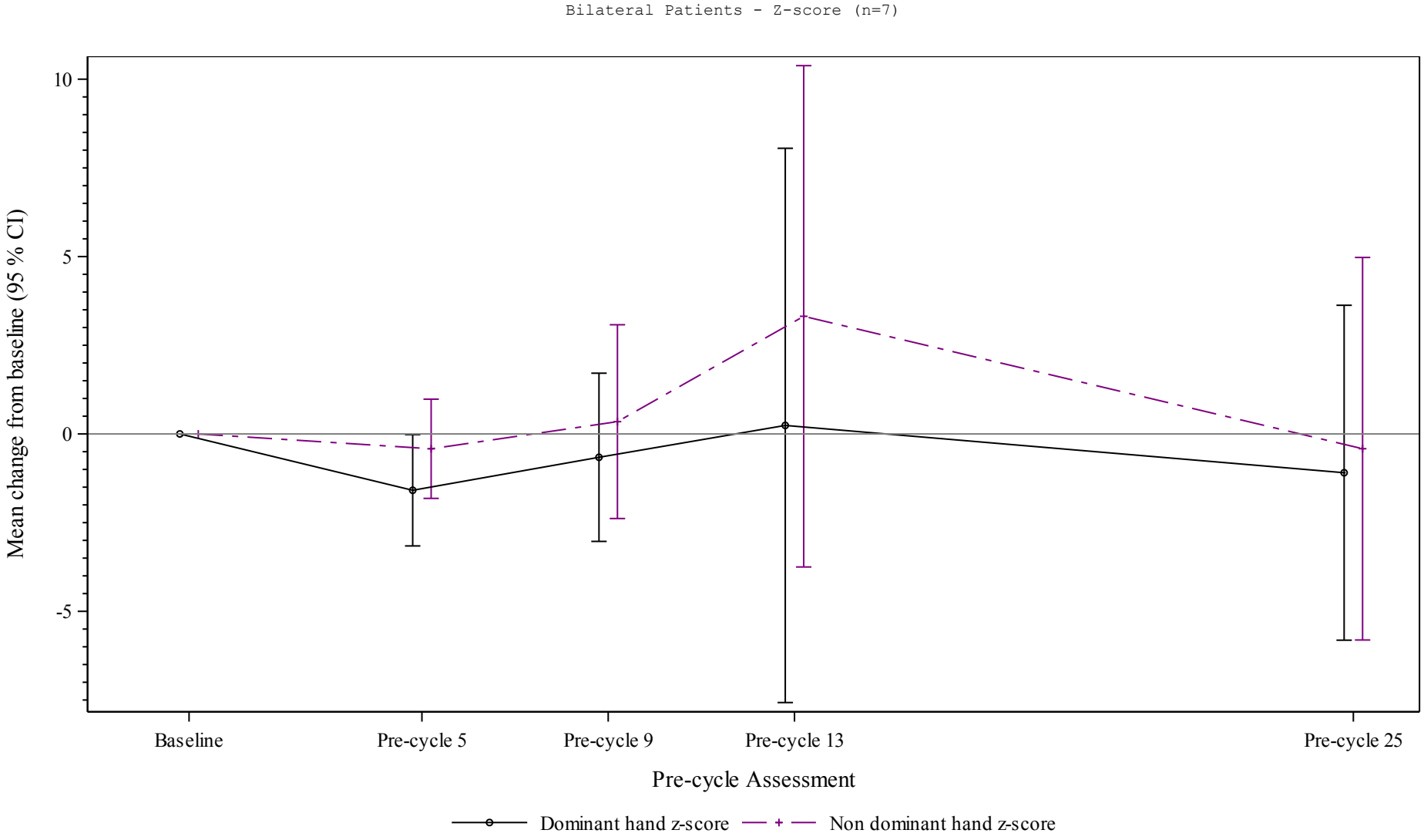
CI = Confidence interval.

Figure 2.6.3.4.1 Mean change from baseline of Grooved pegboard test scores - Gender = Male
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 18



CI = Confidence interval.

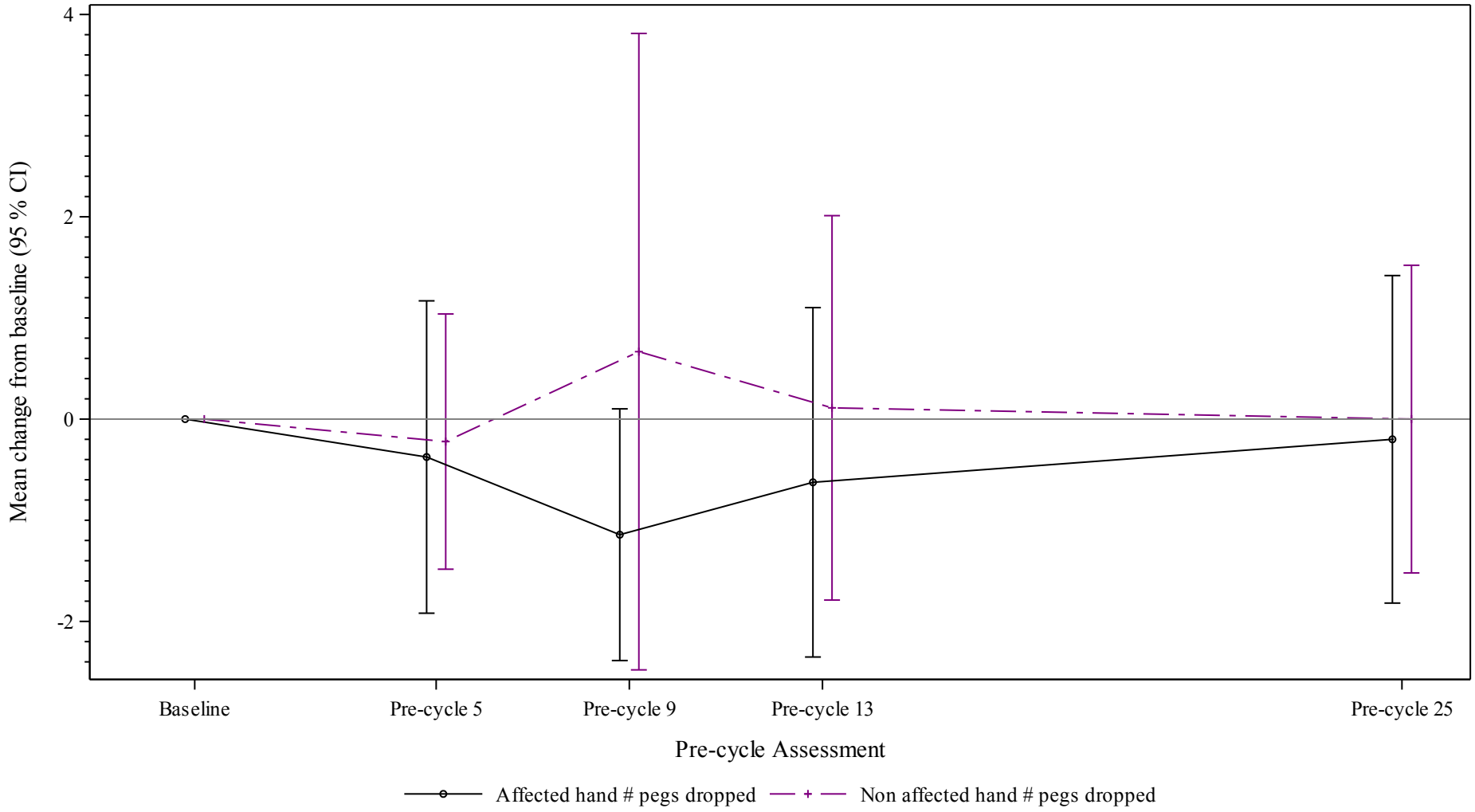
Figure 2.6.3.4.1 Mean change from baseline of Grooved pegboard test scores - Gender = Male
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 18



CI = Confidence interval.

Figure 2.6.3.4.1 Mean change from baseline of Grooved pegboard test scores - Gender = Male
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 18

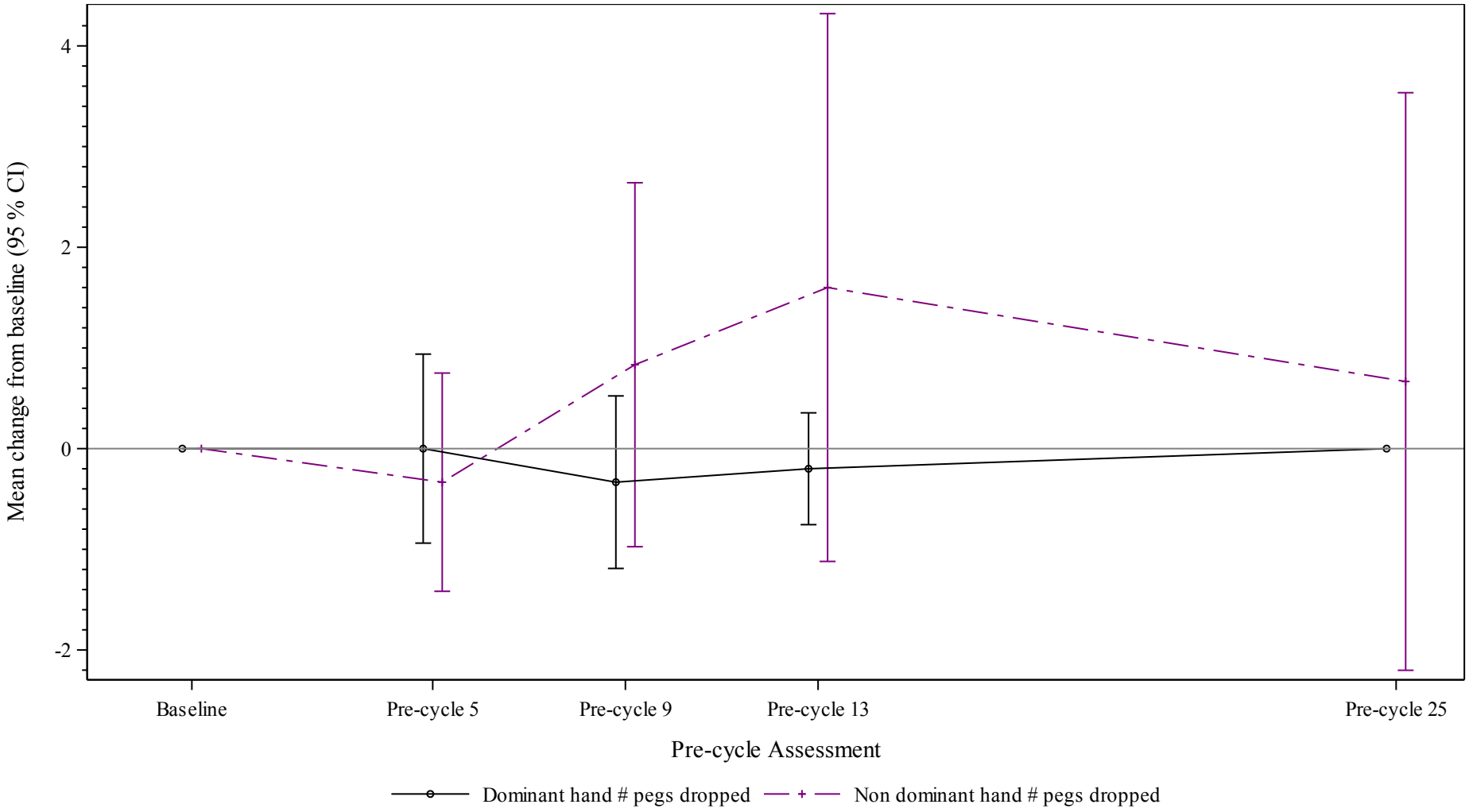
Unilateral Patients - Number of times peg dropped (n=9)



CI = Confidence interval.

Figure 2.6.3.4.1 Mean change from baseline of Grooved pegboard test scores - Gender = Male
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 18

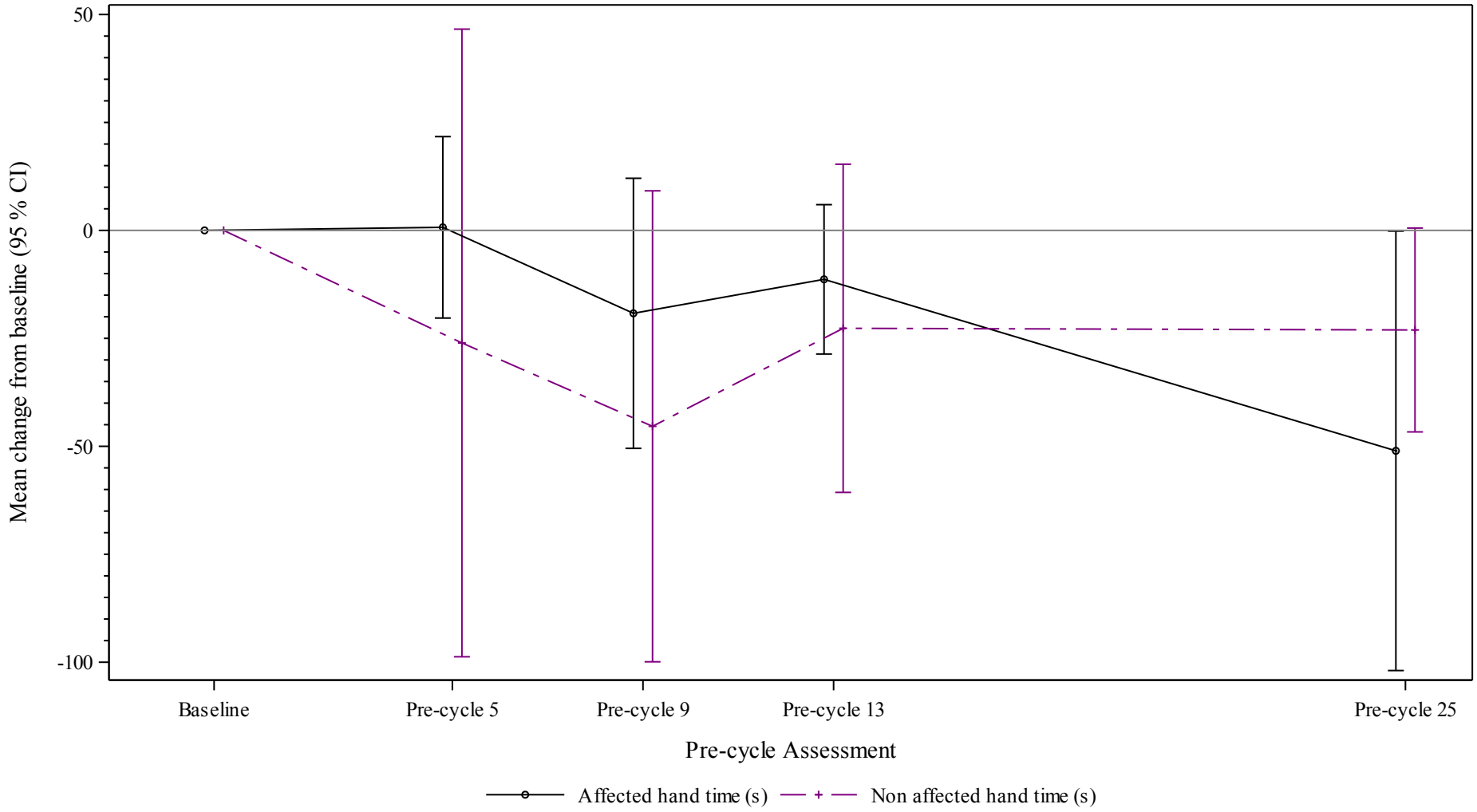
Bilateral Patients - Number of times peg dropped (n=7)



CI = Confidence interval.

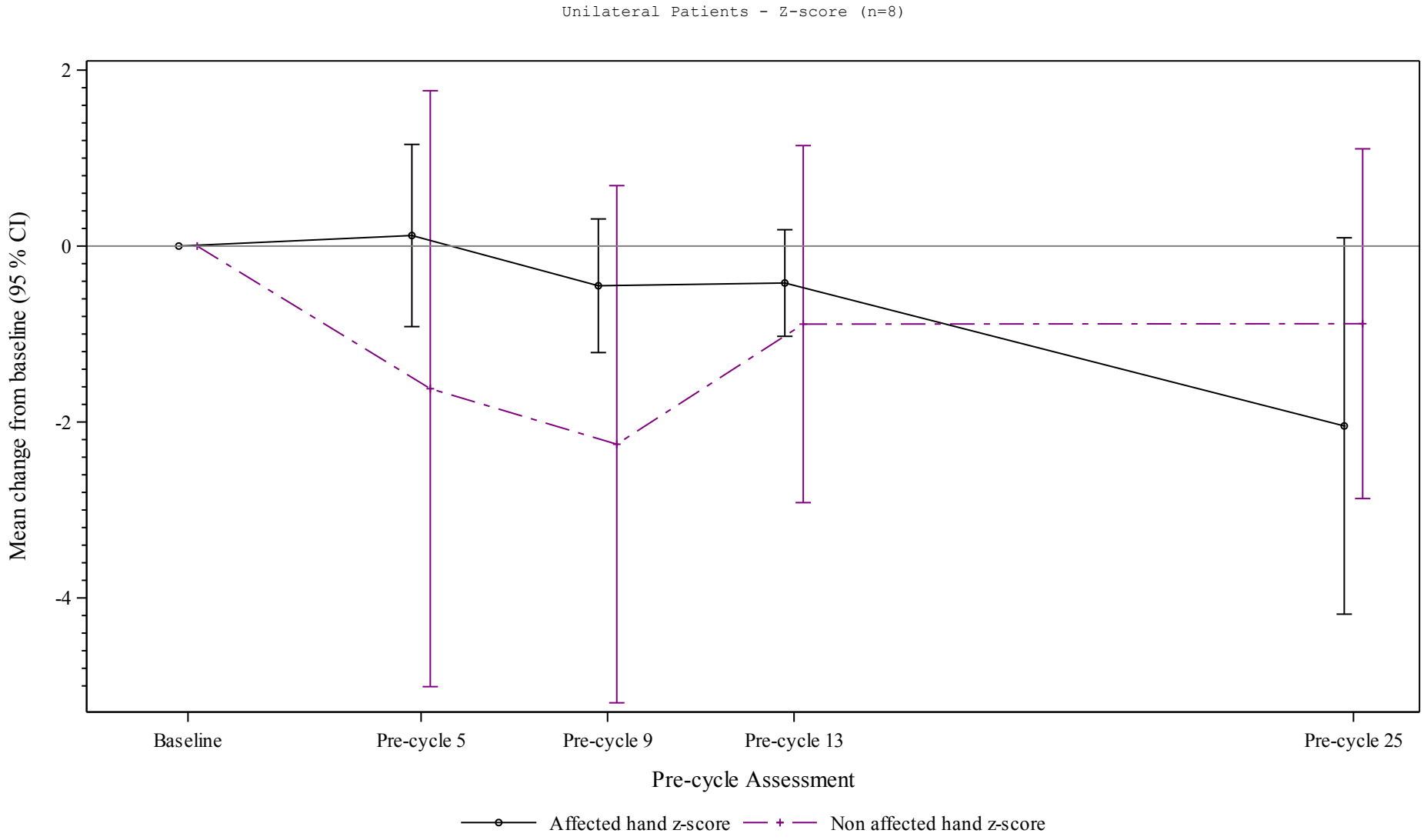
Figure 2.6.3.4.2 Mean change from baseline of Grooved pegboard test scores - Gender = Female
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 9

Unilateral Patients - time to complete Grooved pegboard test (s) (n=8)



CI = Confidence interval.

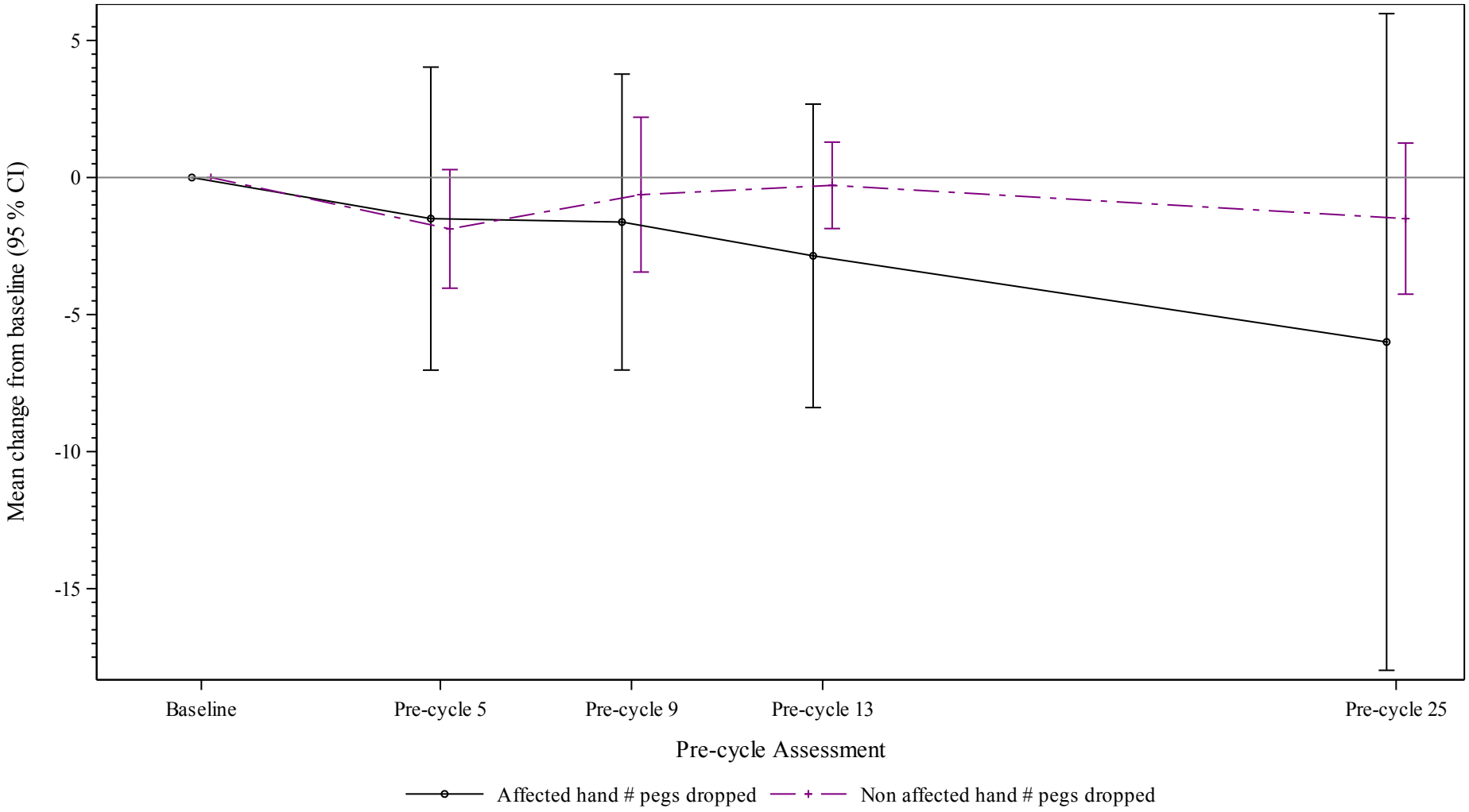
Figure 2.6.3.4.2 Mean change from baseline of Grooved pegboard test scores - Gender = Female
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 9



CI = Confidence interval.

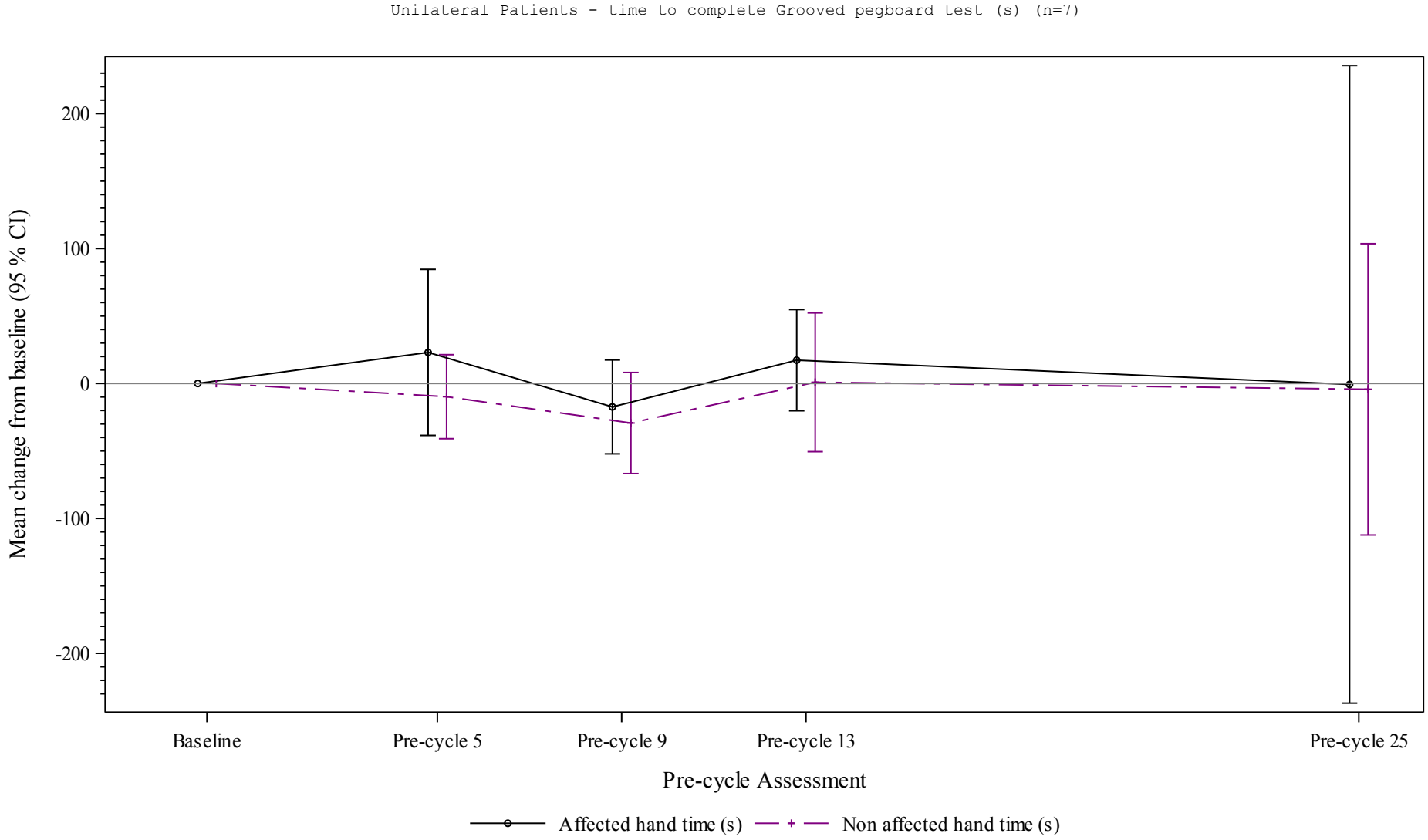
Figure 2.6.3.4.2 Mean change from baseline of Grooved pegboard test scores - Gender = Female
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 9

Unilateral Patients - Number of times peg dropped (n=8)



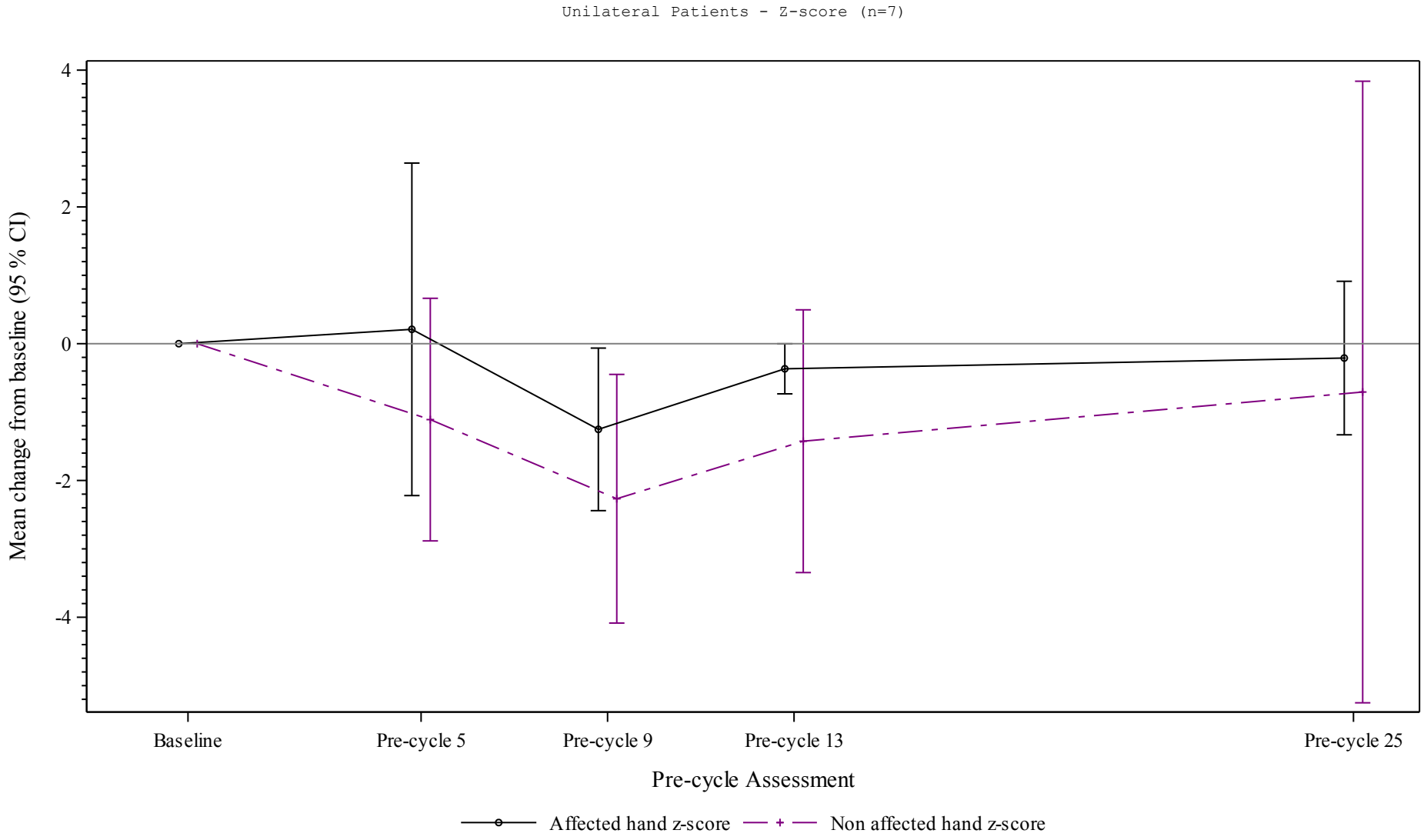
CI = Confidence interval.

Figure 2.6.3.4.3 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 8



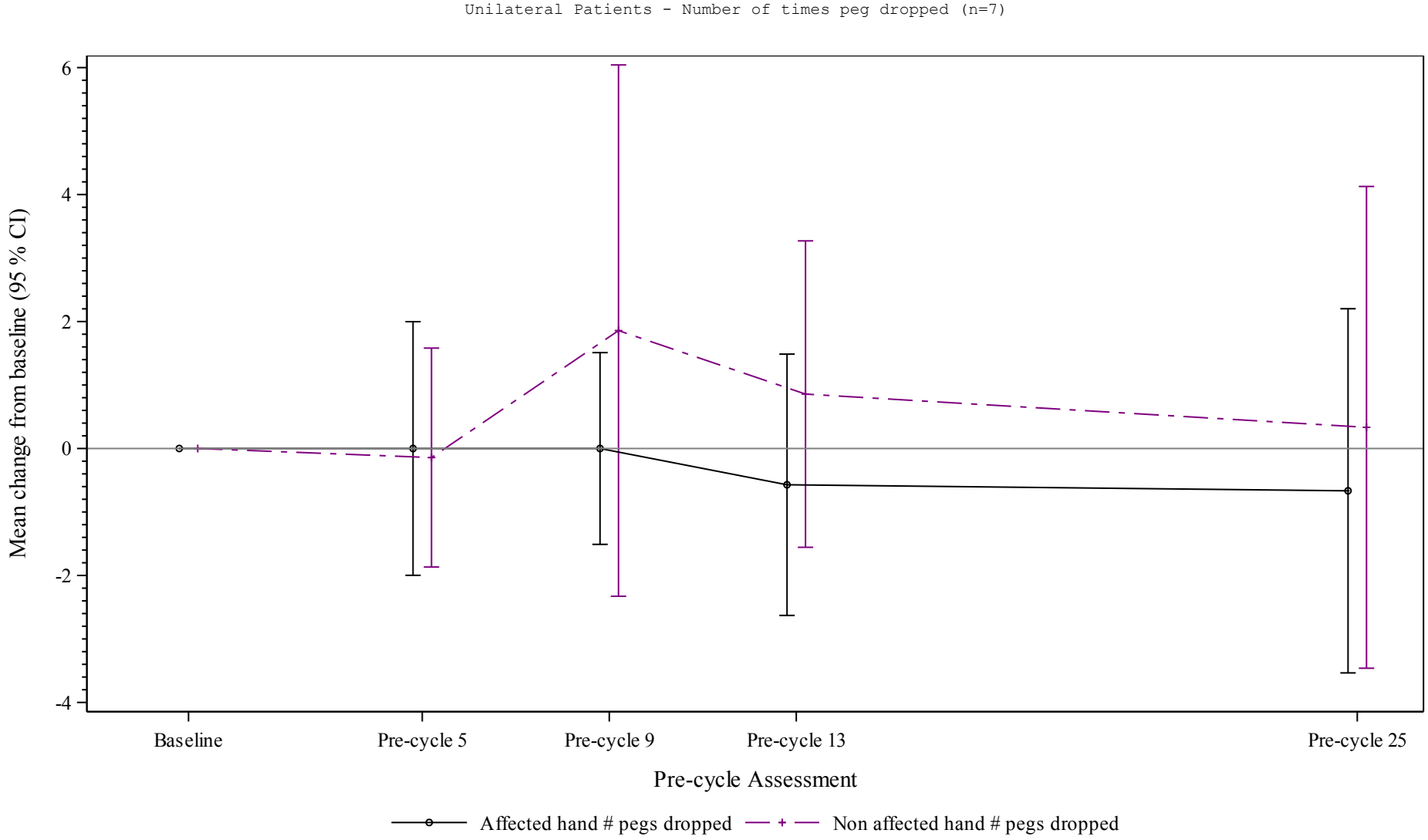
CI = Confidence interval.

Figure 2.6.3.4.3 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 8



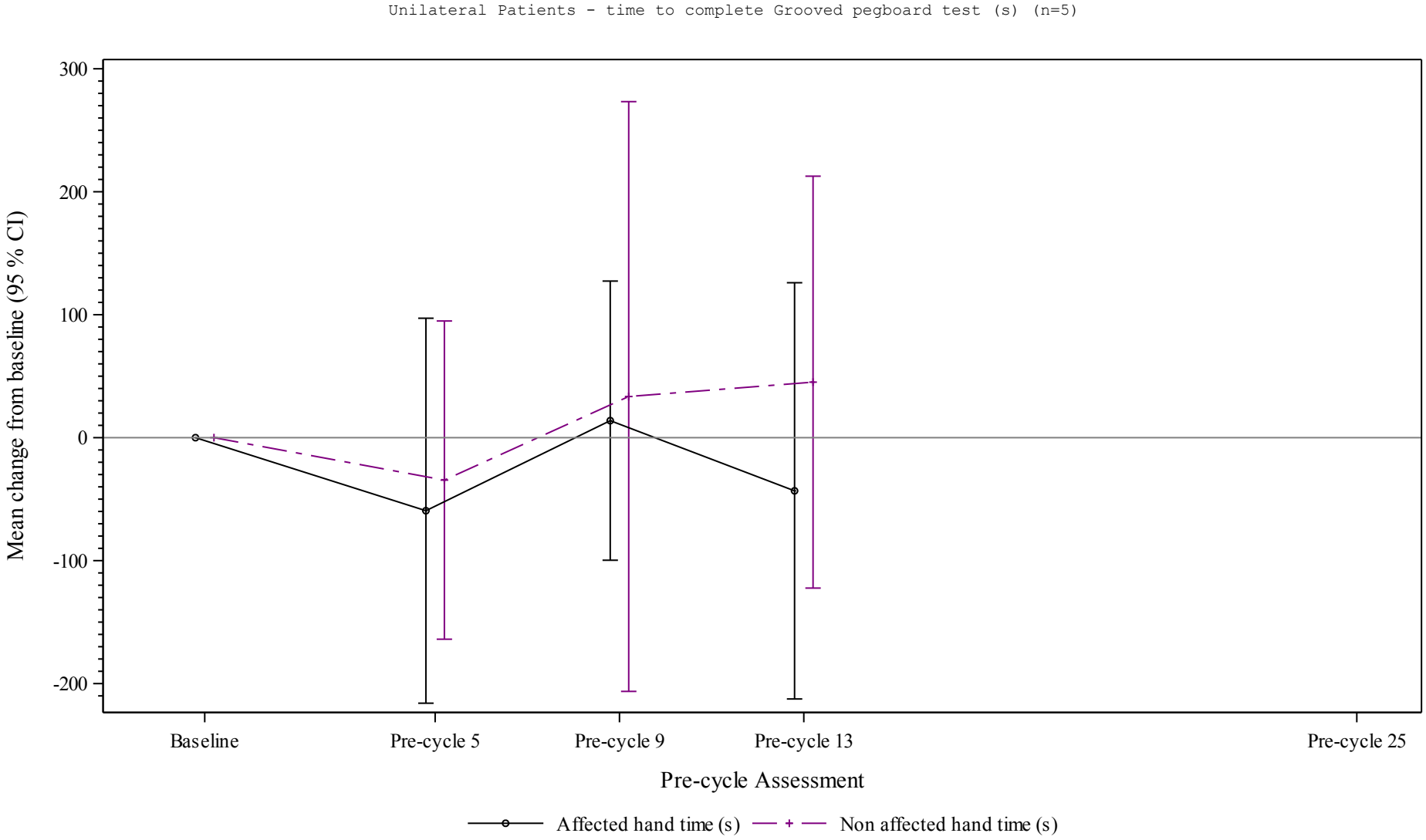
CI = Confidence interval.

Figure 2.6.3.4.3 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 8



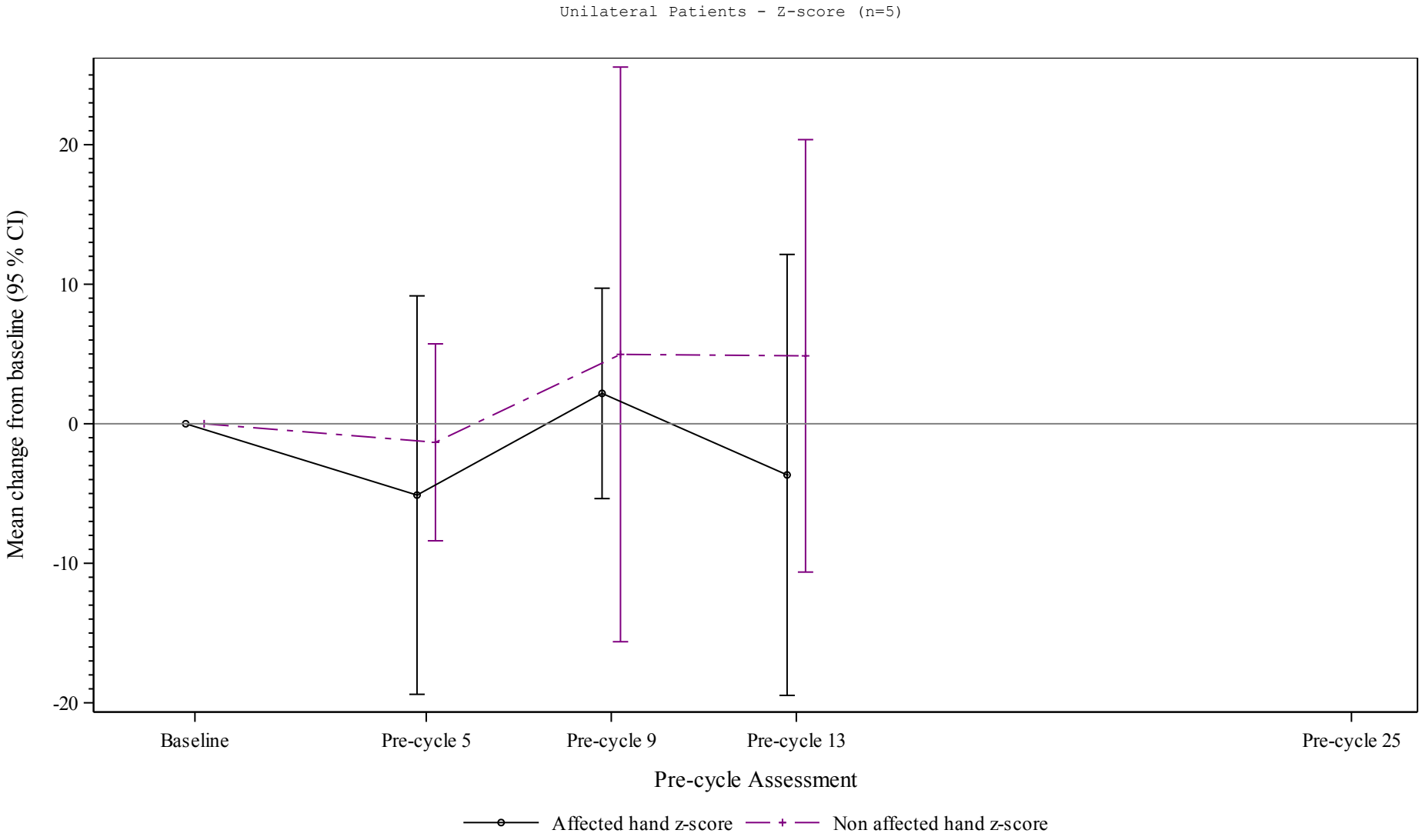
CI = Confidence interval.

Figure 2.6.3.4.4 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Non-progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 8



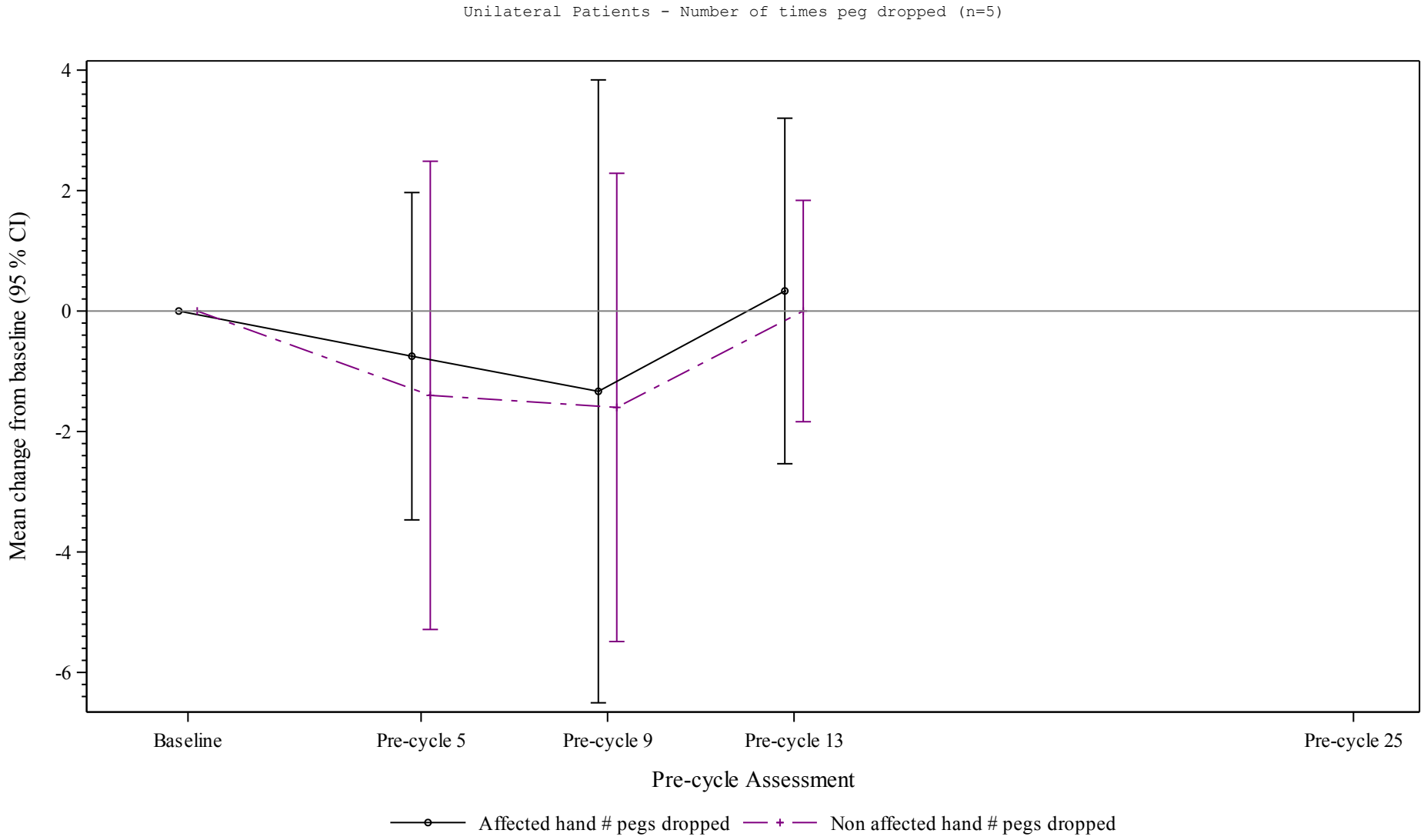
CI = Confidence interval.

Figure 2.6.3.4.4 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Non-progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 8



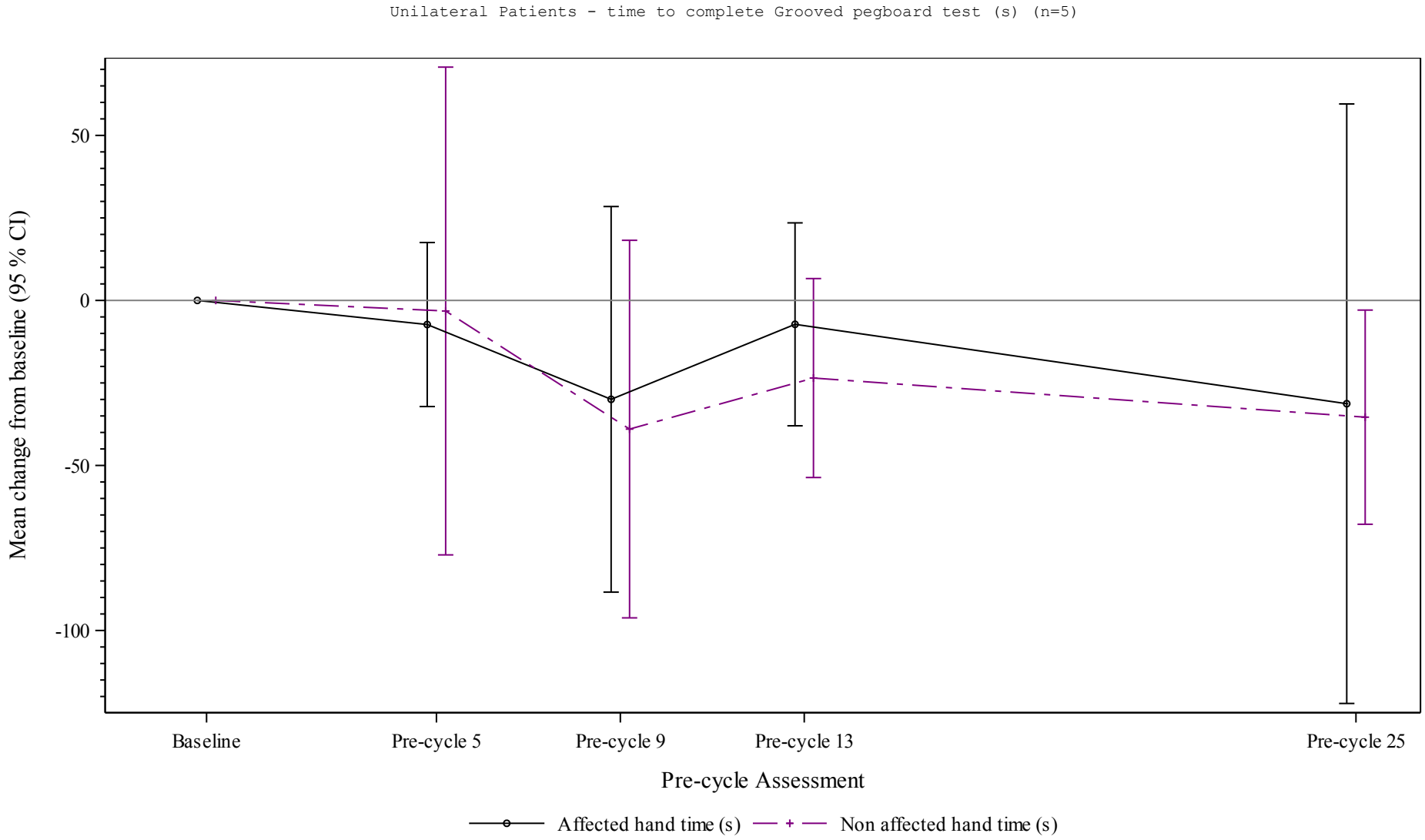
CI = Confidence interval.

Figure 2.6.3.4.4 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Non-progressive
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 8



CI = Confidence interval.

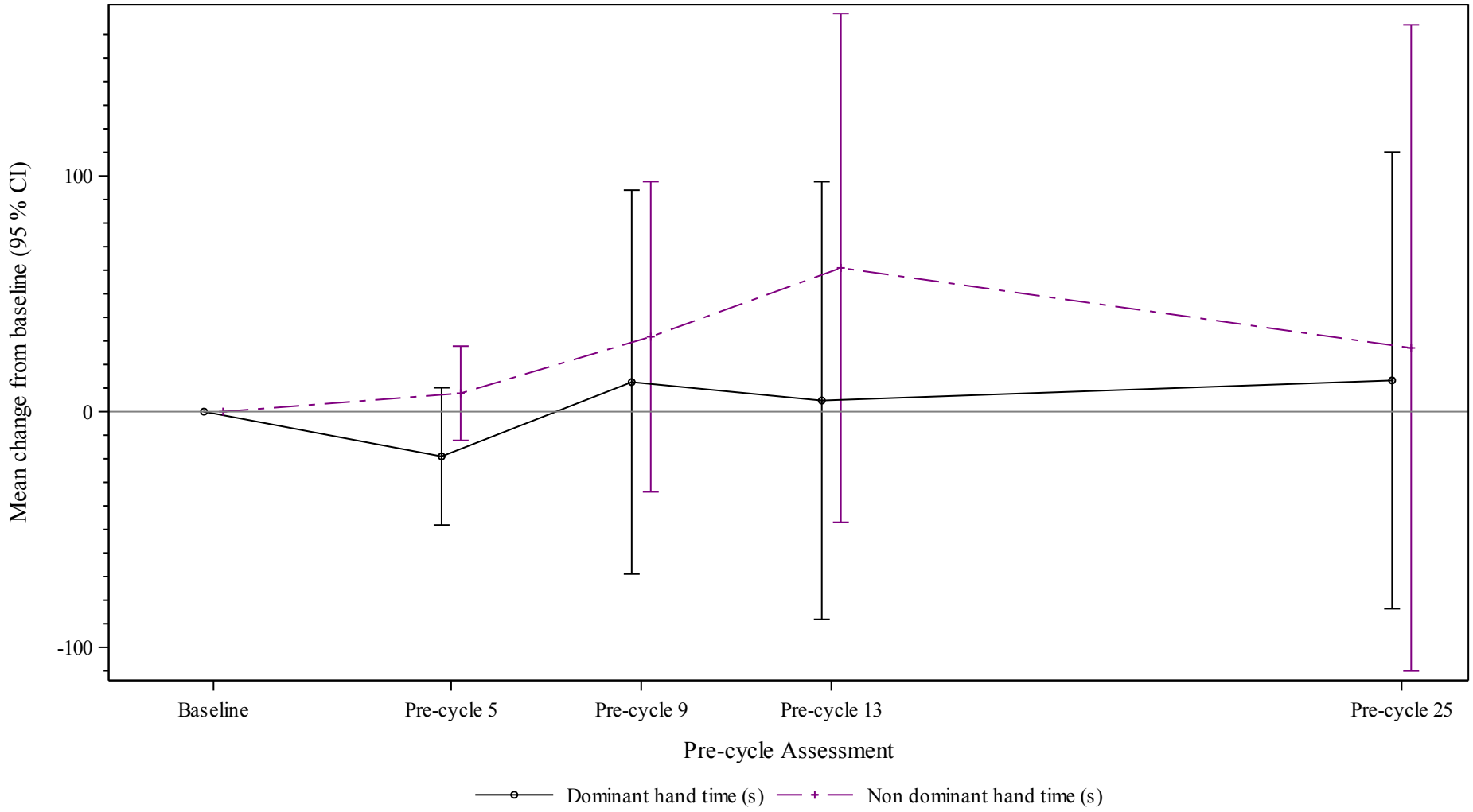
Figure 2.6.3.4.5 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Unknown
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 11



CI = Confidence interval.

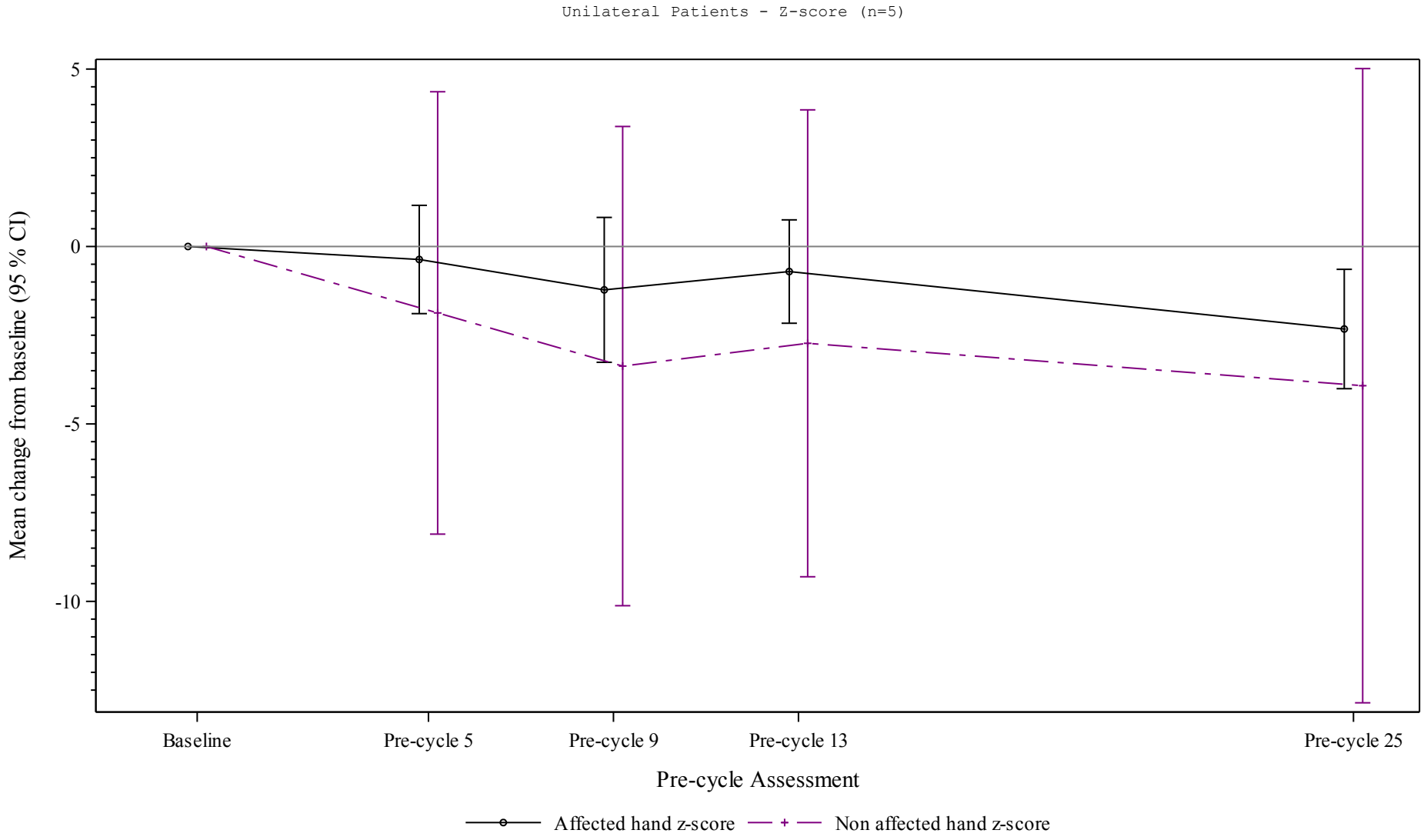
Figure 2.6.3.4.5 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Unknown
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 11

Bilateral Patients - time to complete Grooved pegboard test (s) (n=5)



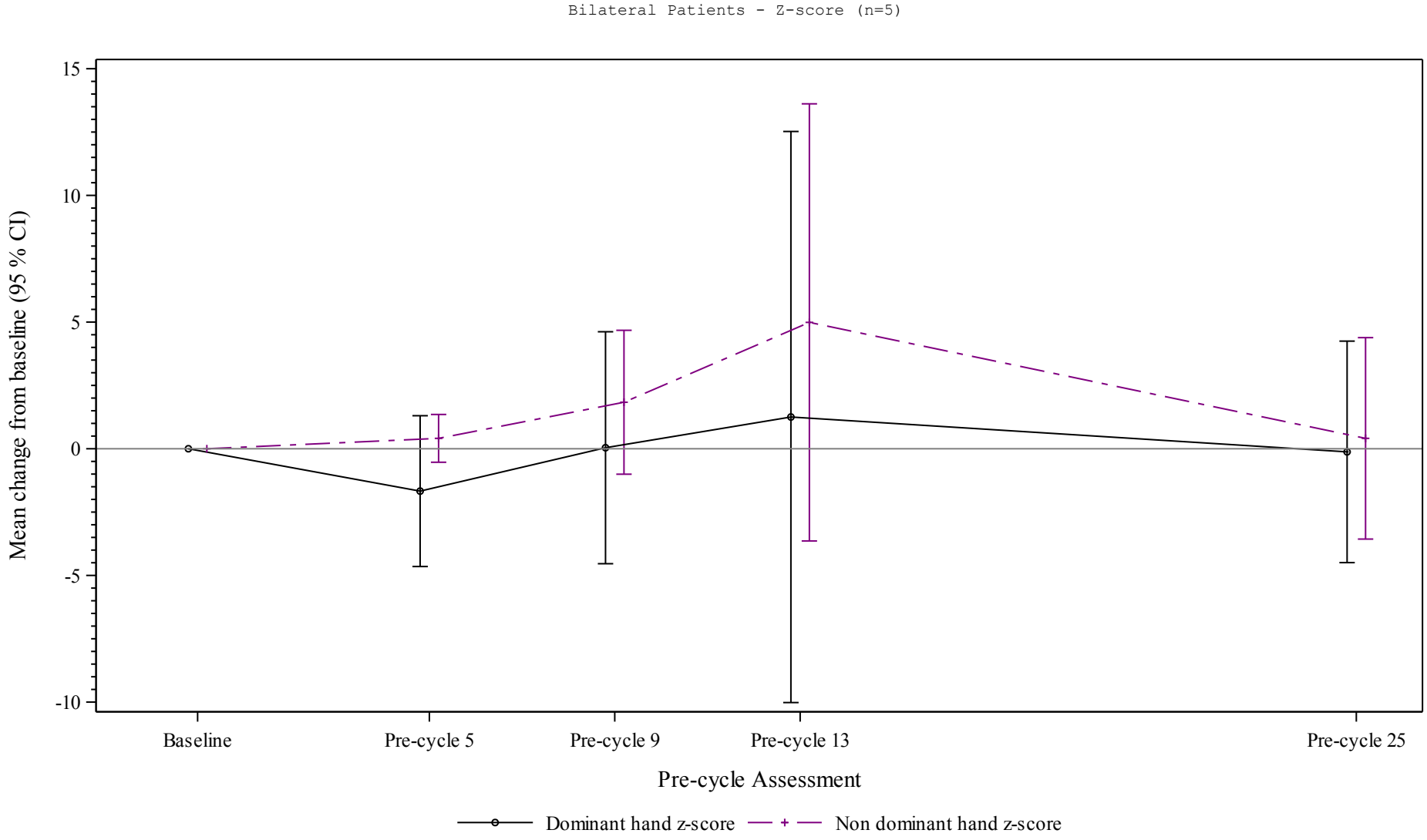
CI = Confidence interval.

Figure 2.6.3.4.5 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Unknown
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 11



CI = Confidence interval.

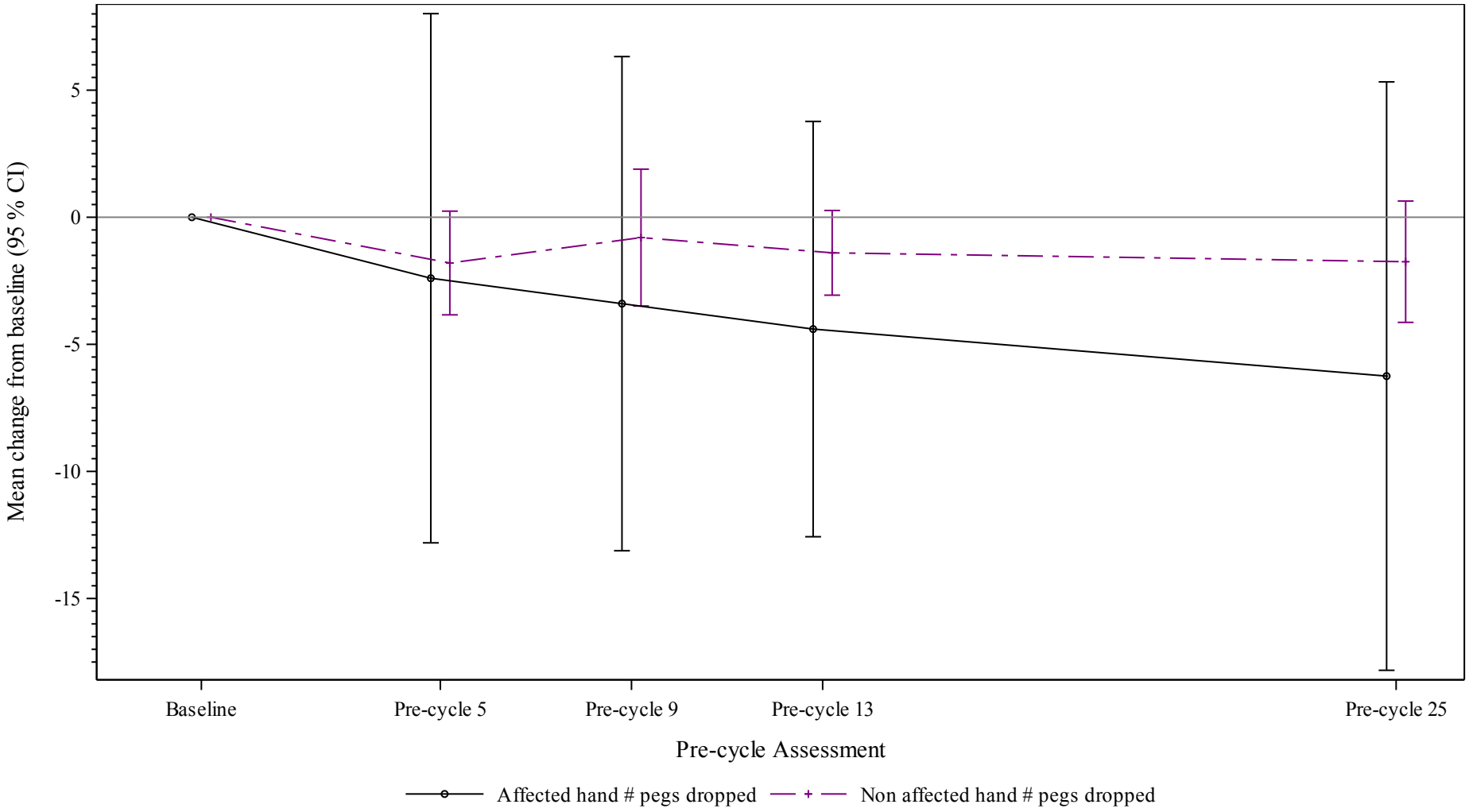
Figure 2.6.3.4.5 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Unknown
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 11



CI = Confidence interval.

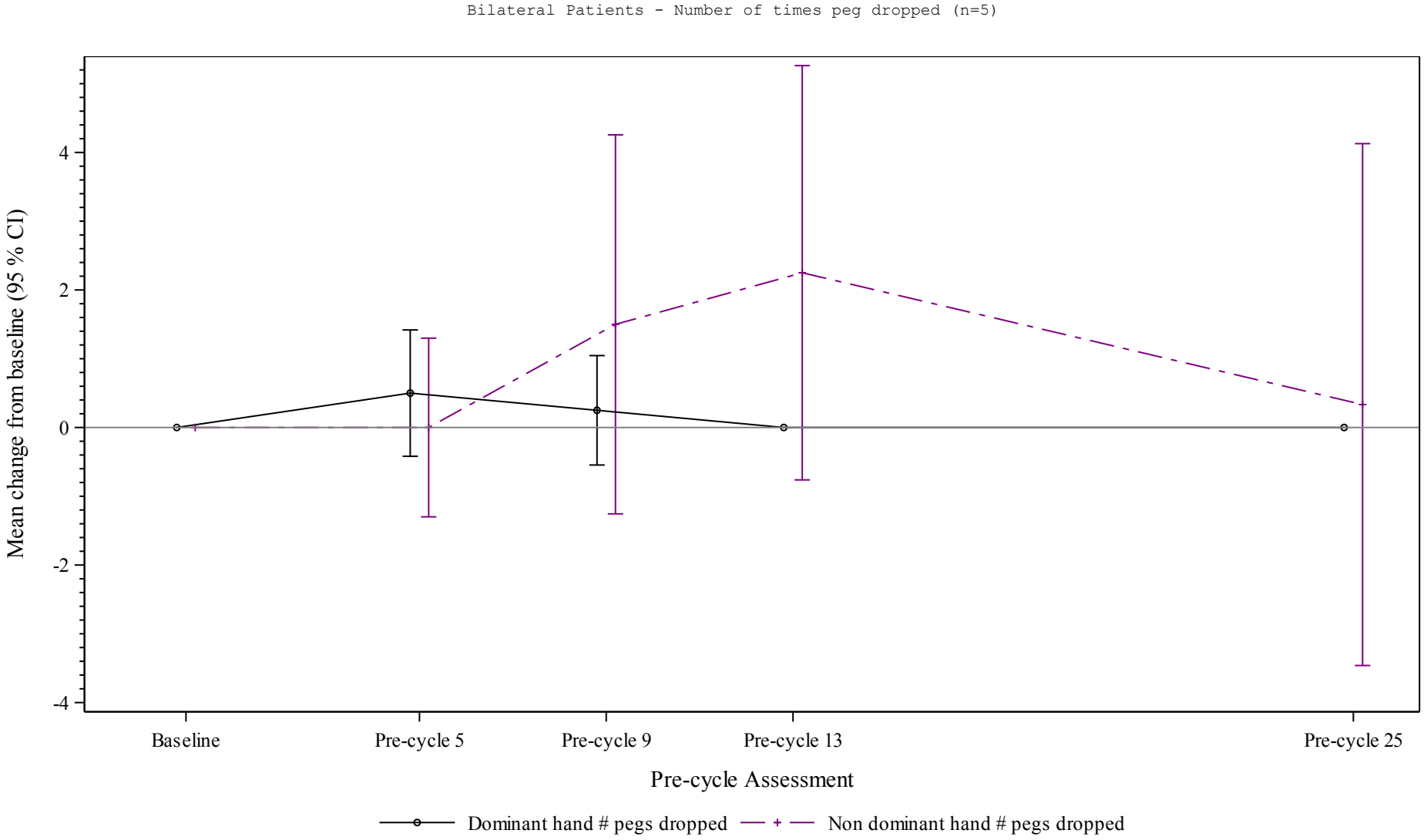
Figure 2.6.3.4.5 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Unknown
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 11

Unilateral Patients - Number of times peg dropped (n=5)



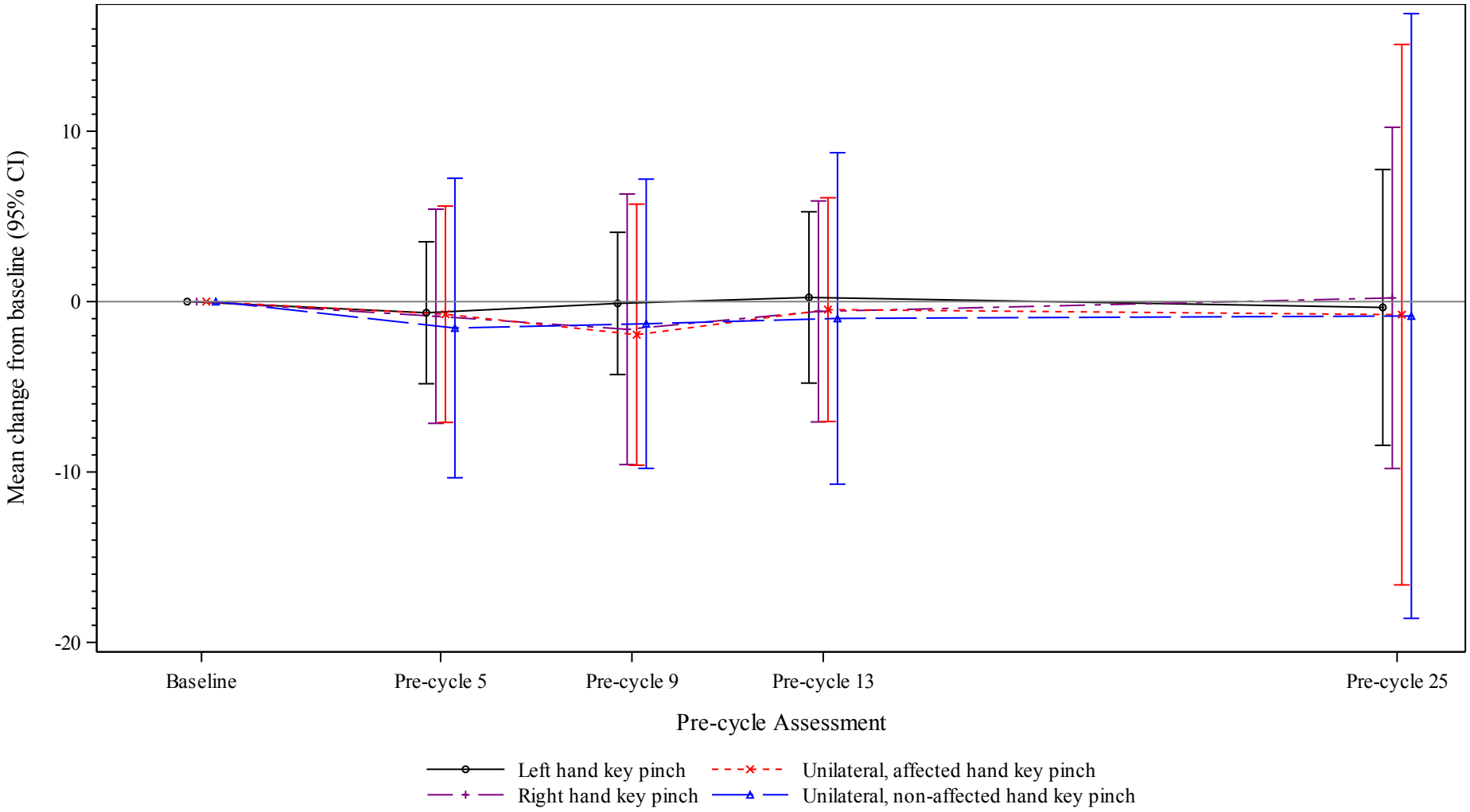
CI = Confidence interval.

Figure 2.6.3.4.5 Mean change from baseline of Grooved pegboard test scores - PN status at enrollment = Unknown
(Full analysis set >=5 years at enrolment with cervical/upper thoracic/upper limb and PN-related morbidity)
N = 11



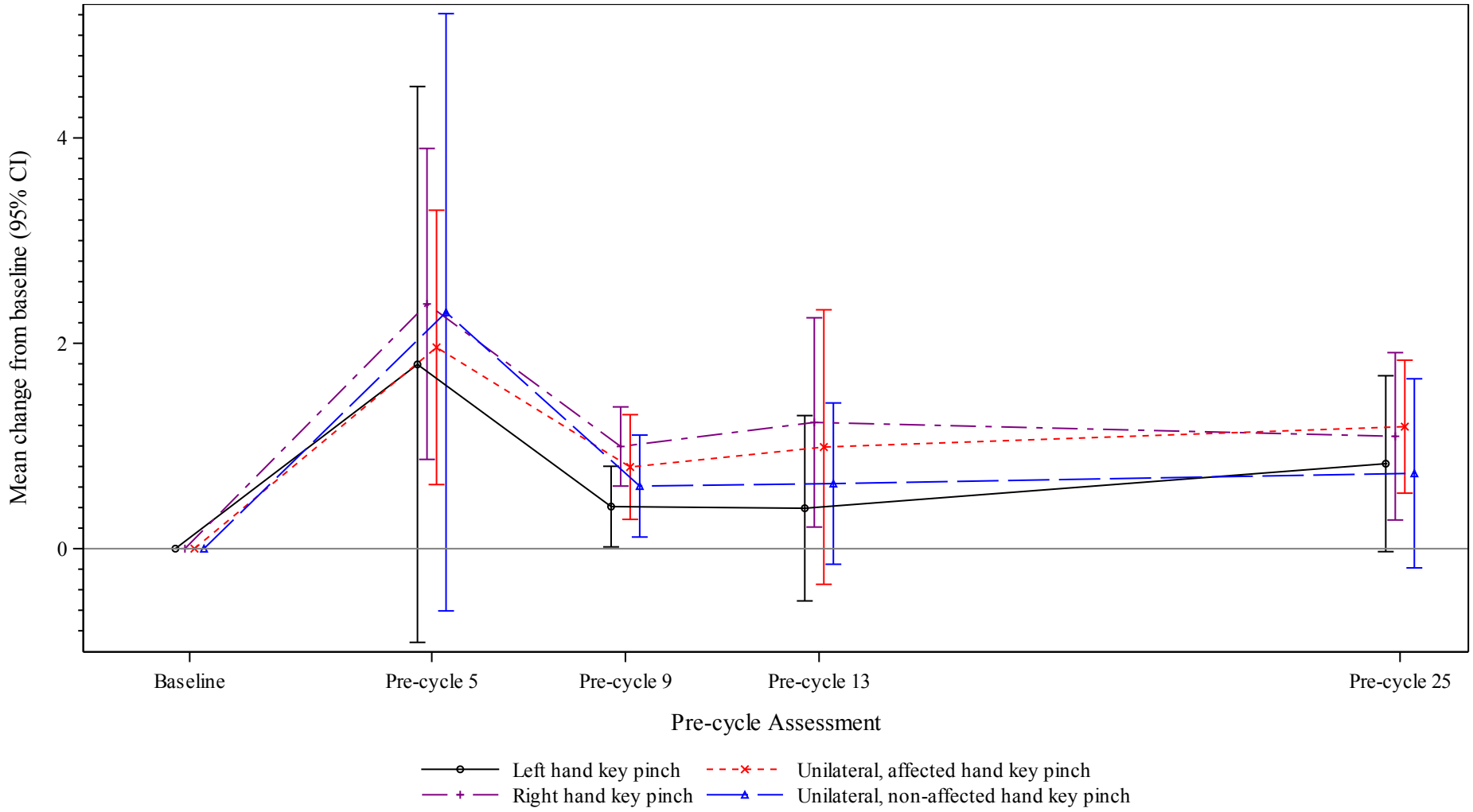
CI = Confidence interval.

Figure 2.6.4.1.1 Mean change from baseline of key pinch test scores
Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 19



CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral patients omitted owing to insufficient data.

Figure 2.6.4.1.2 Mean change from baseline of key pinch test scores
Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 14



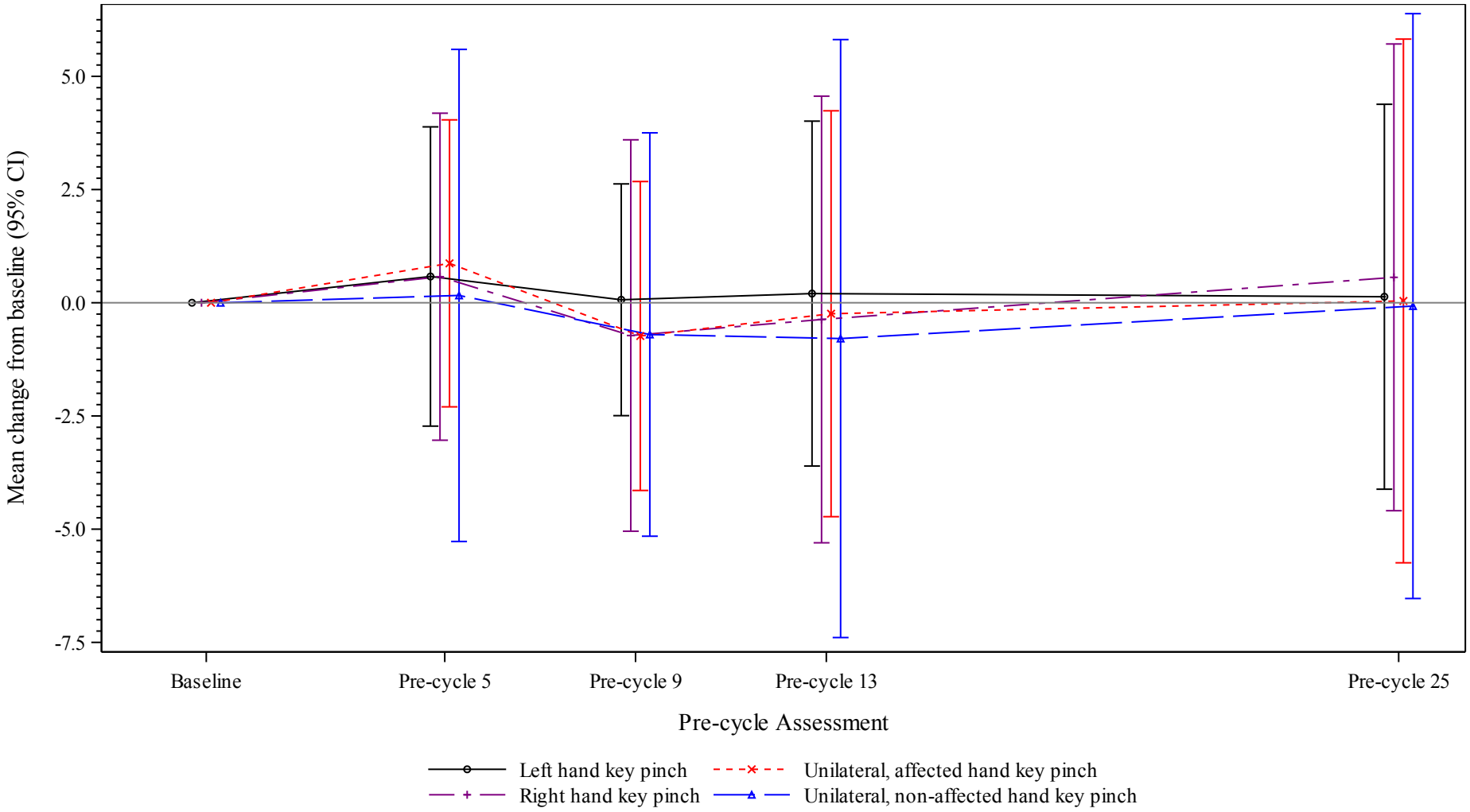
CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral patients omitted owing to insufficient data.

Figure 2.6.4.1.3 Mean change from baseline of key pinch test scores
PN status at enrollment = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.
Timepoints with <3 patients are omitted.
All patients omitted owing to insufficient data.

Figure 2.6.4.1.4 Mean change from baseline of key pinch test scores
PN status at enrollment = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 11



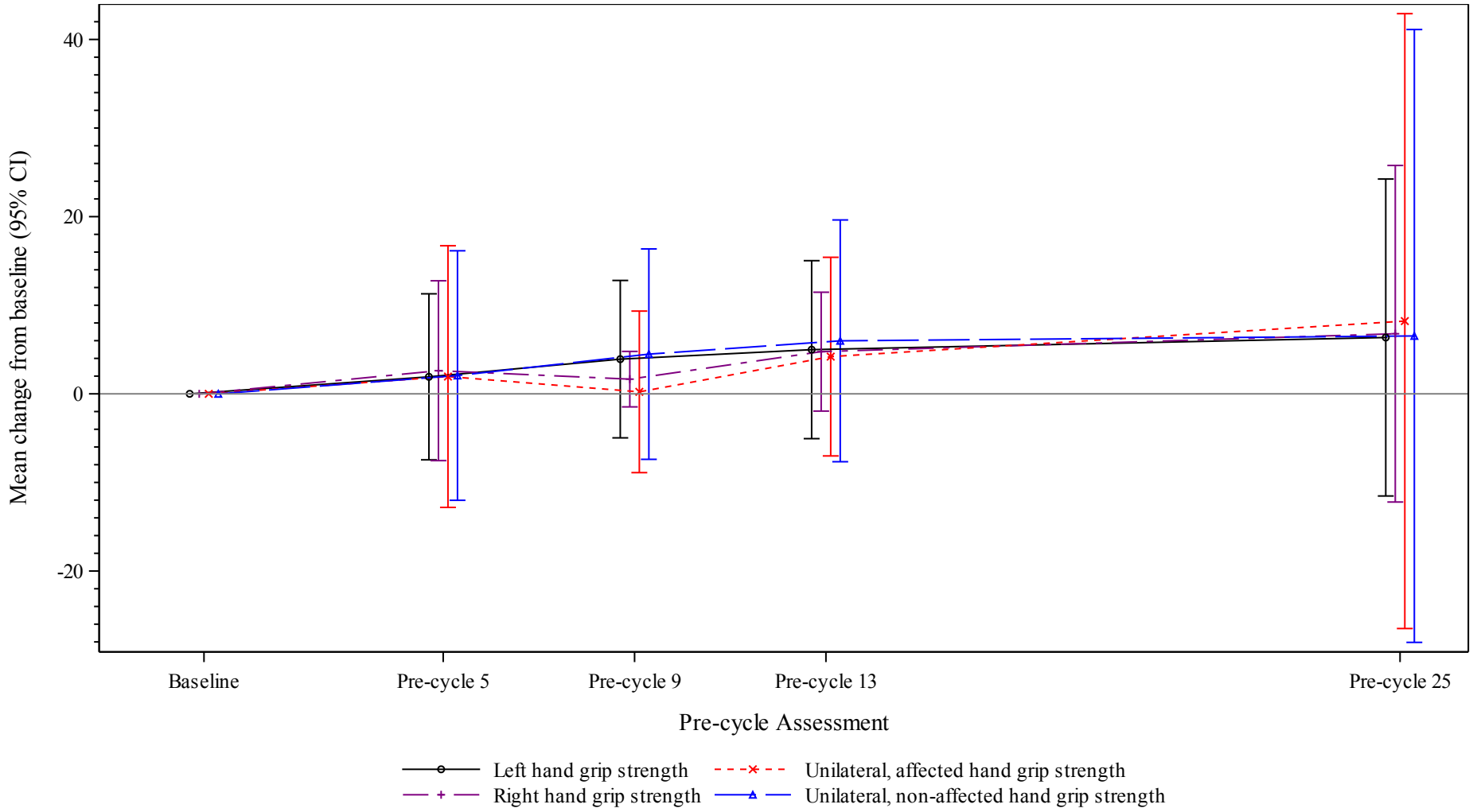
CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral patients omitted owing to insufficient data.

Figure 2.6.4.1.5 Mean change from baseline of key pinch test scores
PN status at enrollment = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

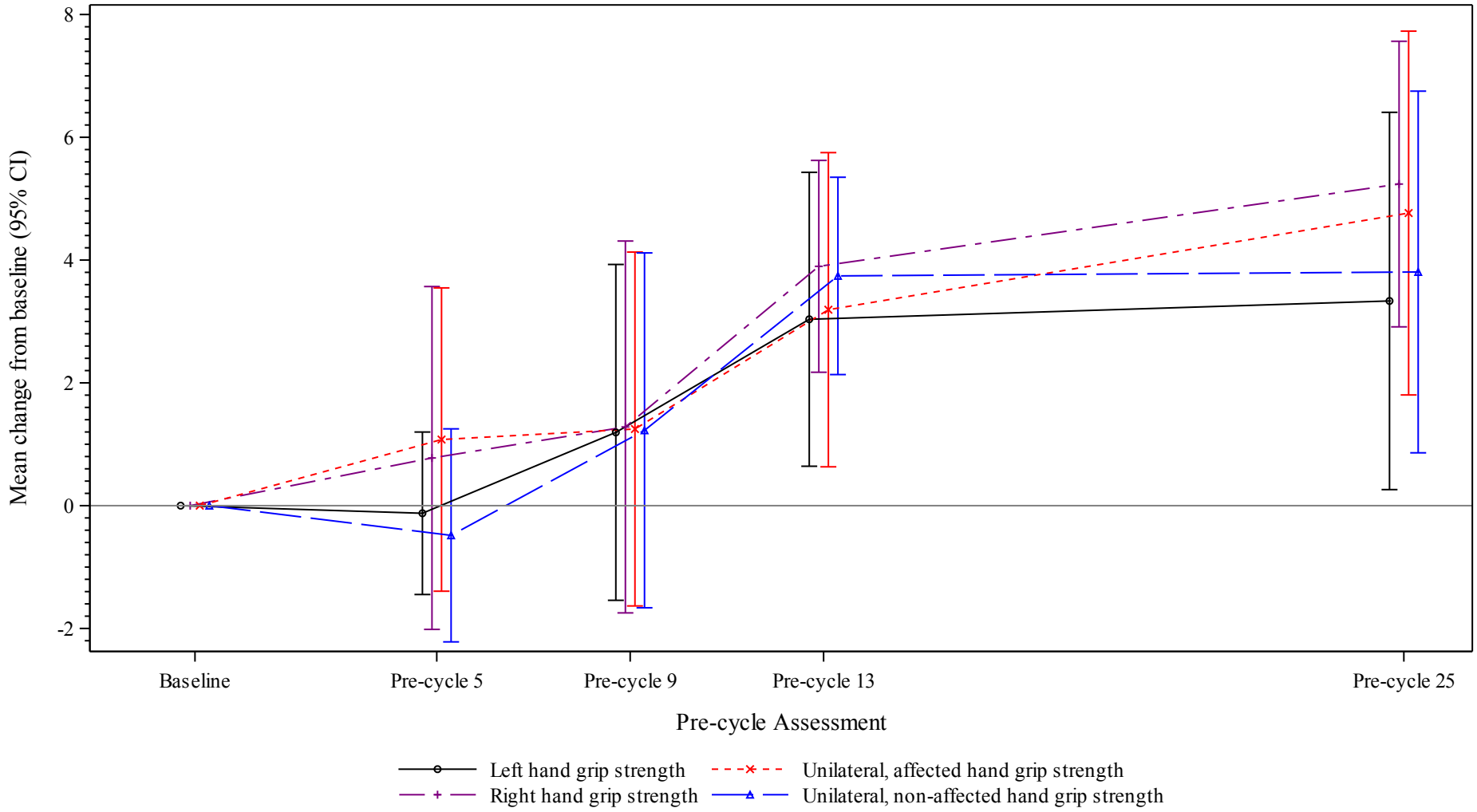
CI = Confidence interval.
Timepoints with <3 patients are omitted.
All patients omitted owing to insufficient data.

Figure 2.6.4.2.1 Mean change from baseline of grip strength test scores
Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 19



CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral patients omitted owing to insufficient data.

Figure 2.6.4.2.2 Mean change from baseline of grip strength test scores
Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 14



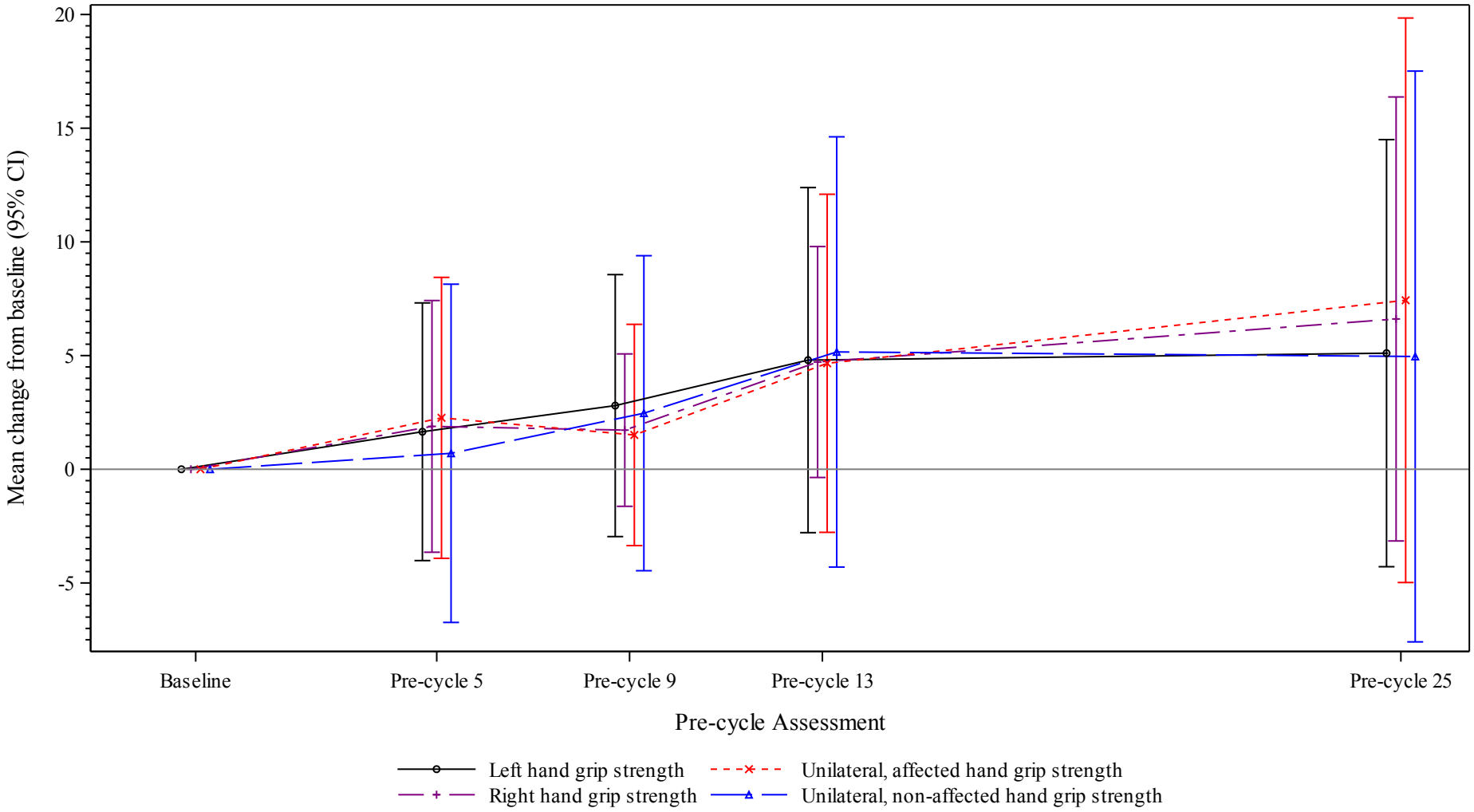
CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral patients omitted owing to insufficient data.

Figure 2.6.4.2.3 Mean change from baseline of grip strength test scores
PN status at enrollment = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.
Timepoints with <3 patients are omitted.
All patients omitted owing to insufficient data.

Figure 2.6.4.2.4 Mean change from baseline of grip strength test scores
PN status at enrollment = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 11



CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral patients omitted owing to insufficient data.

Figure 2.6.4.2.5 Mean change from baseline of grip strength test scores
PN status at enrollment = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.
Timepoints with <3 patients are omitted.
All patients omitted owing to insufficient data.

Table 2.7.1 Airway function test scores categories of change over time - percentage of patients with Improvement
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=16) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
FEV1 (Liters)	Overall (N=11)	Categories of change [d]			
		Improvement	8	72,7	39,0, 94,0
		No improvement	3	27,3	6,0, 61,0
R20 (Resistance)	Overall (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5

[a] Patients with airway PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 12 % for FEV1 (FEV0.75 for pre-school children), 20% for R20 (Resistance) based on REiNS literature (Plotkin et al., 2016).
Five patients with tracheostomy were excluded from the evaluations. NC - not calculated.

Table 2.7.1.1 Airway function test scores categories of change over time - percentage of patients with Improvement - Gender = Male (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=10) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
FEV1 (Liters)	Overall (N=6)	Categories of change [d]			
		Improvement	5	83,3	35,9, 99,6
		No improvement	1	16,7	0,4, 64,1
R20 (Resistance)	Overall (N=5)	Categories of change [d]			
		Improvement	1	20,0	0,5, 71,6
		No improvement	4	80,0	28,4, 99,5

[a] Patients with airway PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 12 % for FEV1 (FEV0.75 for pre-school children), 20% for R20 (Resistance) based on REiNS literature (Plotkin et al., 2016).
Five patients with tracheostomy were excluded from the evaluations. NC - not calculated.

Table 2.7.1.2 Airway function test scores categories of change over time - percentage of patients with Improvement - Gender = Female (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=6) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
FEV1 (Liters)	Overall (N=5)	Categories of change [d]			
		Improvement	3	60,0	14,7, 94,7
		No improvement	2	40,0	5,3, 85,3
R20 (Resistance)	Overall (N=5)	Categories of change [d]			
		Improvement	1	20,0	0,5, 71,6
		No improvement	4	80,0	28,4, 99,5

[a] Patients with airway PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 12 % for FEV1 (FEV0.75 for pre-school children), 20% for R20 (Resistance) based on REiNS literature (Plotkin et al., 2016).
Five patients with tracheostomy were excluded from the evaluations. NC - not calculated.

Table 2.7.1.3 Airway function test scores categories of change over time - percentage of patients with Improvement - PN status at enrollment = Progressive (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=4) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
FEV1 (Liters)	Overall (N=4)	Categories of change [d]			
		Improvement	4	100	39,8, 100
		No improvement	0	0	0, 60,2
R20 (Resistance)	Overall (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4

[a] Patients with airway PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 12 % for FEV1 (FEV0.75 for pre-school children), 20% for R20 (Resistance) based on REiNS literature (Plotkin et al., 2016).
Five patients with tracheostomy were excluded from the evaluations. NC - not calculated.

Table 2.7.1.4 Airway function test scores categories of change over time - percentage of patients with Improvement - PN status at enrollment = Non-progressive (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=5) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
FEV1 (Liters)	Overall (N=4)	Categories of change [d]			
		Improvement	2	50,0	6,8, 93,2
		No improvement	2	50,0	6,8, 93,2
R20 (Resistance)	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100

[a] Patients with airway PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 12 % for FEV1 (FEV0.75 for pre-school children), 20% for R20 (Resistance) based on REiNS literature (Plotkin et al., 2016).
Five patients with tracheostomy were excluded from the evaluations. NC - not calculated.

Table 2.7.1.5 Airway function test scores categories of change over time - percentage of patients with Improvement - PN status at enrollment = Unknown (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=7) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
FEV1 (Liters)	Overall (N=3)	Categories of change [d]			
		Improvement	2	66,7	9,4, 99,2
		No improvement	1	33,3	0,8, 90,6
R20 (Resistance)	Overall (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2

[a] Patients with airway PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 12 % for FEV1 (FEV0.75 for pre-school children), 20% for R20 (Resistance) based on REiNS literature (Plotkin et al., 2016).
Five patients with tracheostomy were excluded from the evaluations. NC - not calculated.

Table 2.7.2.1 Airway function test scores and change from baseline over time - Gender = Male
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=10) [a]											
		Absolute values						Change from baseline					
Parameter	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
FEV1 or FEV 0.75 (Liters)	Baseline (n=6)	1,760	1,1265	1,515	0,64	3,84	40,0							
	Pre-cycle 5 (n=6)	1,855	1,2513	1,705	0,67	4,09	40,0	6	0,095	0,1958	0,160	-0,27	0,25	40,0
	Pre-cycle 9 (n=6)	1,905	1,2260	1,675	0,79	4,09	40,0	6	0,145	0,1816	0,175	-0,19	0,34	40,0
	Pre-cycle 13 (n=6)	1,990	1,2057	1,700	0,72	4,08	40,0	6	0,230	0,1748	0,200	0,06	0,53	40,0
	Pre-cycle 25 (n=5)	2,438	1,1920	2,070	1,41	4,26	50,0	5	0,538	0,3209	0,420	0,20	0,97	50,0
R20 (Resistance)	Baseline (n=5)	3,868	0,8906	3,990	2,54	4,85	50,0							
	Pre-cycle 5 (n=5)	4,168	0,9221	4,400	3,15	5,43	50,0	5	0,300	0,5889	0,490	-0,45	1,00	50,0
	Pre-cycle 9 (n=5)	4,176	1,2148	4,470	2,55	5,63	50,0	5	0,308	0,5513	0,010	-0,14	1,20	50,0
	Pre-cycle 13 (n=5)	3,698	0,9940	3,640	2,54	4,78	50,0	5	-0,170	0,3641	-0,240	-0,61	0,35	50,0
	Pre-cycle 25 (n=4)	3,573	0,8701	3,580	2,51	4,62	60,0	4	-0,265	0,5832	-0,065	-1,12	0,19	60,0
Apnea-hypopnea Index (AHI, events / hour)	Baseline (n=9)	1,044	1,1706	0,400	0,20	3,20	10,0							
	Pre-cycle 5 (n=4)	3,275	4,5169	1,600	0,00	9,90	60,0	4	1,325	4,8624	-0,450	-2,30	8,50	60,0
	Pre-cycle 9 (n=4)	1,375	1,6132	1,200	0,00	3,10	60,0	4	0,175	1,8768	-0,400	-1,40	2,90	60,0
	Pre-cycle 13 (n=8)	2,313	2,7168	1,250	0,70	8,60	20,0	8	1,188	3,3736	0,350	-2,00	8,40	20,0
	Pre-cycle 25 (n=3)	1,600	1,4731	1,300	0,30	3,20	70,0	3	-0,567	1,7214	0,000	-2,50	0,80	70,0

[a] Patients with airway PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.
Five patients with tracheostomy were excluded from the evaluations.

Table 2.7.2.2 Airway function test scores and change from baseline over time - Gender = Female
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=6) [a]											
		Absolute values						Change from baseline					
Parameter	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
FEV1 or FEV 0.75 (Liters)	Baseline (n=5)	1,586	1,0001	1,320	0,69	2,96	16,7							
	Pre-cycle 5 (n=5)	1,650	0,9534	1,430	0,64	2,79	16,7	5	0,064	0,1740	0,110	-0,17	0,23	16,7
	Pre-cycle 9 (n=5)	1,712	1,0055	1,420	0,57	2,86	16,7	5	0,126	0,2486	0,100	-0,13	0,40	16,7
	Pre-cycle 13 (n=5)	1,884	0,9664	1,360	0,93	3,12	16,7	5	0,298	0,2675	0,230	-0,02	0,67	16,7
	Pre-cycle 25 (n=4)	2,025	0,9507	2,085	1,02	2,91	33,3	4	0,373	0,4196	0,485	-0,20	0,72	33,3
	Pre-cycle 37 (n=1)	NC	NC	NC	1,35	1,35	83,3	1	NC	NC	NC	0,66	0,66	83,3
R20 (Resistance)	Baseline (n=5)	3,864	1,2003	3,380	2,80	5,81	16,7							
	Pre-cycle 5 (n=5)	4,240	1,9592	3,600	2,68	7,64	16,7	5	0,376	0,9759	0,500	-0,58	1,83	16,7
	Pre-cycle 9 (n=5)	4,206	1,6962	3,790	2,98	7,16	16,7	5	0,342	0,8156	-0,170	-0,39	1,35	16,7
	Pre-cycle 13 (n=5)	3,876	0,9368	3,480	3,00	5,17	16,7	5	0,012	1,0546	-0,150	-0,99	1,74	16,7
	Pre-cycle 25 (n=4)	3,928	1,3862	3,430	2,88	5,97	33,3	4	-0,058	0,5979	-0,055	-0,76	0,64	33,3
	Pre-cycle 37 (n=1)	NC	NC	NC	3,45	3,45	83,3	1	NC	NC	NC	0,65	0,65	83,3
Apnea-hypopnea Index (AHI, events / hour)	Baseline (n=5)	2,060	1,7344	1,800	0,40	4,90	16,7							
	Pre-cycle 5 (n=3)	1,467	1,5044	0,700	0,50	3,20	50,0	3	-1,233	0,6429	-1,500	-1,70	-0,50	50,0
	Pre-cycle 9 (n=2)	NC	NC	NC	0,50	2,60	66,7	2	NC	NC	NC	-2,30	-1,70	66,7
	Pre-cycle 13 (n=5)	1,080	0,7259	1,000	0,00	1,80	16,7	5	-0,980	1,9409	-1,000	-3,90	1,40	16,7
	Pre-cycle 25 (n=3)	2,667	1,8339	3,300	0,60	4,10	50,0	3	0,300	1,1533	0,200	-0,80	1,50	50,0

[a] Patients with airway PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.
Five patients with tracheostomy were excluded from the evaluations.

Table 2.7.2.3 Airway function test scores and change from baseline over time - PN status at enrollment = Progressive
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=4) [a]											
		Absolute values						Change from baseline					
Parameter	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
FEV1 or FEV 0.75 (Liters)	Baseline (n=4)	1,195	0,4394	1,175	0,69	1,74	0,0							
	Pre-cycle 5 (n=4)	1,275	0,5468	1,165	0,79	1,98	0,0	4	0,080	0,2371	0,175	-0,27	0,24	0,0
	Pre-cycle 9 (n=4)	1,318	0,4718	1,230	0,87	1,94	0,0	4	0,123	0,2310	0,160	-0,19	0,36	0,0
	Pre-cycle 13 (n=4)	1,495	0,3755	1,355	1,22	2,05	0,0	4	0,300	0,2672	0,235	0,06	0,67	0,0
	Pre-cycle 25 (n=3)	1,657	0,3602	1,490	1,41	2,07	25,0	3	0,417	0,2706	0,330	0,20	0,72	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	1,35	1,35	75,0	1	NC	NC	NC	0,66	0,66	75,0
R20 (Resistance)	Baseline (n=4)	3,793	0,8585	3,760	2,80	4,85	0,0							
	Pre-cycle 5 (n=4)	3,890	0,6368	3,890	3,30	4,48	0,0	4	0,098	0,4751	0,170	-0,45	0,50	0,0
	Pre-cycle 9 (n=4)	4,150	0,6373	4,185	3,39	4,84	0,0	4	0,358	0,5624	0,235	-0,14	1,10	0,0
	Pre-cycle 13 (n=4)	3,928	0,8039	4,090	2,92	4,61	0,0	4	0,135	1,0812	-0,295	-0,61	1,74	0,0
	Pre-cycle 25 (n=3)	3,533	0,1704	3,440	3,43	3,73	25,0	3	-0,193	0,8837	-0,100	-1,12	0,64	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	3,45	3,45	75,0	1	NC	NC	NC	0,65	0,65	75,0
Apnea-hypopnea Index (AHI, events / hour)	Baseline (n=4)	1,350	1,1733	1,150	0,30	2,80	0,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	2,30	2,30	75,0	1	NC	NC	NC	-0,50	-0,50	75,0
	Pre-cycle 9 (n=1)	NC	NC	NC	2,40	2,40	75,0	1	NC	NC	NC	-0,40	-0,40	75,0
	Pre-cycle 13 (n=4)	1,175	0,4272	1,150	0,70	1,70	0,0	4	-0,175	1,1442	0,150	-1,80	0,80	0,0
	Pre-cycle 25 (n=3)	1,633	1,5275	1,300	0,30	3,30	25,0	3	-0,067	2,1362	0,800	-2,50	1,50	25,0

[a] Patients with airway PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.
Five patients with tracheostomy were excluded from the evaluations.

Table 2.7.2.4 Airway function test scores and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=5) [a]											
		Absolute values						Change from baseline					
Parameter	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
FEV1 or FEV 0.75 (Liters)	Baseline (n=4)	2,358	1,3718	2,475	0,64	3,84	20,0							
	Pre-cycle 5 (n=4)	2,430	1,4201	2,480	0,67	4,09	20,0	4	0,073	0,1859	0,105	-0,17	0,25	20,0
	Pre-cycle 9 (n=4)	2,518	1,3674	2,595	0,79	4,09	20,0	4	0,160	0,1899	0,200	-0,10	0,34	20,0
	Pre-cycle 13 (n=4)	2,610	1,4144	2,820	0,72	4,08	20,0	4	0,253	0,1962	0,200	0,08	0,53	20,0
	Pre-cycle 25 (n=4)	2,848	1,1665	2,860	1,41	4,26	20,0	4	0,490	0,5131	0,595	-0,20	0,97	20,0
R20 (Resistance)	Baseline (n=3)	3,373	0,9646	3,150	2,54	4,43	40,0							
	Pre-cycle 5 (n=3)	3,753	1,4709	3,150	2,68	5,43	40,0	3	0,380	0,7615	0,610	-0,47	1,00	40,0
	Pre-cycle 9 (n=3)	3,720	1,6680	2,980	2,55	5,63	40,0	3	0,347	0,7445	0,010	-0,17	1,20	40,0
	Pre-cycle 13 (n=3)	3,440	1,1830	3,000	2,54	4,78	40,0	3	0,067	0,2566	0,000	-0,15	0,35	40,0
	Pre-cycle 25 (n=3)	3,337	1,1267	2,880	2,51	4,62	40,0	3	-0,037	0,2301	-0,030	-0,27	0,19	40,0
Apnea-hypopnea Index (AHI, events / hour)	Baseline (n=5)	1,480	1,2538	1,400	0,20	3,20	0,0							
	Pre-cycle 5 (n=4)	2,875	4,6992	0,800	0,00	9,90	20,0	4	1,075	5,0109	-0,950	-2,30	8,50	20,0
	Pre-cycle 9 (n=3)	0,167	0,2887	0,000	0,00	0,50	40,0	3	-1,167	0,6807	-1,400	-1,70	-0,40	40,0
	Pre-cycle 13 (n=5)	1,560	1,2198	1,200	0,70	3,70	0,0	5	0,080	2,1218	-0,100	-2,00	3,50	0,0
	Pre-cycle 25 (n=1)	NC	NC	NC	3,20	3,20	80,0	1	NC	NC	NC	0,00	0,00	80,0

[a] Patients with airway PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.
Five patients with tracheostomy were excluded from the evaluations.

Table 2.7.2.5 Airway function test scores and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=7) [a]											
		Absolute values						Change from baseline					
Parameter	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
FEV1 or FEV 0.75 (Liters)	Baseline (n=3)	1,427	0,7855	1,320	0,70	2,26	57,1							
	Pre-cycle 5 (n=3)	1,520	0,9283	1,430	0,64	2,49	57,1	3	0,093	0,1457	0,110	-0,06	0,23	57,1
	Pre-cycle 9 (n=3)	1,550	1,0510	1,420	0,57	2,66	57,1	3	0,123	0,2658	0,100	-0,13	0,40	57,1
	Pre-cycle 13 (n=3)	1,647	0,9393	1,300	0,93	2,71	57,1	3	0,220	0,2352	0,230	-0,02	0,45	57,1
	Pre-cycle 25 (n=2)	NC	NC	NC	1,02	2,91	71,4	2	NC	NC	NC	0,32	0,65	71,4
R20 (Resistance)	Baseline (n=3)	4,457	1,2384	4,180	3,38	5,81	57,1							
	Pre-cycle 5 (n=3)	5,073	2,2309	3,980	3,60	7,64	57,1	3	0,617	1,2051	0,600	-0,58	1,83	57,1
	Pre-cycle 9 (n=3)	4,717	2,1365	3,790	3,20	7,16	57,1	3	0,260	0,9498	-0,180	-0,39	1,35	57,1
	Pre-cycle 13 (n=3)	3,947	1,0693	3,480	3,19	5,17	57,1	3	-0,510	0,5565	-0,640	-0,99	0,10	57,1
	Pre-cycle 25 (n=2)	NC	NC	NC	3,42	5,97	71,4	2	NC	NC	NC	-0,76	0,16	71,4
Apnea-hypopnea Index (AHI, events / hour)	Baseline (n=5)	1,380	1,9905	0,400	0,20	4,90	28,6							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,50	3,20	71,4	2	NC	NC	NC	-1,70	-0,50	71,4
	Pre-cycle 9 (n=2)	NC	NC	NC	2,60	3,10	71,4	2	NC	NC	NC	-2,30	2,90	71,4
	Pre-cycle 13 (n=4)	2,850	3,9034	1,400	0,00	8,60	42,9	4	1,225	5,2513	0,200	-3,90	8,40	42,9
	Pre-cycle 25 (n=2)	NC	NC	NC	0,60	4,10	71,4	2	NC	NC	NC	-0,80	0,20	71,4

[a] Patients with airway PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.
Five patients with tracheostomy were excluded from the evaluations.

Table 2.7.3.1 Airway function test percentage change from baseline over time - Gender = Male
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=10) [a] Percentage change from baseline						
Parameter	Time point	n	Mean	SD	Median	Min	Max	%missing [b]
FEV1 or FEV 0.75 (Liters)	Pre-cycle 5	6	3,24	14,423	7,78	-25	14	40,0
	Pre-cycle 9	6	8,32	14,202	10,40	-18	23	40,0
	Pre-cycle 13	6	13,82	8,061	13,80	5	27	40,0
	Pre-cycle 25	5	42,89	45,749	18,97	11	120	50,0
R20 (Resistance)	Pre-cycle 5	5	9,07	15,249	12,28	-9	24	50,0
	Pre-cycle 9	5	7,07	12,695	0,39	-4	27	50,0
	Pre-cycle 13	5	-4,62	9,431	-4,95	-17	8	50,0
	Pre-cycle 25	4	-5,70	11,985	-2,01	-23	4	60,0

[a] Patients with airway PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.
Five patients with tracheostomy were excluded from the evaluations.

Table 2.7.3.2 Airway function test percentage change from baseline over time - Gender = Female
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=6) [a] Percentage change from baseline						
Parameter	Time point	n	Mean	SD	Median	Min	Max	%missing [b]
FEV1 or FEV 0.75 (Liters)	Pre-cycle 5	5	6,93	15,539	8,33	-9	30	16,7
	Pre-cycle 9	5	11,10	26,613	7,58	-19	52	16,7
	Pre-cycle 13	5	30,75	39,395	19,91	-2	97	16,7
	Pre-cycle 25	4	43,02	46,366	37,24	-7	104	33,3
	Pre-cycle 37	1	NC	NC	NC	96	96	83,3
R20 (Resistance)	Pre-cycle 5	5	7,66	20,903	17,75	-15	31	16,7
	Pre-cycle 9	5	8,49	21,605	-5,33	-9	39	16,7
	Pre-cycle 13	5	5,13	33,332	-4,76	-24	62	16,7
	Pre-cycle 25	4	-0,29	17,642	-2,91	-18	23	33,3
	Pre-cycle 37	1	NC	NC	NC	23	23	83,3

[a] Patients with airway PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.
Five patients with tracheostomy were excluded from the evaluations.

Table 2.7.3.3 Airway function test percentage change from baseline over time - PN status at enrollment = Progressive
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=4) [a] Percentage change from baseline						
Parameter	Time point	n	Mean	SD	Median	Min	Max	%missing [b]
FEV1 or FEV 0.75 (Liters)	Pre-cycle 5	4	7,40	23,551	12,32	-25	30	0,0
	Pre-cycle 9	4	13,76	28,894	10,40	-18	52	0,0
	Pre-cycle 13	4	33,67	42,669	16,46	5	97	0,0
	Pre-cycle 25	3	46,27	50,325	18,97	16	104	25,0
	Pre-cycle 37	1	NC	NC	NC	96	96	75,0
R20 (Resistance)	Pre-cycle 5	4	4,15	12,973	4,02	-9	18	0,0
	Pre-cycle 9	4	11,79	19,564	5,91	-4	39	0,0
	Pre-cycle 13	4	7,79	36,603	-6,86	-17	62	0,0
	Pre-cycle 25	3	-1,02	23,028	-2,83	-23	23	25,0
	Pre-cycle 37	1	NC	NC	NC	23	23	75,0

[a] Patients with airway PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.
Five patients with tracheostomy were excluded from the evaluations.

Table 2.7.3.4 Airway function test percentage change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=5) [a] Percentage change from baseline						
Parameter	Time point	n	Mean	SD	Median	Min	Max	%missing [b]
FEV1 or FEV 0.75 (Liters)	Pre-cycle 5	4	3,62	6,496	5,60	-6	9	20,0
	Pre-cycle 9	4	10,91	11,812	11,80	-3	23	20,0
	Pre-cycle 13	4	12,70	9,815	9,38	5	27	20,0
	Pre-cycle 25	4	43,31	56,313	29,84	-7	120	20,0
R20 (Resistance)	Pre-cycle 5	3	10,56	22,075	22,57	-15	24	40,0
	Pre-cycle 9	3	7,36	17,327	0,39	-5	27	40,0
	Pre-cycle 13	3	1,05	6,396	0,00	-5	8	40,0
	Pre-cycle 25	3	-1,82	6,454	-1,18	-9	4	40,0

[a] Patients with airway PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.
Five patients with tracheostomy were excluded from the evaluations.

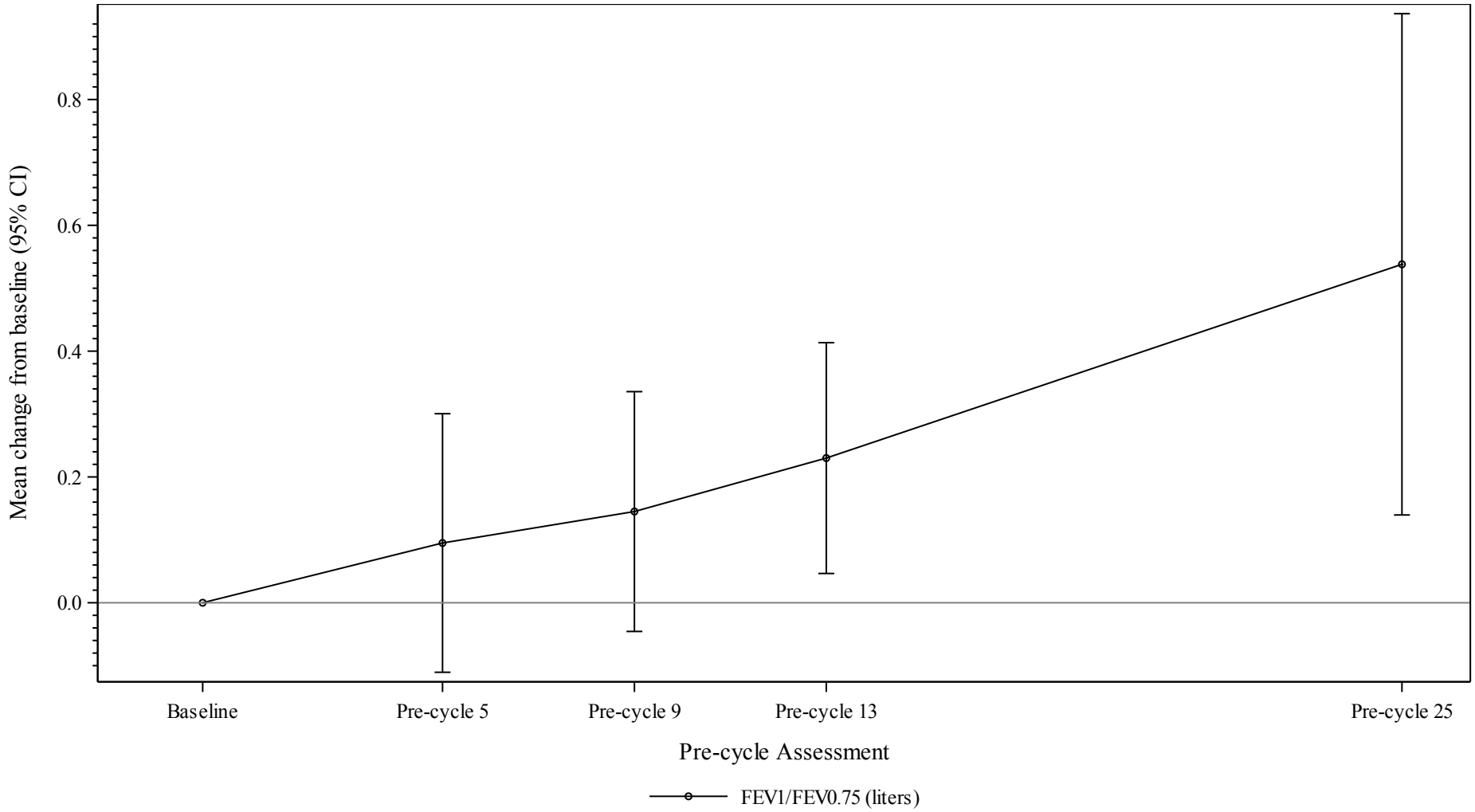
Table 2.7.3.5 Airway function test percentage change from baseline over time - PN status at enrollment = Unknown
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=7) [a] Percentage change from baseline						
Parameter	Time point	n	Mean	SD	Median	Min	Max	%missing [b]
FEV1 or FEV 0.75 (Liters)	Pre-cycle 5	3	3,31	10,333	8,33	-9	10	57,1
	Pre-cycle 9	3	2,23	18,716	7,58	-19	18	57,1
	Pre-cycle 13	3	17,08	17,360	19,91	-2	33	57,1
	Pre-cycle 25	2	NC	NC	NC	29	46	71,4
R20 (Resistance)	Pre-cycle 5	3	11,79	23,266	17,75	-14	31	57,1
	Pre-cycle 9	3	2,86	17,759	-5,33	-9	23	57,1
	Pre-cycle 13	3	-10,58	13,327	-11,02	-24	3	57,1
	Pre-cycle 25	2	NC	NC	NC	-18	3	71,4

[a] Patients with airway PN-related morbidity.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.1 Mean change from baseline of FEV - Gender = Male
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

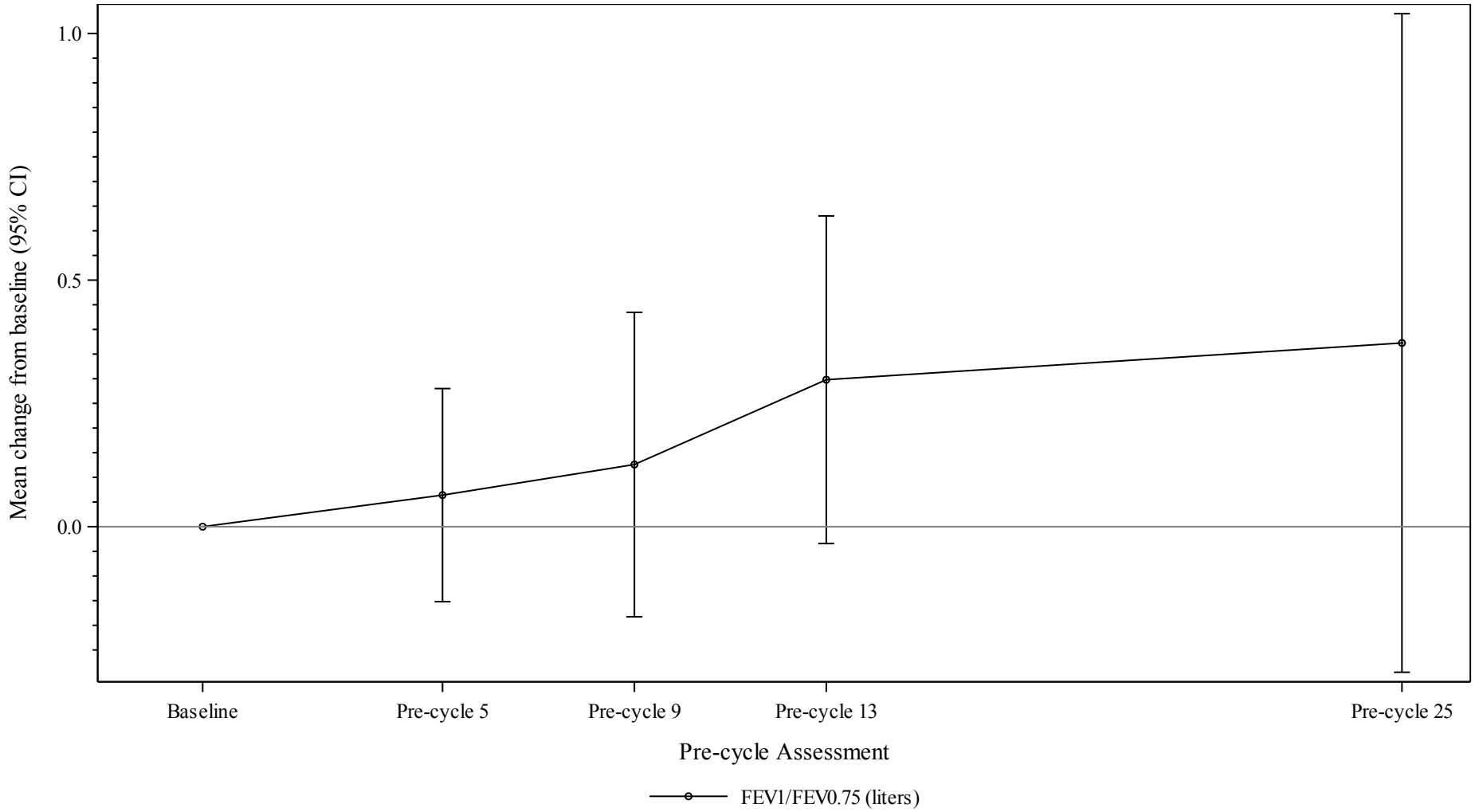
N = 10



FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.2 Mean change from baseline of FEV - Gender = Female
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

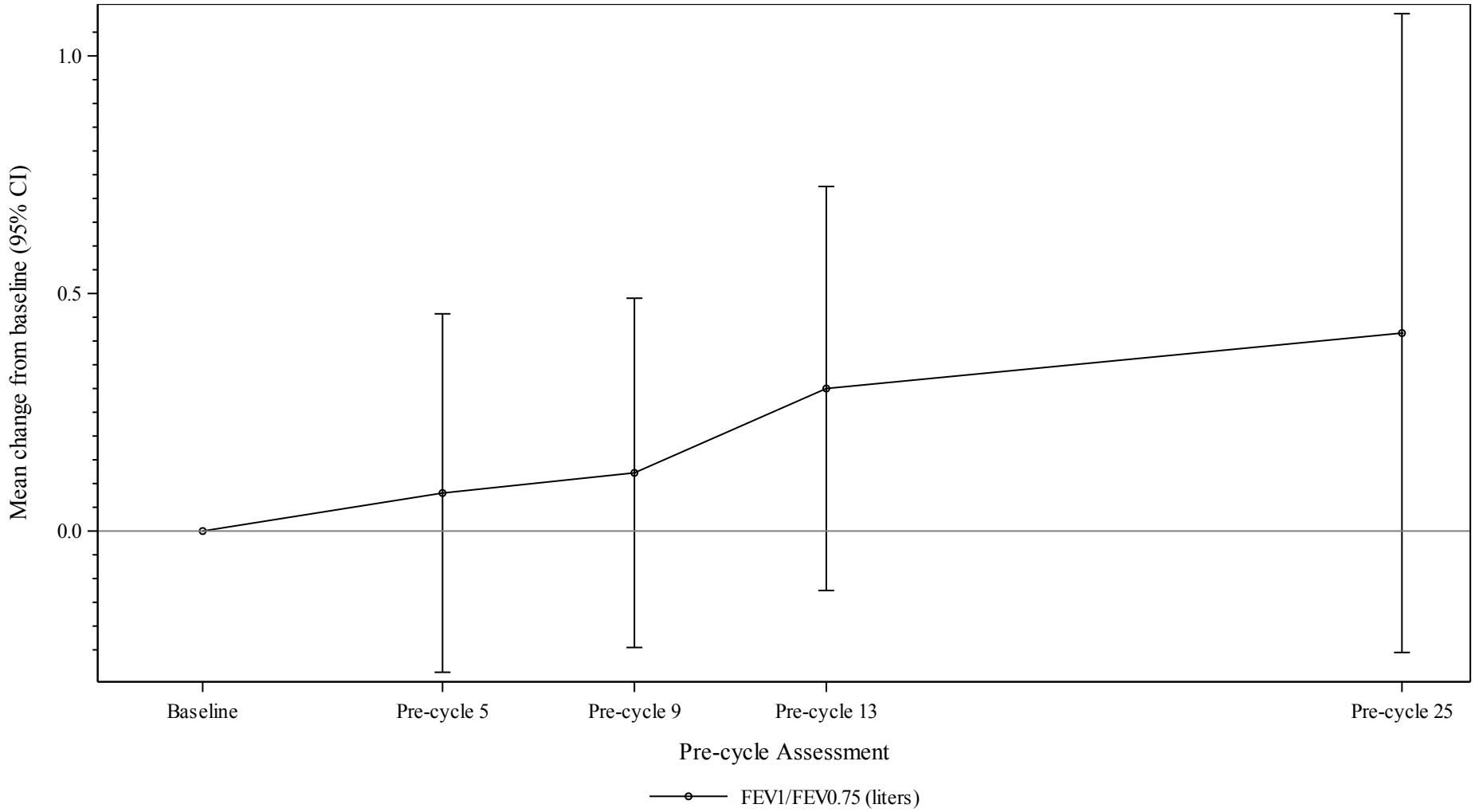
N = 6



FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.3 Mean change from baseline of FEV - PN status at enrollment = Progressive
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

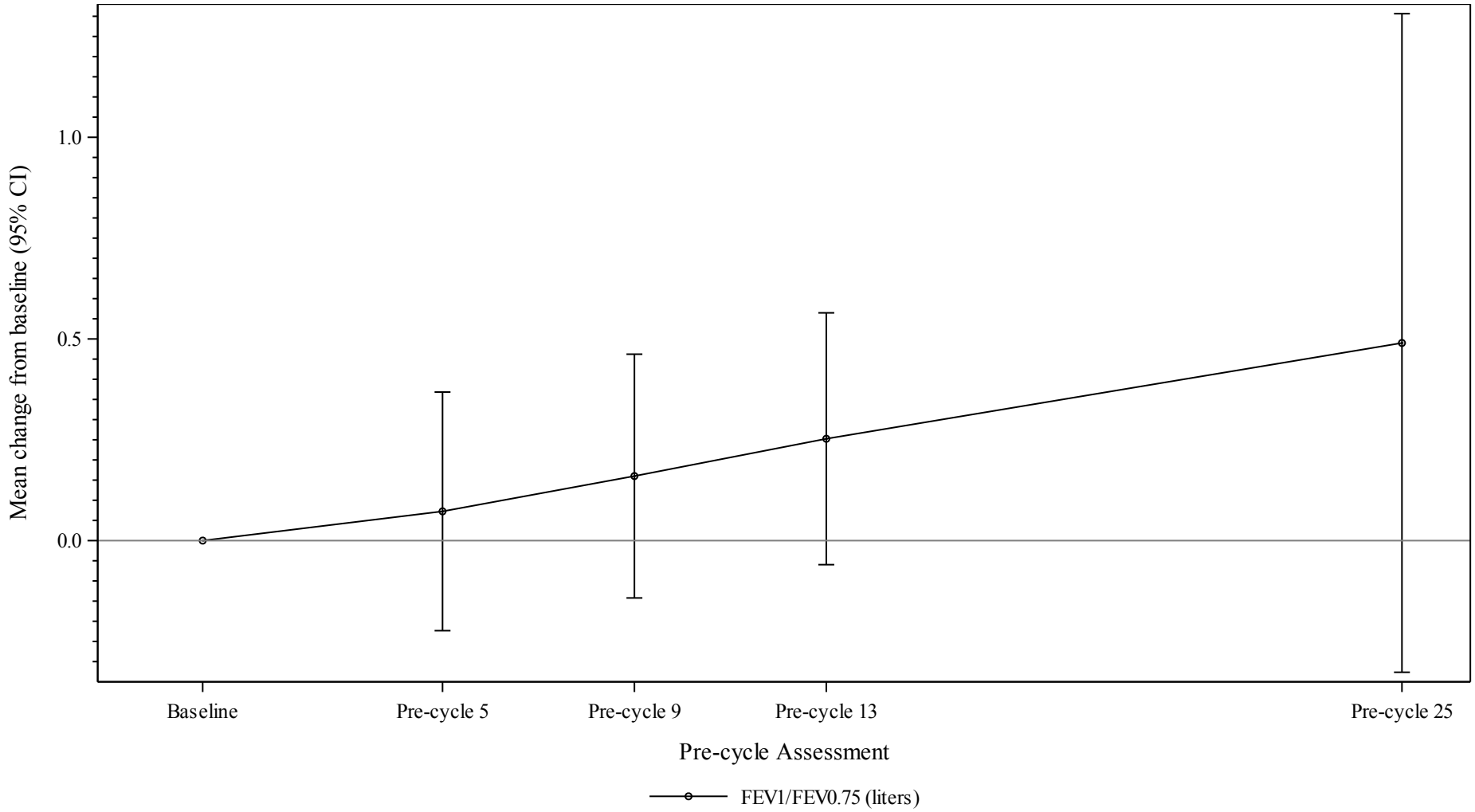
N = 4



FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.4 Mean change from baseline of FEV - PN status at enrollment = Non-progressive
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

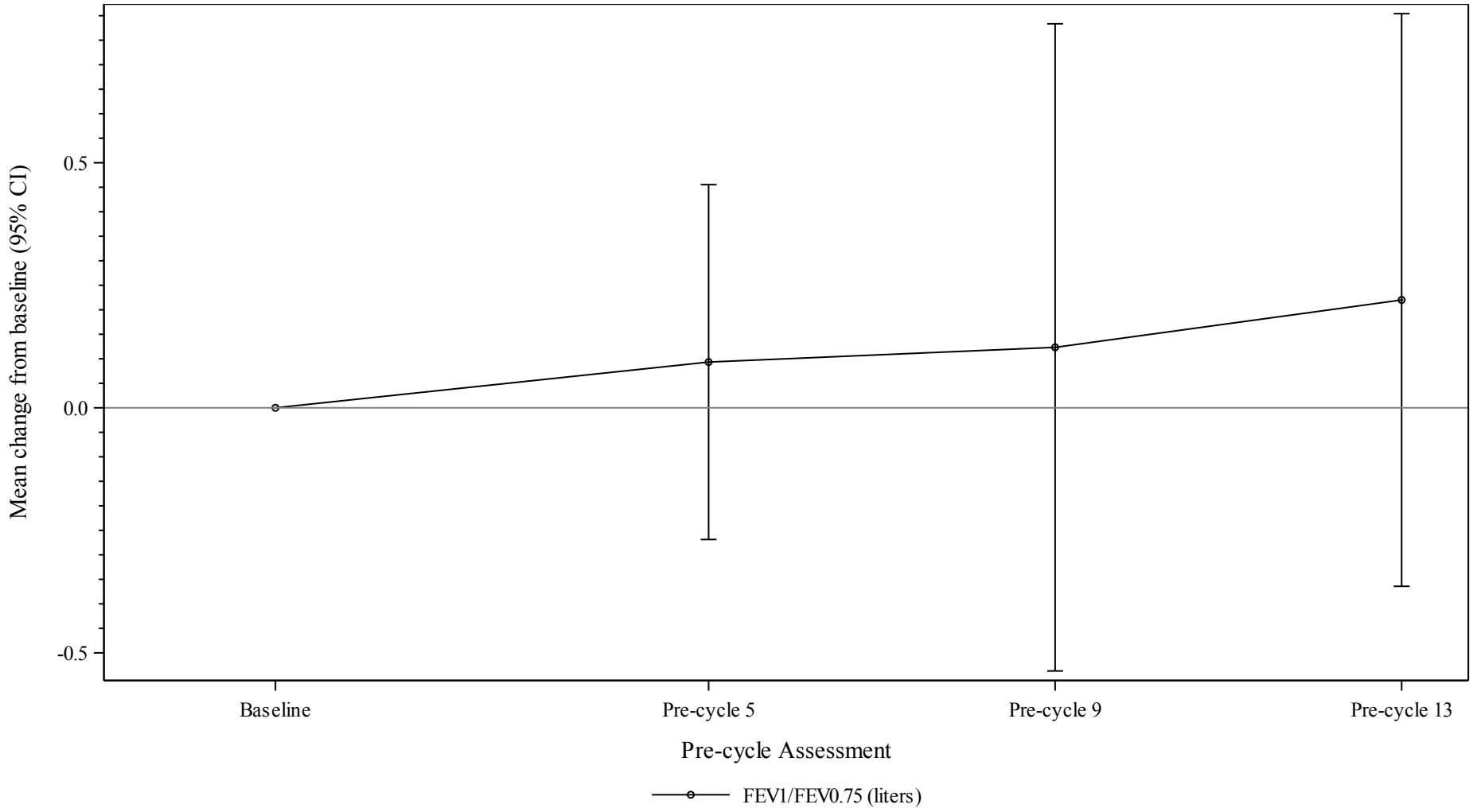
N = 5



FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.5 Mean change from baseline of FEV - PN status at enrollment = Unknown
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

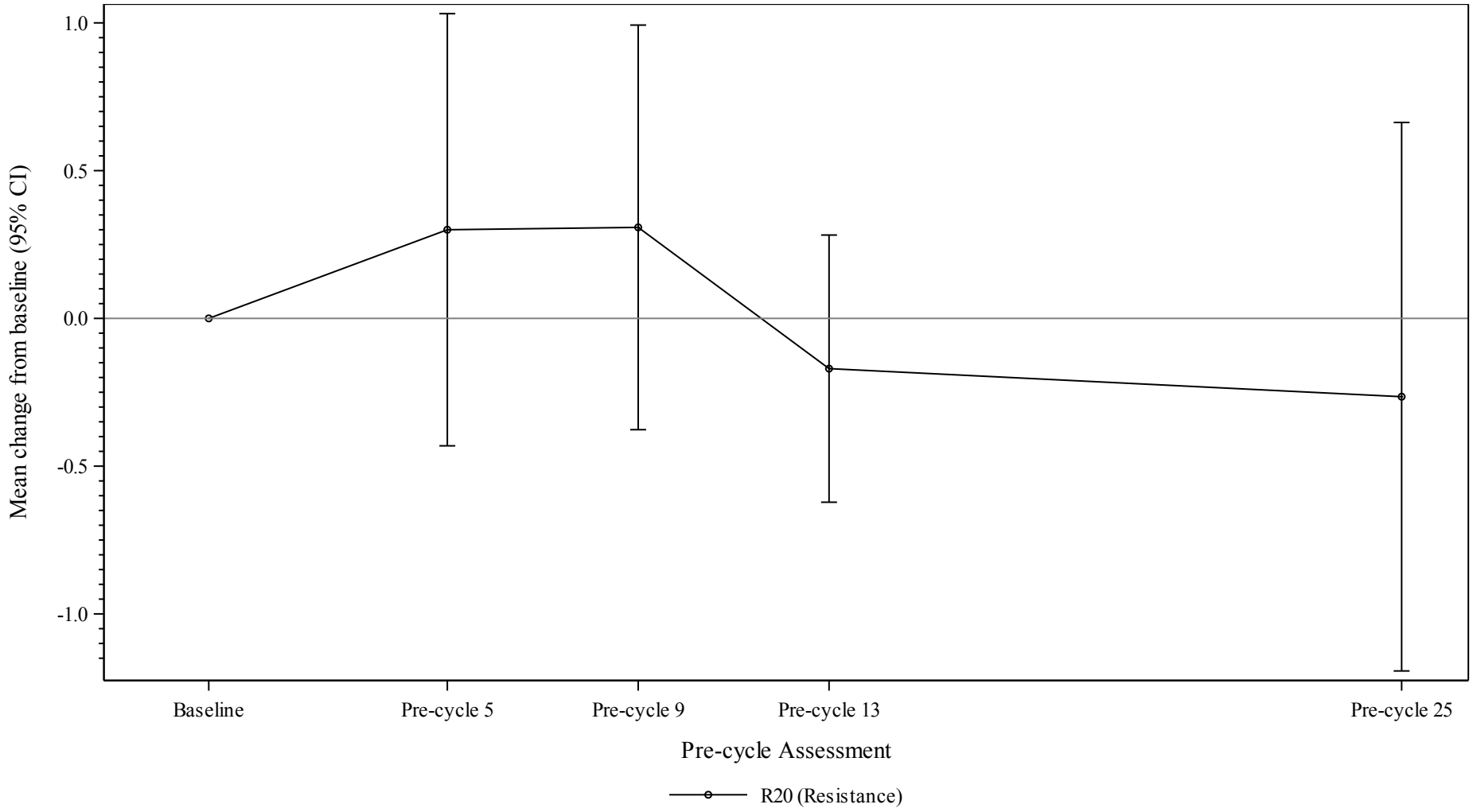
N = 7



FEV1 measurements are used when patients have both FEV1 and FEV0.75 measurements at an analysis visit.
CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.6 Mean change from baseline of R20 - Gender = Male
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

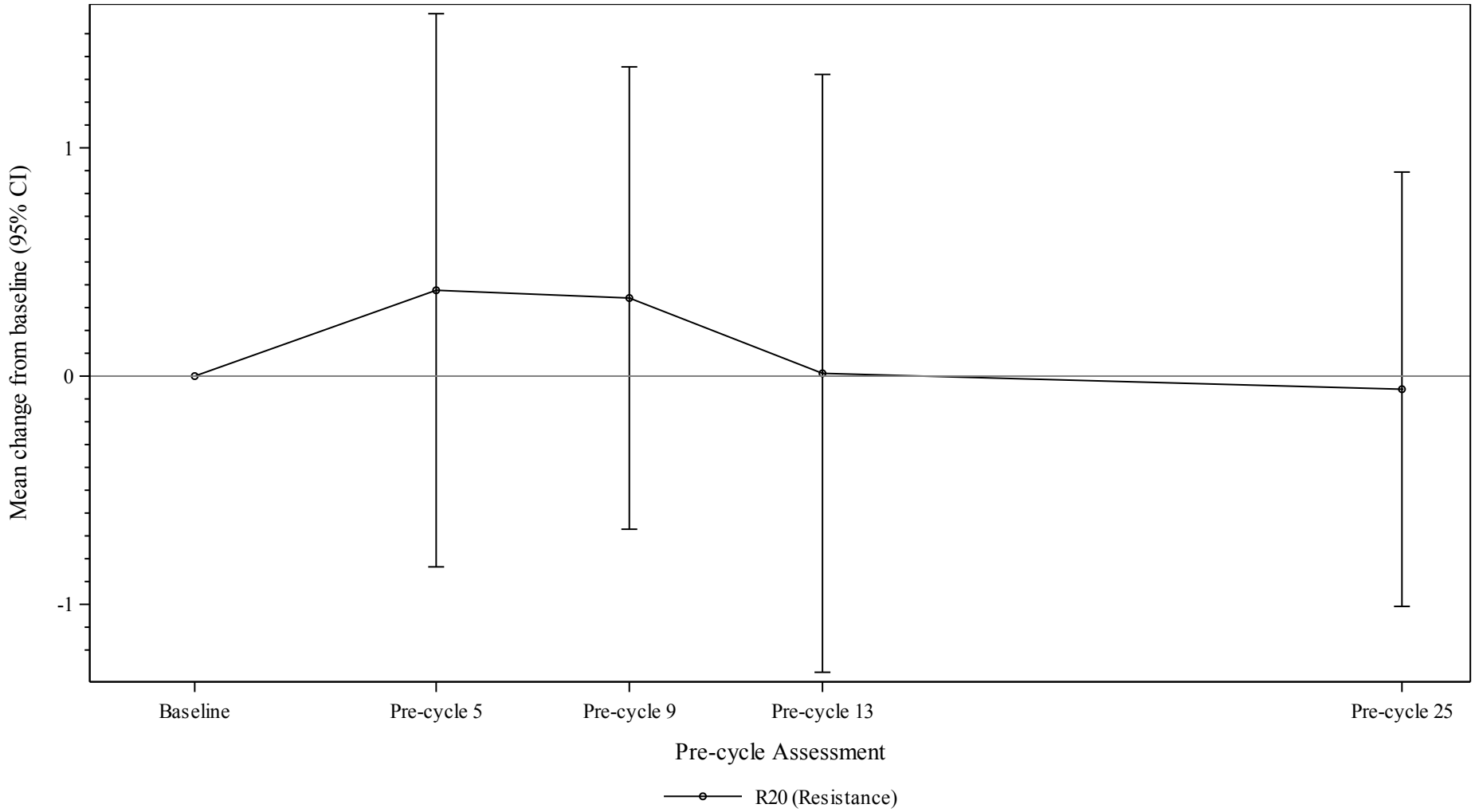
N = 10



CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.7 Mean change from baseline of R20 - Gender = Female
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

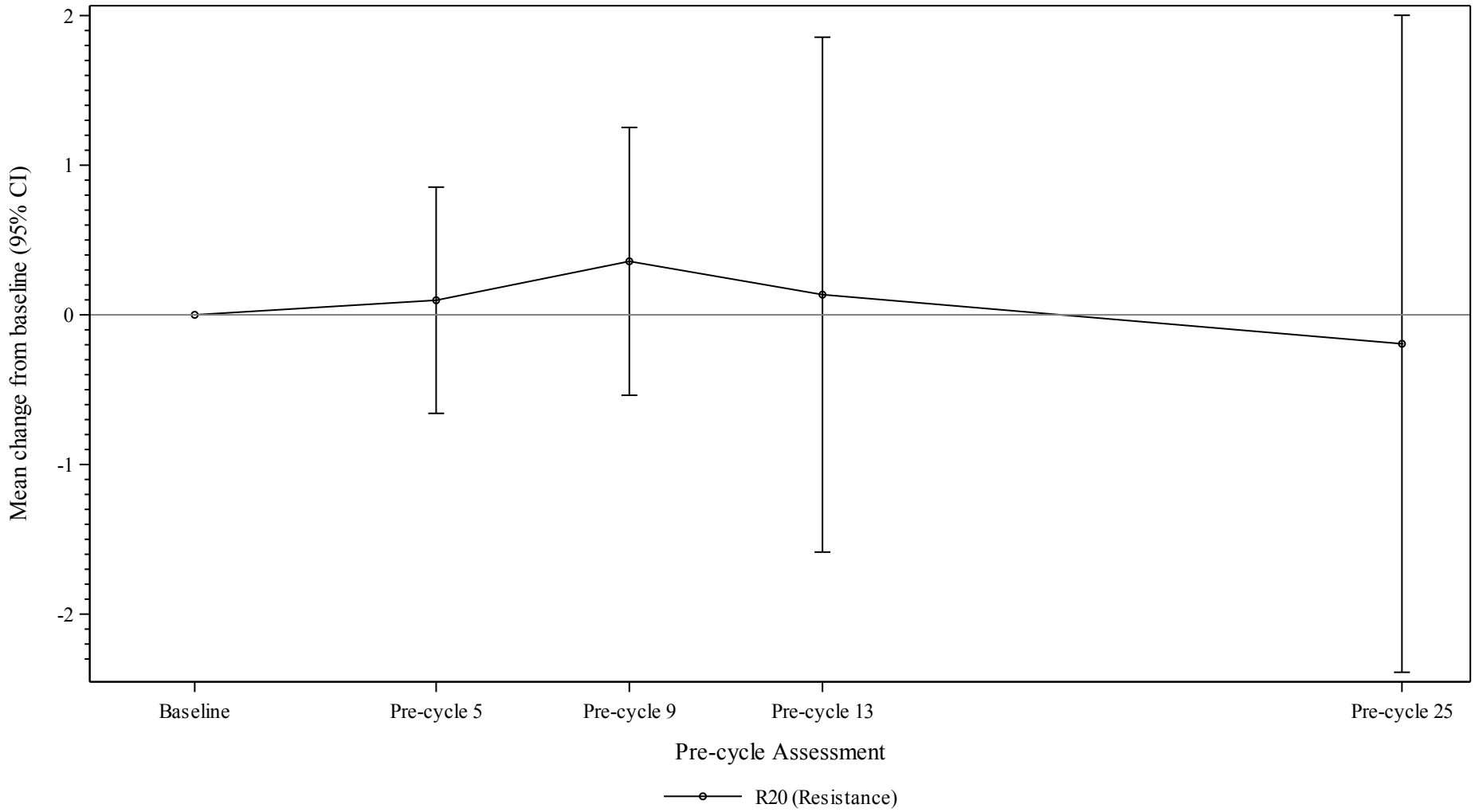
N = 6



CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.8 Mean change from baseline of R20 - PN status at enrollment = Progressive
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

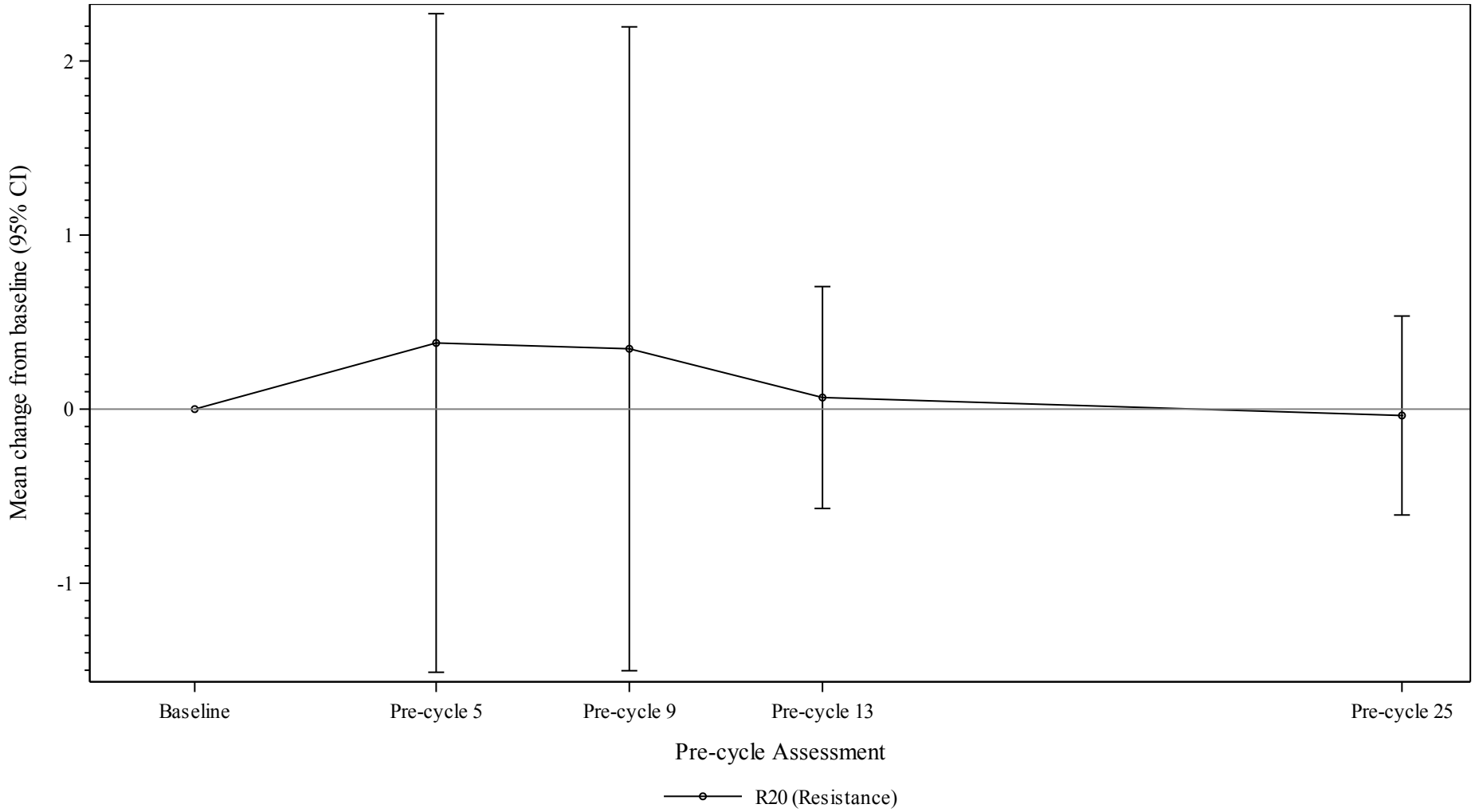
N = 4



CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.9 Mean change from baseline of R20 - PN status at enrollment = Non-progressive
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

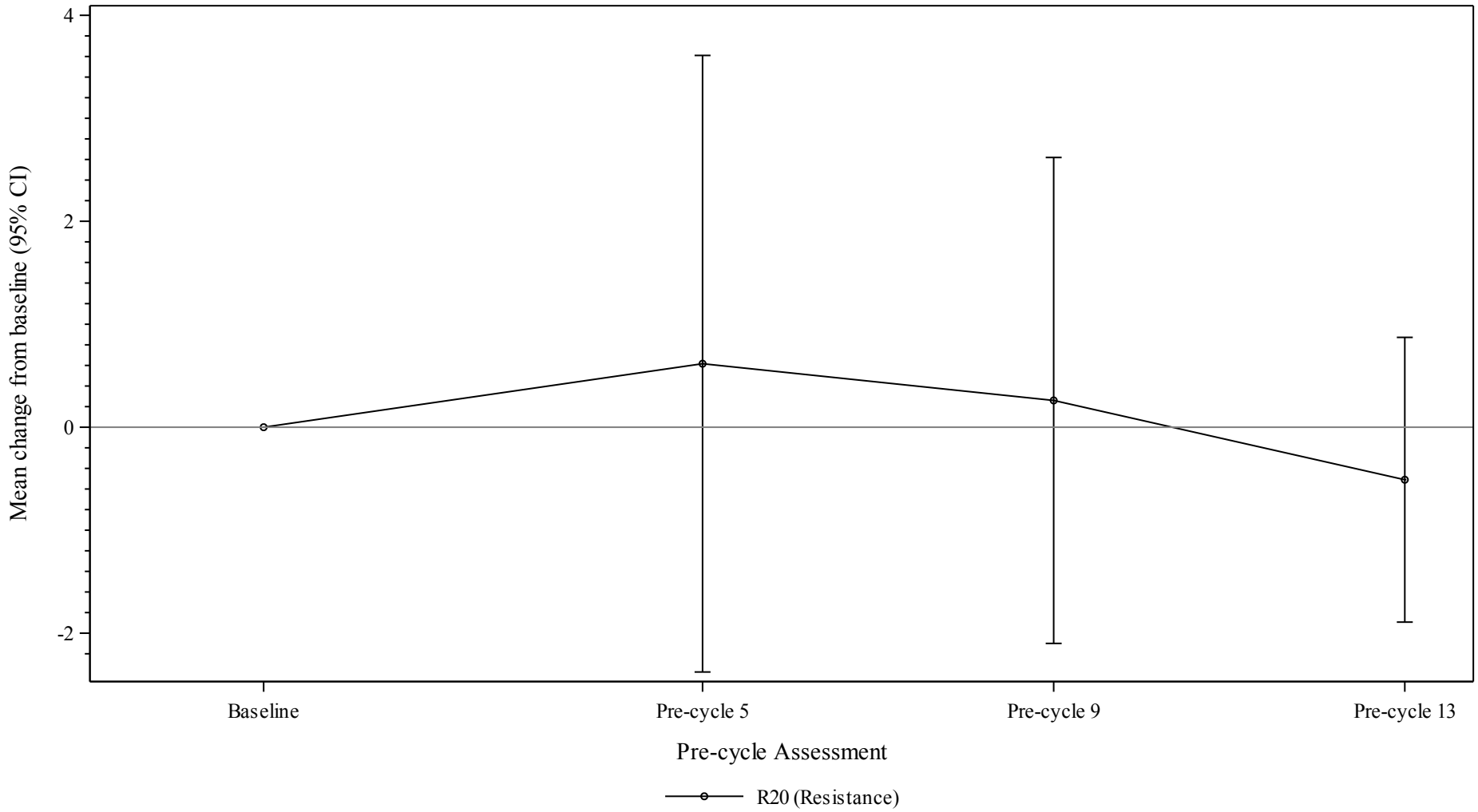
N = 5



CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.10 Mean change from baseline of R20 - PN status at enrollment = Unknown
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

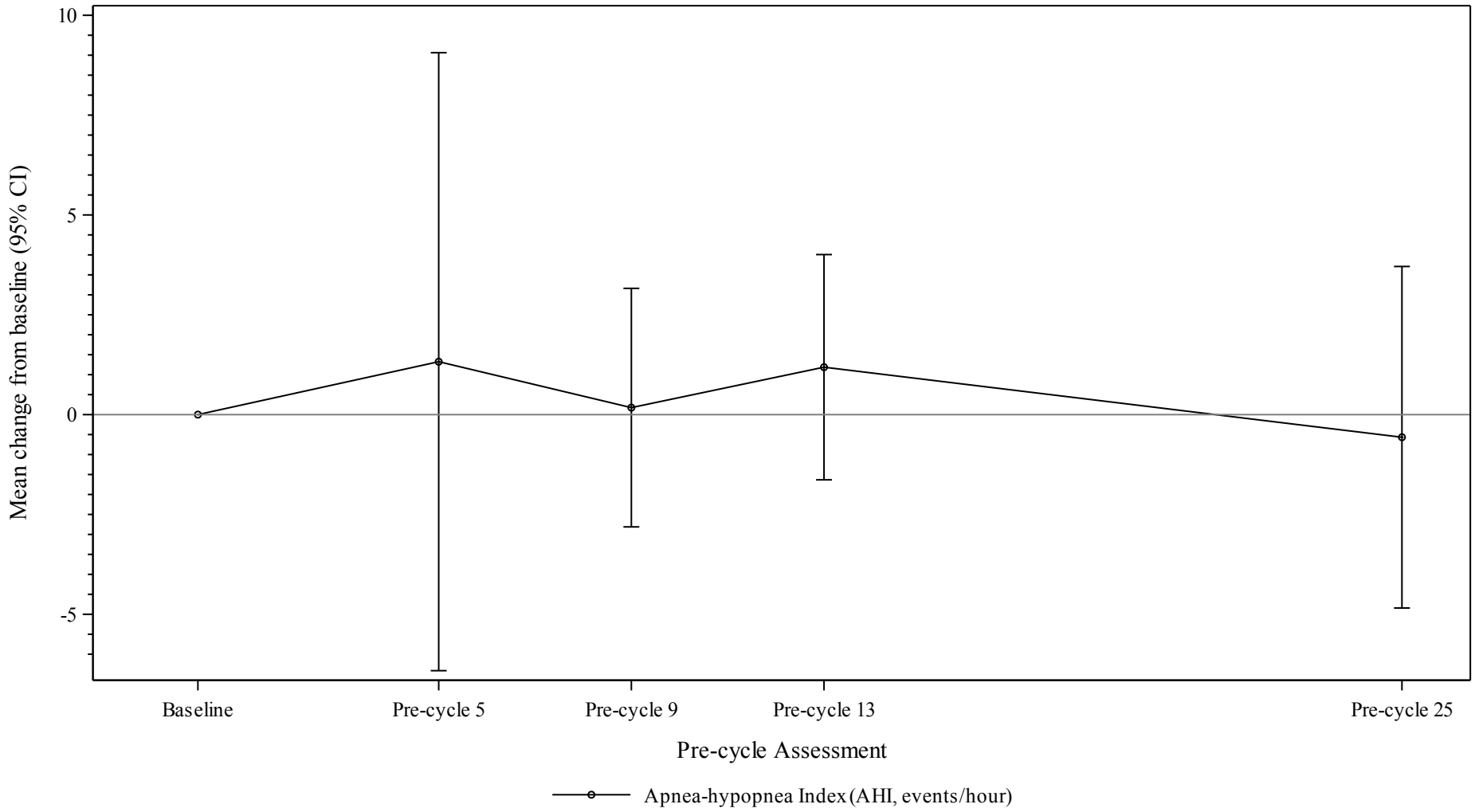
N = 7



CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.11 Mean change from baseline of Apnea-hypopnea Index - Gender = Male
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

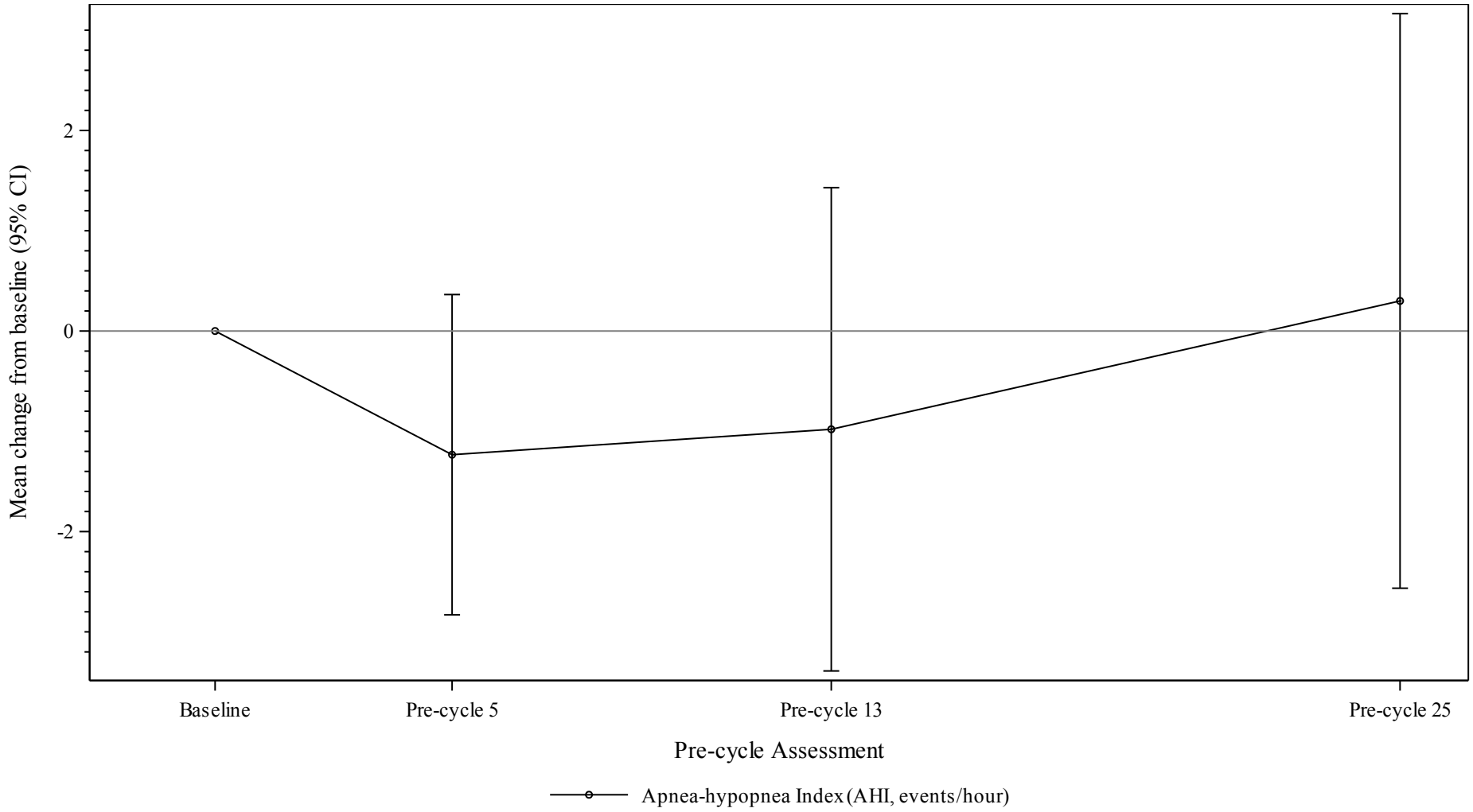
N = 10



CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.12 Mean change from baseline of Apnea-hypopnea Index Gender = Female
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

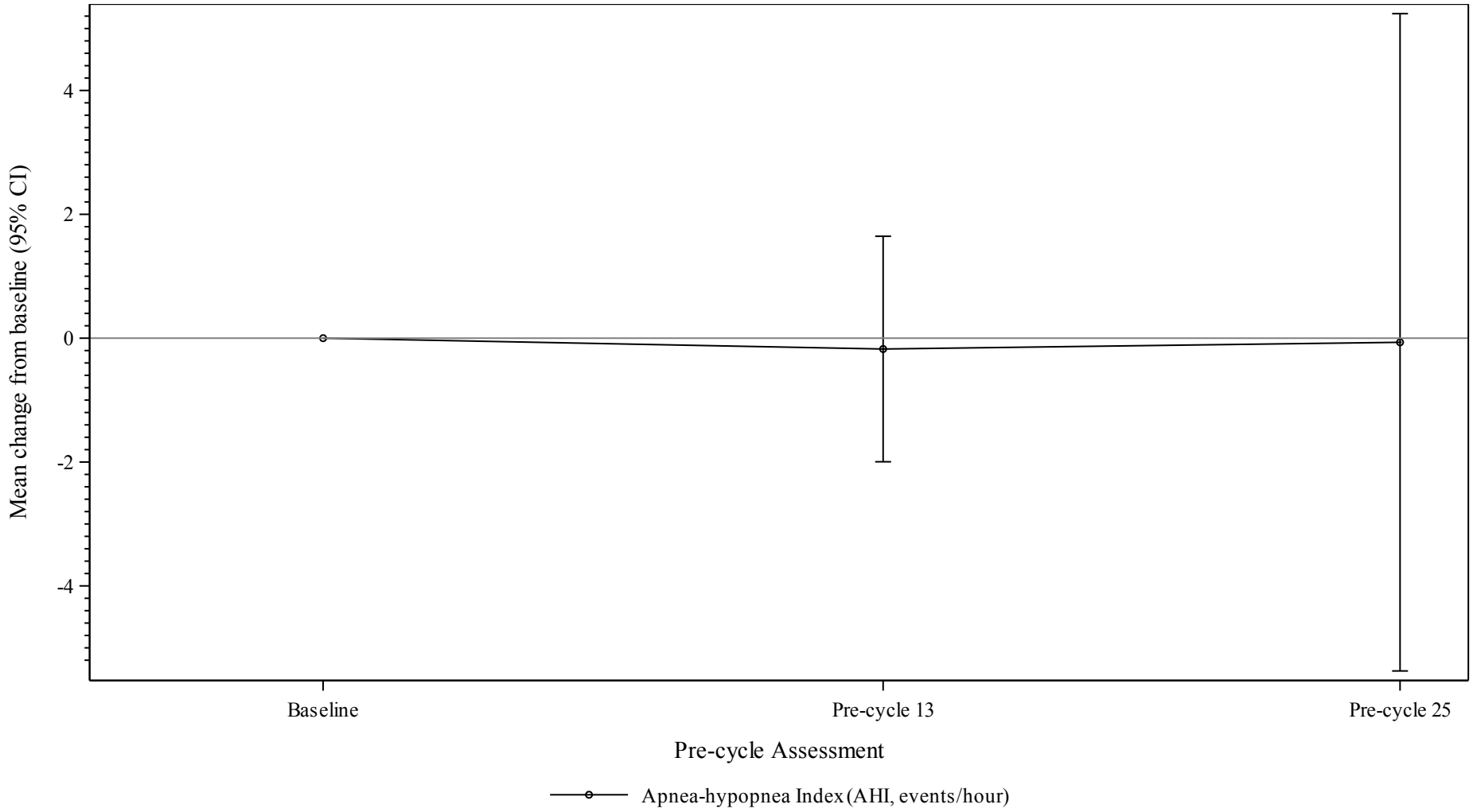
N = 6



CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.13 Mean change from baseline of Apnea-hypopnea Index - PN status at enrollment = Progressive
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

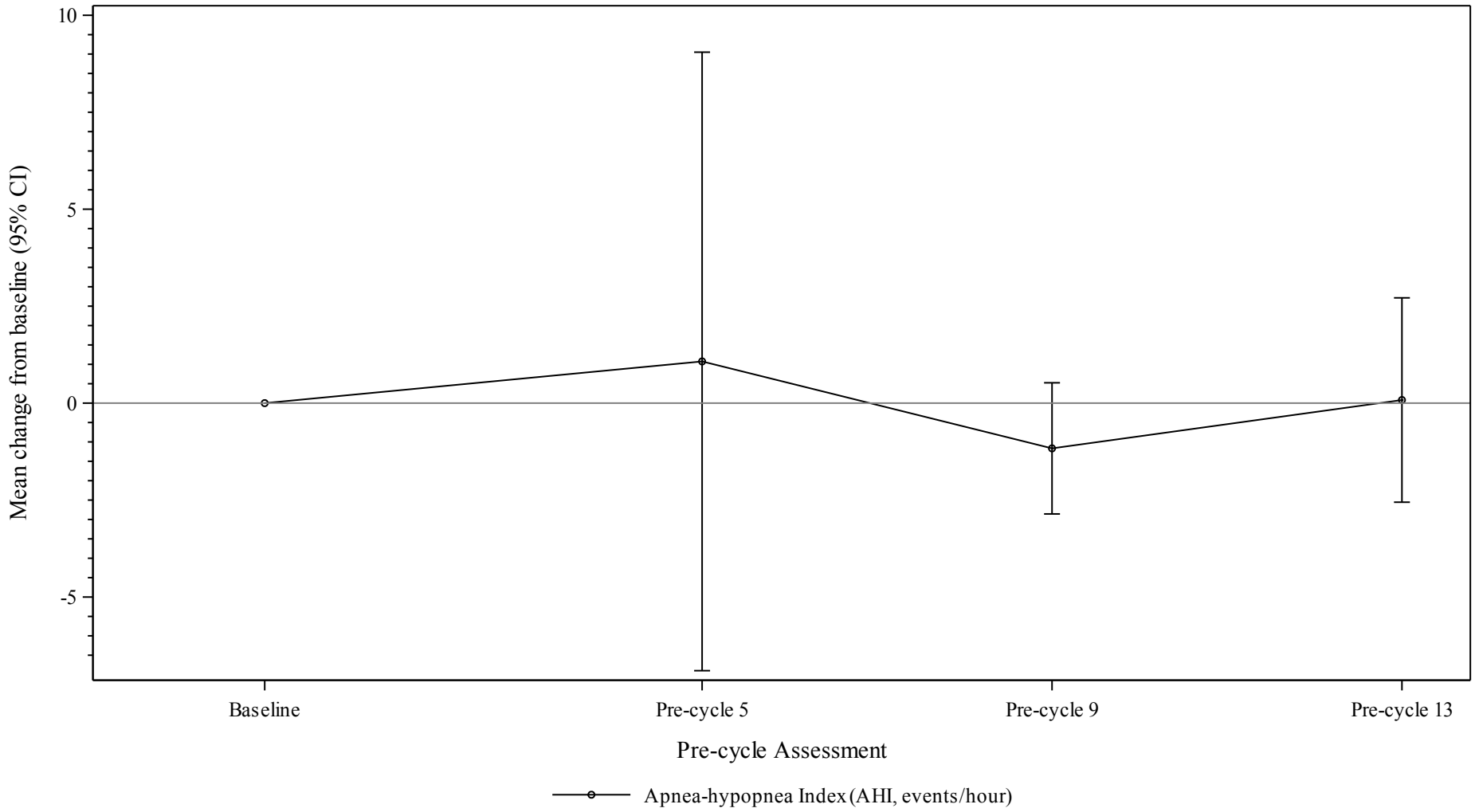
N = 4



CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.14 Mean change from baseline of Apnea-hypopnea Index - PN status at enrollment = Non-progressive (Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

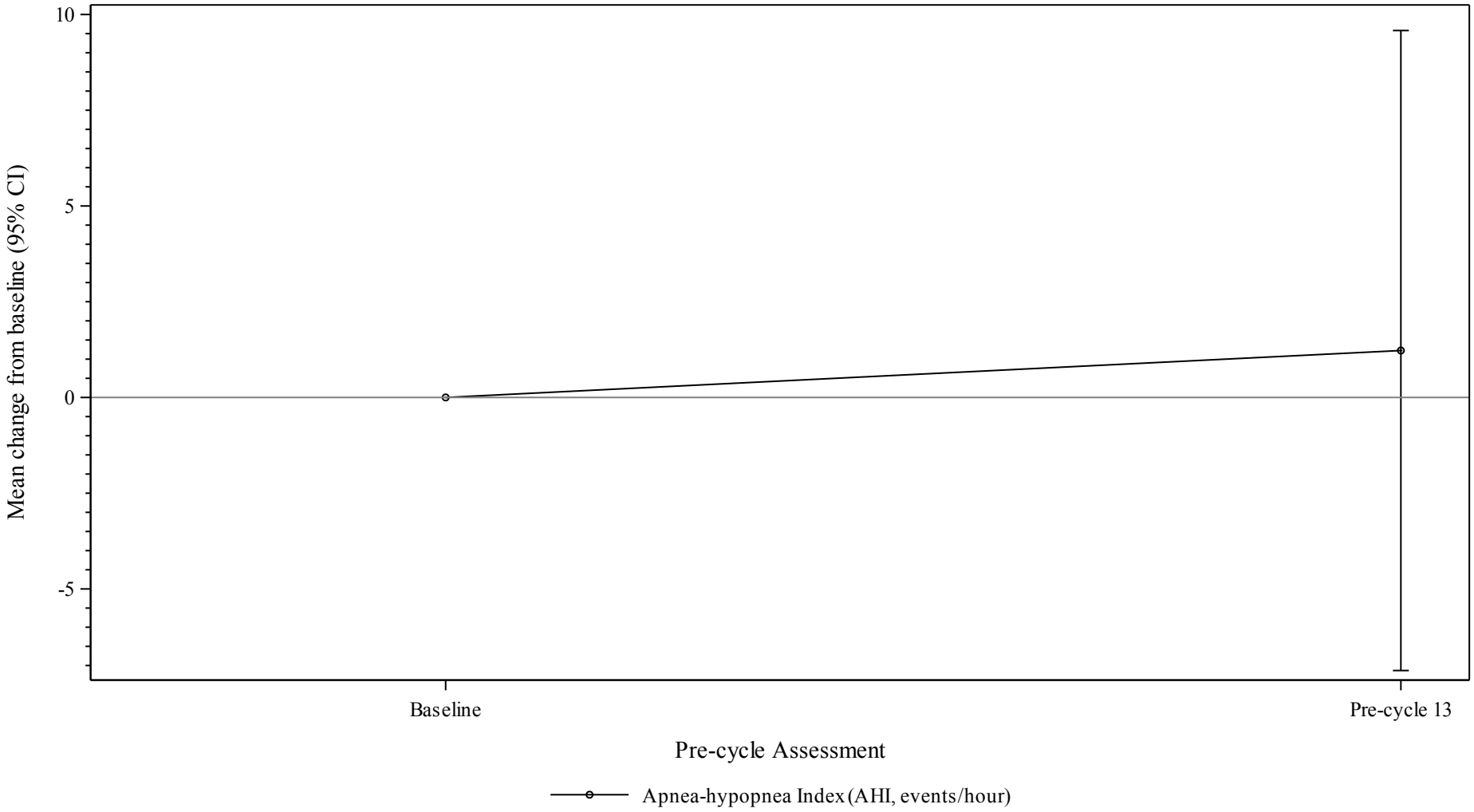
N = 5



CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Figure 2.7.4.15 Mean change from baseline of Apnea-hypopnea Index - PN status at enrollment = Unknown
(Full analysis set with airway PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 7



CI = Confidence interval.
Five patients with tracheostomy were excluded from the evaluations.

Table 2.8.1 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Improvement
(Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=10) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Scale Score	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.1.1.1 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Improvement - Gender = Male (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.1.1.2 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Improvement - Gender = Female (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=5) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Scale Score	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.1.1.3 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Improvement - PN status at enrol. = Progressive (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=5) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Scale Score	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.1.1.4 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Improvement - PN status at enrol. = Non-Progressive (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.1.1.5 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Improvement - PN status at enrol. = Unknown (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.1.2.1 Bowel and Bladder function self-report change from baseline over time - Gender = Male
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.8.1.2.2 Bowel and Bladder function self-report change from baseline over time - Gender = Female
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=5) [a]												
		Absolute values						Change from baseline						
Bowel and Bladder function self-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=2)	NC	NC	NC	4	21	60,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	12	12	80,0	1	NC	NC	NC	-9	-9	80,0
	Pre-cycle 9 (n=1)	NC	NC	NC	9	9	80,0	1	NC	NC	NC	-12	-12	80,0
	Pre-cycle 13 (n=1)	NC	NC	NC	6	6	80,0	1	NC	NC	NC	-15	-15	80,0
	Pre-cycle 25 (n=1)	NC	NC	NC	9	9	80,0	0	NC	NC	NC	NC	NC	100,0

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.8.1.2.3 Bowel and Bladder function self-report change from baseline over time - PN status at enrollment = Progressive
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=5) [a]											
		Absolute values						Change from baseline					
Bowel and Bladder function self-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=2)	NC	NC	NC	4	21	60,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	12	12	80,0	1	NC	NC	NC	-9	-9	80,0
	Pre-cycle 9 (n=1)	NC	NC	NC	9	9	80,0	1	NC	NC	NC	-12	-12	80,0
	Pre-cycle 13 (n=1)	NC	NC	NC	6	6	80,0	1	NC	NC	NC	-15	-15	80,0
	Pre-cycle 25 (n=1)	NC	NC	NC	9	9	80,0	0	NC	NC	NC	NC	NC	100,0

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.8.1.2.4 Bowel and Bladder function self-report change from baseline over time - PN status at enrol. = Non-progressive
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.8.1.2.5 Bowel and Bladder function self-report change from baseline over time - PN status at enrollment = Unknown
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

[a] Patients with a bowel/bladder PN-related morbidity who completed the self-report bowel/bladder questionnaire.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Figure 2.8.1.3.1 Mean change from baseline of Bowel and Bladder function self-report score - Gender = Male
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

Figure 2.8.1.3.2 Mean change from baseline of Bowel and Bladder function self-report score - Gender = Female
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

Figure 2.8.1.3.3 Mean change from baseline of Bowel and Bladder function self-report score - PN status at enrol. = Progressive
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

Figure 2.8.1.3.4 Mean change from baseline of Bowel and Bladder function self-report score - PN status at enrol. = Non-progressive (Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

Figure 2.8.1.3.5 Mean change from baseline of Bowel and Bladder function self-report score - PN status at enrollment = Unknown
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

Table 2.8.2 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Improvement
(Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=10) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Scale Score	Pre-cycle 5 (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8
	Pre-cycle 13 (N=7)	Categories of change [d]			
		Improvement	2	28,6	3,7, 71,0
		No improvement	5	71,4	29,0, 96,3
	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Overall (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.2.1.1 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Improvement - Gender = Male (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=5) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Scale Score	Pre-cycle 5 (N=5)	Categories of change [d]			
		Improvement	1	20,0	0,5, 71,6
		No improvement	4	80,0	28,4, 99,5
	Pre-cycle 9 (N=5)	Categories of change [d]			
		Improvement	1	20,0	0,5, 71,6
		No improvement	4	80,0	28,4, 99,5
	Pre-cycle 13 (N=5)	Categories of change [d]			
		Improvement	1	20,0	0,5, 71,6
		No improvement	4	80,0	28,4, 99,5
	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
	Overall (N=5)	Categories of change [d]			
		Improvement	1	20,0	0,5, 71,6
		No improvement	4	80,0	28,4, 99,5

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.2.1.2 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Improvement - Gender = Female (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=5) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Scale Score	Pre-cycle 5 (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
	Pre-cycle 9 (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
	Pre-cycle 13 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.2.1.3 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Improvement - PN status at enrol. = Progressive (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=5) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Scale Score	Pre-cycle 5 (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
	Pre-cycle 9 (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
	Pre-cycle 13 (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
	Overall (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.2.1.4 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Improvement - PN status at enrol. = Non-Progressive (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=3) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Scale Score	Pre-cycle 5 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Pre-cycle 9 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Pre-cycle 13 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.2.1.5 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Improvement - PN status at enrol. = Unknown (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

			Selumetinib 25 mg/m² BID (N=2) [a]		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Scale Score	Pre-cycle 5 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 9 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 13 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

Table 2.8.2.2.1 Bowel and Bladder function parent-report change from baseline over time - Gender = Male
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=5) [a]											
		Absolute values						Change from baseline					
Bowel and Bladder function parent-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total score	Baseline (n=5)	14,0	6,32	13,0	5	21	0,0							
	Pre-cycle 5 (n=5)	12,6	7,50	11,0	4	24	0,0	5	-1,4	12,50	-3,0	-15	19	0,0
	Pre-cycle 9 (n=5)	12,0	7,38	12,0	2	22	0,0	5	-2,0	12,35	-4,0	-17	17	0,0
	Pre-cycle 13 (n=5)	10,2	6,10	9,0	2	18	0,0	5	-3,8	9,23	-3,0	-17	9	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	4	8	60,0	2	NC	NC	NC	-5	-1	60,0

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.8.2.2.2 Bowel and Bladder function parent-report change from baseline over time - Gender = Female
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=5) [a]											
		Absolute values						Change from baseline					
Bowel and Bladder function parent-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total score	Baseline (n=3)	18,3	1,53	18,0	17	20	40,0							
	Pre-cycle 5 (n=4)	13,3	10,31	13,0	3	24	20,0	3	-1,7	8,96	3,0	-12	4	40,0
	Pre-cycle 9 (n=4)	12,3	8,54	13,0	3	20	20,0	3	-3,0	7,00	0,0	-11	2	40,0
	Pre-cycle 13 (n=3)	8,3	8,39	4,0	3	18	40,0	2	NC	NC	NC	-14	-2	60,0
	Pre-cycle 25 (n=2)	NC	NC	NC	3	20	60,0	1	NC	NC	NC	0	0	80,0

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.8.2.2.3 Bowel and Bladder function parent-report change from baseline over time - PN status at enrollment = Progressive
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=5) [a]											
		Absolute values						Change from baseline					
Bowel and Bladder function parent-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total score	Baseline (n=3)	17,0	4,58	18,0	12	21	40,0							
	Pre-cycle 5 (n=4)	8,3	5,12	7,5	3	15	20,0	3	-7,0	4,58	-6,0	-12	-3	40,0
	Pre-cycle 9 (n=4)	9,3	5,32	9,5	3	15	20,0	3	-5,7	5,51	-6,0	-11	0	40,0
	Pre-cycle 13 (n=4)	8,5	6,86	6,5	3	18	20,0	3	-6,7	6,35	-3,0	-14	-3	40,0
	Pre-cycle 25 (n=1)	NC	NC	NC	3	3	80,0	0	NC	NC	NC	NC	NC	100,0

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.8.2.2.4 Bowel and Bladder function parent-report change from baseline over time - PN status at enrol. = Non-progressive (Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=3) [a]											
		Absolute values						Change from baseline					
Bowel and Bladder function parent-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total score	Baseline (n=3)	14,0	7,94	17,0	5	20	0,0							
	Pre-cycle 5 (n=3)	22,7	2,31	24,0	20	24	0,0	3	8,7	8,96	4,0	3	19	0,0
	Pre-cycle 9 (n=3)	20,3	1,53	20,0	19	22	0,0	3	6,3	9,29	2,0	0	17	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	14	18	33,3	2	NC	NC	NC	-2	9	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	4	20	33,3	2	NC	NC	NC	-1	0	33,3

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

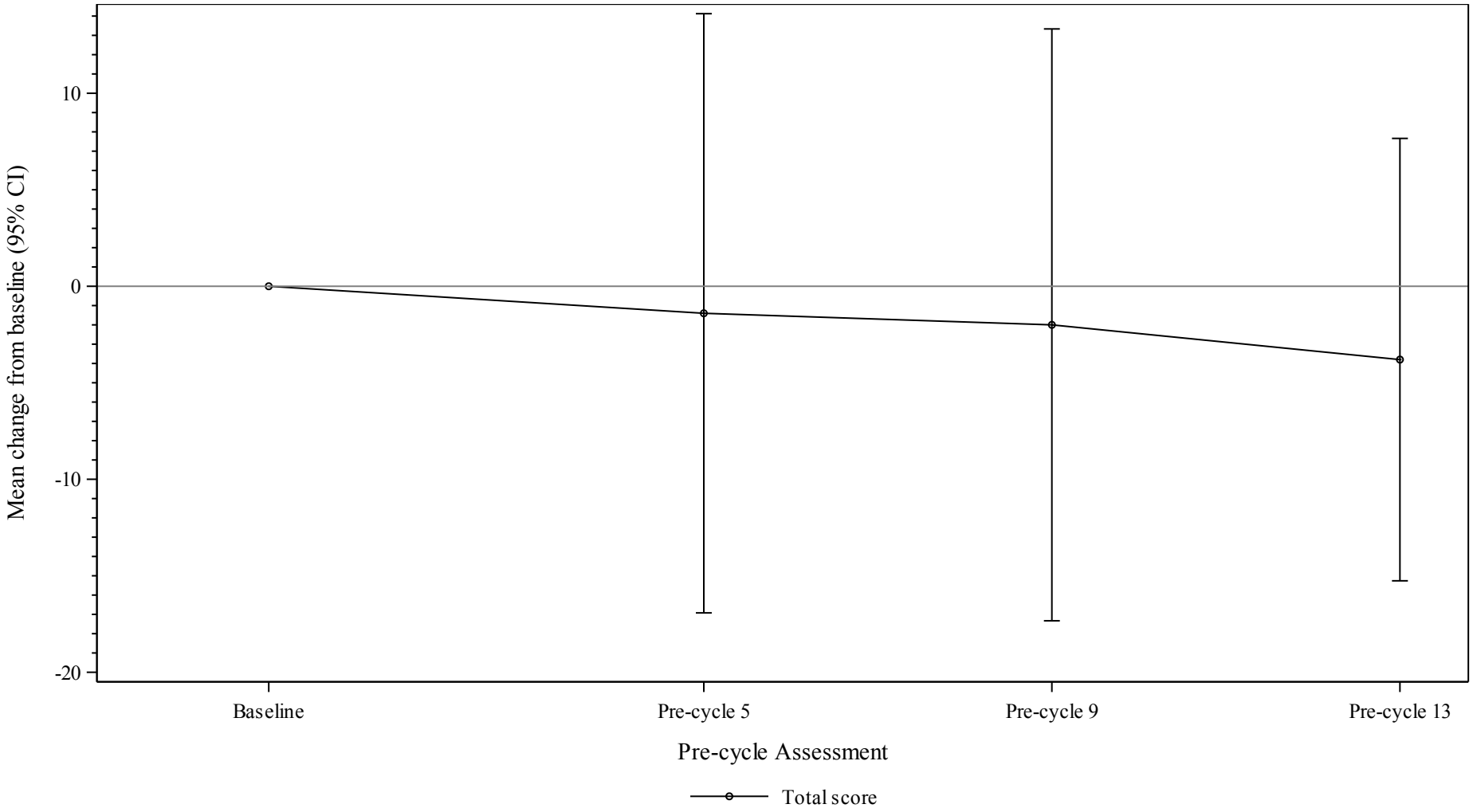
Table 2.8.2.2.5 Bowel and Bladder function parent-report change from baseline over time - PN status at enrollment = Unknown
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=2) [a]											
		Absolute values						Change from baseline					
Bowel and Bladder function parent-report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total score	Baseline (n=2)	NC	NC	NC	13	19	0,0							
	Pre-cycle 5 (n=2)	NC	NC	NC	4	11	0,0	2	NC	NC	NC	-15	-2	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	2	9	0,0	2	NC	NC	NC	-17	-4	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	2	8	0,0	2	NC	NC	NC	-17	-5	0,0
	Pre-cycle 25 (n=1)	NC	NC	NC	8	8	50,0	1	NC	NC	NC	-5	-5	50,0

[a] Patients with a bowel/bladder PN-related morbidity whose parent/legal guardian completed the parent proxy bowel/bladder questionnaire.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Figure 2.8.2.3.1 Mean change from baseline of Bowel and Bladder function parent-report score - Gender = Male
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

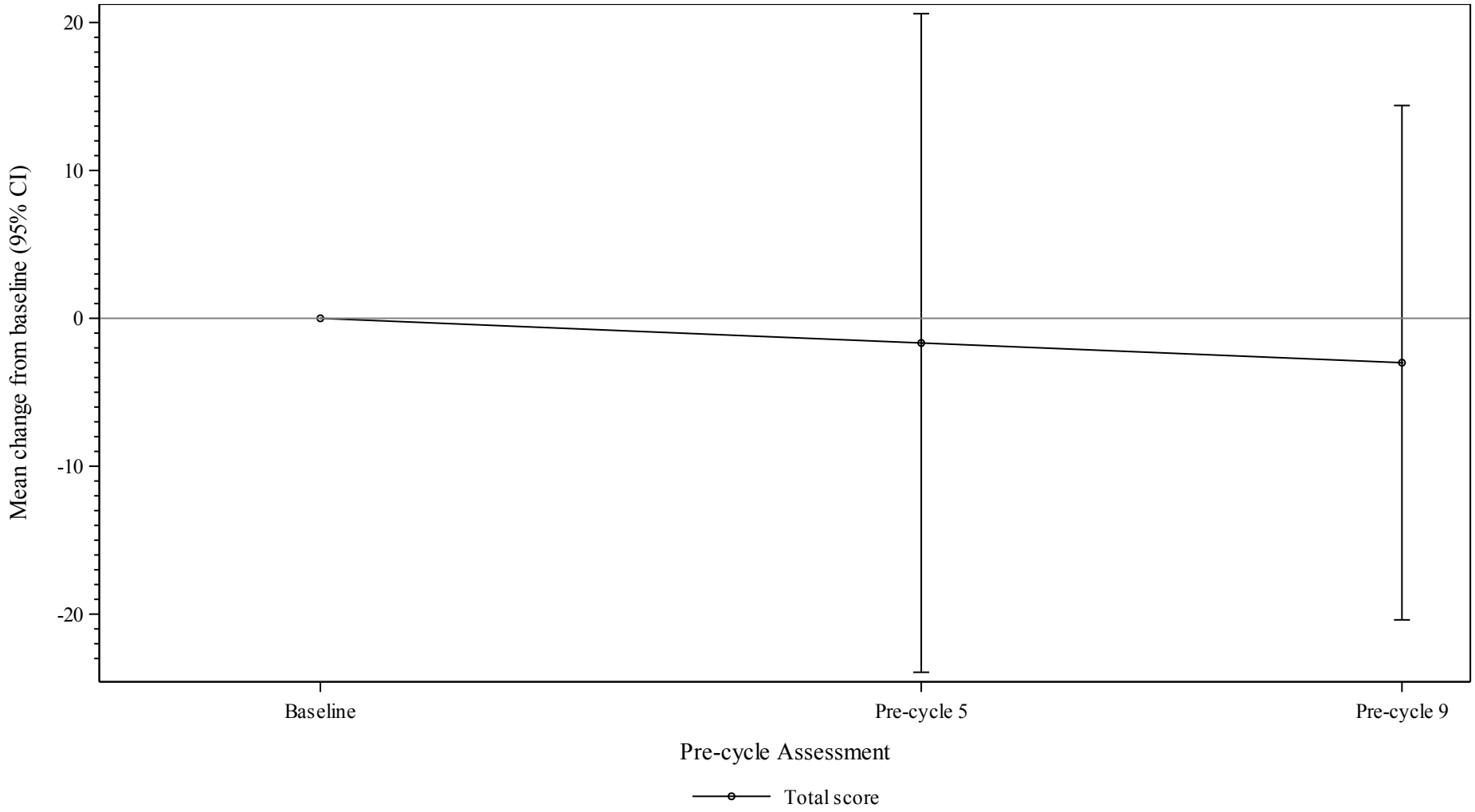
N = 5



CI = Confidence interval.

Figure 2.8.2.3.2 Mean change from baseline of Bowel and Bladder function parent-report score - Gender = Female
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

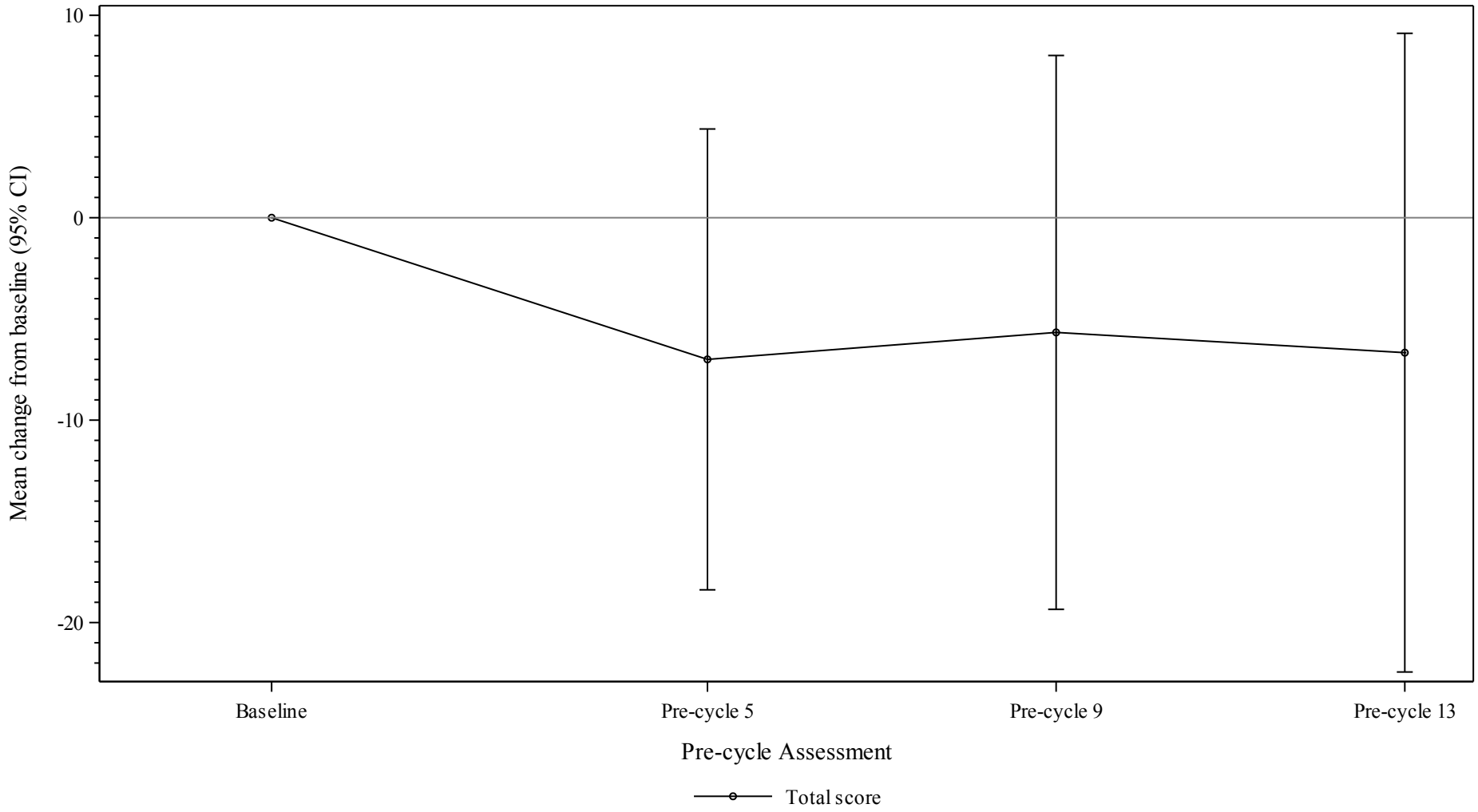
N = 5



CI = Confidence interval.

Figure 2.8.2.3.3 Mean change from baseline of Bowel and Bladder function parent-report score - PN status at enrol. = Progressive (Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

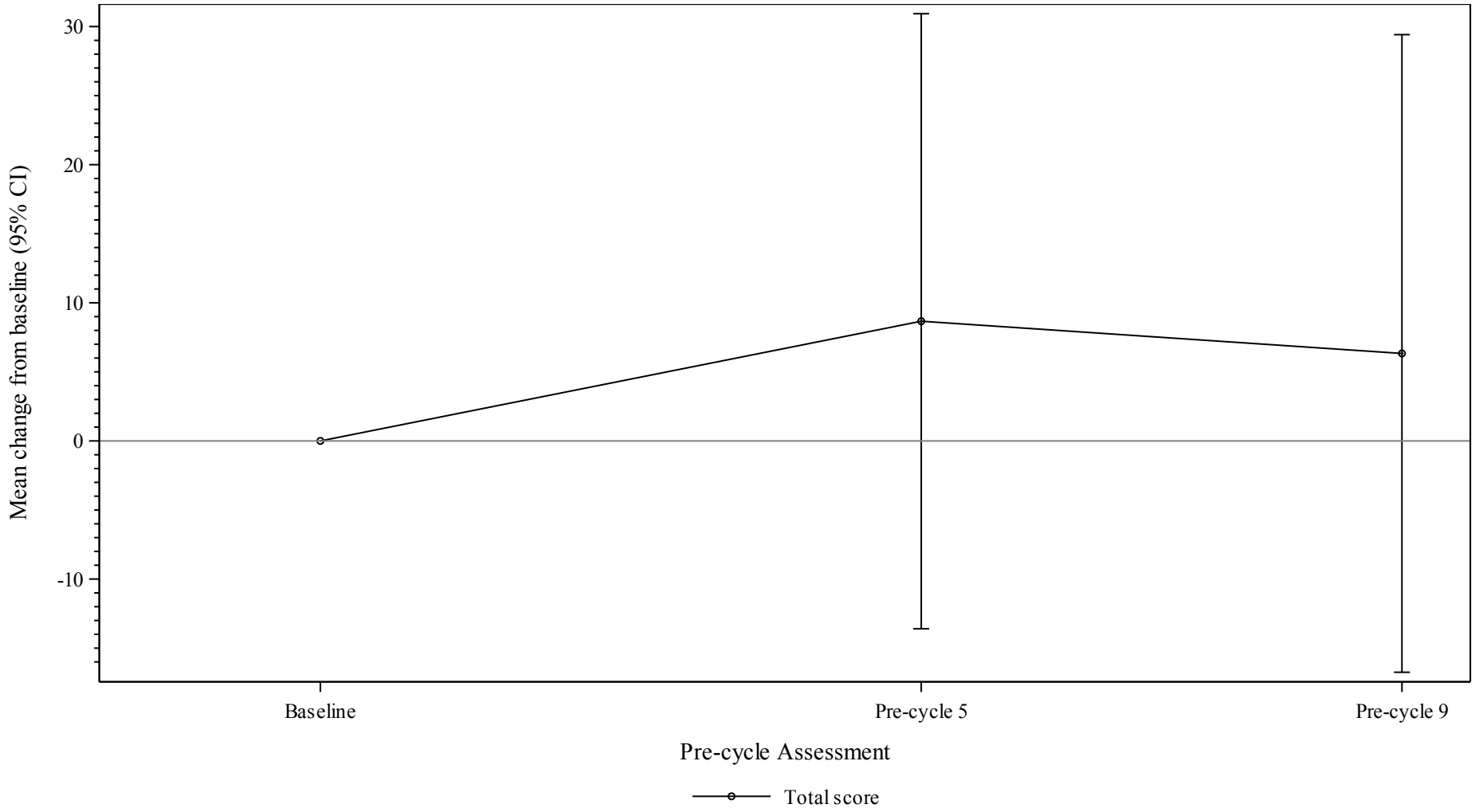
N = 5



CI = Confidence interval.

Figure 2.8.2.3.4 Mean change from baseline of Bowel and Bladder funct. parent-report score - PN status at enrol. = Non-progressive (Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 3



CI = Confidence interval.

Figure 2.8.2.3.5 Mean change from baseline of Bowel and Bladder function parent-report score - PN status at enrollment = Unknown
(Full analysis set with a bowel and/or bladder PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

Table 2.9.1 Visual Acuity and Exophthalmometry test score categories of overall change - percentage of patients with Improvement
(Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Overall (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
Exophthalmometry (mm) - OS	Overall (N=7)	Categories of change [d]			
		Improvement	2	28,6	3,7, 71,0
		No improvement	5	71,4	29,0, 96,3
HOTV (logMAR) - OD	Overall (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100
HOTV (logMAR) - OS	Overall (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52,2
		No improvement	5	100	47,8, 100
Teller Acuity Cards (logMAR) - OS	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV, Teller Acuity Cards.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
NC = Not Calculated.

Table 2.9.1.1.1 Visual Acuity and Exophthalmometry test score categories of overall change - percentage of patients with Improvement - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
Exophthalmometry (mm) - OS	Overall (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
HOTV (logMAR) - OD	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
HOTV (logMAR) - OS	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
Teller Acuity Cards (logMAR) - OS	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV, Teller Acuity Cards.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
NC = Not Calculated.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.9.1.1.2 Visual Acuity and Exophthalmometry test score categories of overall change - percentage of patients with Improvement - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Overall (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
Exophthalmometry (mm) - OS	Overall (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
HOTV (logMAR) - OD	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
HOTV (logMAR) - OS	Overall (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV, Teller Acuity Cards.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
NC = Not Calculated.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.9.1.1.3 Visual Acuity and Exophthalmometry test score categories of overall change - percentage of patients with Improvement - PN status at enrollment = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=3) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
Exophthalmometry (mm) - OS	Overall (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
HOTV (logMAR) - OD	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
HOTV (logMAR) - OS	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV, Teller Acuity Cards.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
NC = Not Calculated.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.9.1.1.4 Visual Acuity and Exophthalmometry test score categories of overall change - percentage of patients with Improvement - PN status at enrollment = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
Exophthalmometry (mm) - OS	Overall (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
HOTV (logMAR) - OD	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
Teller Acuity Cards (logMAR) - OS	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV, Teller Acuity Cards.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
NC = Not Calculated.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.9.1.1.5 Visual Acuity and Exophthalmometry test score categories of overall change - percentage of patients with Improvement - PN status at enrollment = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=3) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Overall (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
Exophthalmometry (mm) - OS	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
HOTV (logMAR) - OD	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
HOTV (logMAR) - OS	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV, Teller Acuity Cards.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
NC = Not Calculated.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.9.1.2.1 Visual Acuity and Exophthalmometry scores and change from baseline over time - Gender = Male
(Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=4) [a]												
		Absolute values						Change from baseline						
Visual Acuity/Exophthalmom-etry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Exophthalmom-etry (mm) - OD	Baseline (n=4)	12,8	14,17	9,0	0	33	0,0							
	Pre-cycle 5 (n=3)	20,0	13,45	16,0	9	35	25,0	3	3,0	2,65	2,0	1	6	25,0
	Pre-cycle 9 (n=3)	18,7	15,62	10,7	9	37	25,0	3	1,7	1,73	0,7	1	4	25,0
	Pre-cycle 13 (n=3)	17,9	16,55	8,7	8	37	25,0	3	0,9	3,01	0,7	-2	4	25,0
	Pre-cycle 25 (n=3)	18,0	15,88	9,0	9	36	25,0	3	1,0	2,33	1,0	-1	3	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	11	11	75,0	1	NC	NC	NC	1	1	75,0
Exophthalmom-etry (mm) - OS	Baseline (n=4)	10,3	10,08	8,5	0	24	0,0							
	Pre-cycle 5 (n=3)	12,9	3,15	14,0	9	15	25,0	3	-0,8	8,13	2,3	-10	5	25,0
	Pre-cycle 9 (n=3)	16,6	6,85	20,0	9	21	25,0	3	2,9	6,59	1,7	-3	10	25,0
	Pre-cycle 13 (n=3)	9,6	10,03	8,7	0	20	25,0	3	-4,1	17,72	1,7	-24	10	25,0
	Pre-cycle 25 (n=3)	15,0	5,20	18,0	9	18	25,0	3	1,3	7,02	2,0	-6	8	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	14	14	75,0	1	NC	NC	NC	-10	-10	75,0
HOTV (logMAR) - OD	Baseline (n=2)	NC	NC	NC	0,0	0,1	50,0							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	0,0	50,0	2	NC	NC	NC	-0,1	0,0	50,0
	Pre-cycle 9 (n=2)	NC	NC	NC	-0,1	0,0	50,0	2	NC	NC	NC	-0,2	0,0	50,0
	Pre-cycle 13 (n=2)	NC	NC	NC	0,0	0,0	50,0	2	NC	NC	NC	-0,1	0,0	50,0
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	0,1	50,0	2	NC	NC	NC	0,0	0,0	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	-0,1	-0,1	75,0	1	NC	NC	NC	-0,1	-0,1	75,0
HOTV(logMAR) - OS	Baseline (n=1)	NC	NC	NC	0,3	0,3	75,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	0,6	0,6	75,0	1	NC	NC	NC	0,3	0,3	75,0
	Pre-cycle 13 (n=1)	NC	NC	NC	1,0	1,0	75,0	1	NC	NC	NC	0,7	0,7	75,0
	Pre-cycle 25 (n=1)	NC	NC	NC	1,0	1,0	75,0	1	NC	NC	NC	0,7	0,7	75,0
Teller Acuity Cards (logMAR) - OS	Baseline (n=1)	NC	NC	NC	6,5	6,5	75,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	4,8	4,8	75,0	1	NC	NC	NC	-1,7	-1,7	75,0
	Pre-cycle 9 (n=1)	NC	NC	NC	6,5	6,5	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 13 (n=1)	NC	NC	NC	2,4	2,4	75,0	1	NC	NC	NC	-4,1	-4,1	75,0
	Pre-cycle 25 (n=1)	NC	NC	NC	9,8	9,8	75,0	1	NC	NC	NC	3,3	3,3	75,0

[a] Patients with orbit PN-related morbidity at enrolment.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.1.2.2 Visual Acuity and Exophthalmometry scores and change from baseline over time - Gender = Female
(Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=6) [a]												
		Absolute values						Change from baseline						
Visual Acuity/Exophthalmom-etry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Exophthalmom-etry (mm) - OD	Baseline (n=5)	8,9	8,13	14,0	0	16	16,7							
	Pre-cycle 5 (n=4)	17,9	5,36	18,3	12	23	33,3	4	10,3	14,13	11,2	-4	23	33,3
	Pre-cycle 9 (n=4)	19,0	4,63	19,2	15	23	33,3	4	11,4	13,38	11,7	-1	23	33,3
	Pre-cycle 13 (n=4)	13,8	10,03	15,7	0	24	33,3	4	6,3	11,84	0,5	0	24	33,3
	Pre-cycle 25 (n=4)	8,2	9,57	7,7	0	18	33,3	4	0,7	0,82	0,5	0	2	33,3
	Pre-cycle 37 (n=1)	NC	NC	NC	13	13	83,3	1	NC	NC	NC	-1	-1	83,3
Exophthalmom-etry (mm) - OS	Baseline (n=5)	8,3	7,68	11,7	0	16	16,7							
	Pre-cycle 5 (n=4)	12,8	0,96	12,7	12	14	33,3	4	6,3	7,31	6,3	0	13	33,3
	Pre-cycle 9 (n=4)	13,9	0,69	14,0	13	15	33,3	4	7,5	6,97	7,7	1	14	33,3
	Pre-cycle 13 (n=4)	14,7	1,16	15,0	13	16	33,3	4	8,3	6,72	8,2	2	15	33,3
	Pre-cycle 25 (n=4)	9,6	6,63	11,7	0	15	33,3	4	3,2	6,89	1,7	-3	13	33,3
	Pre-cycle 37 (n=1)	NC	NC	NC	13	13	83,3	1	NC	NC	NC	-1	-1	83,3
HOTV (logMAR) - OD	Baseline (n=4)	0,48	0,512	0,35	0,0	1,2	33,3							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,6	1,1	66,7	2	NC	NC	NC	-0,1	0,2	66,7
	Pre-cycle 9 (n=3)	0,77	0,551	0,50	0,4	1,4	50,0	3	0,13	0,058	0,10	0,1	0,2	50,0
	Pre-cycle 13 (n=3)	0,77	0,379	0,60	0,5	1,2	50,0	3	0,13	0,153	0,10	0,0	0,3	50,0
	Pre-cycle 25 (n=3)	0,80	0,520	0,50	0,5	1,4	50,0	3	0,17	0,058	0,20	0,1	0,2	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	0,4	0,4	83,3	1	NC	NC	NC	0,1	0,1	83,3
HOTV(logMAR) - OS	Baseline (n=5)	0,10	0,255	0,10	-0,2	0,5	16,7							
	Pre-cycle 5 (n=3)	0,07	0,115	0,00	0,0	0,2	50,0	3	0,10	0,100	0,10	0,0	0,2	50,0
	Pre-cycle 9 (n=4)	0,13	0,250	0,15	-0,2	0,4	33,3	4	0,13	0,126	0,10	0,0	0,3	33,3
	Pre-cycle 13 (n=4)	0,15	0,238	0,05	0,0	0,5	33,3	4	0,15	0,191	0,10	0,0	0,4	33,3
	Pre-cycle 25 (n=4)	0,18	0,206	0,15	0,0	0,4	33,3	4	0,18	0,126	0,20	0,0	0,3	33,3
	Pre-cycle 37 (n=1)	NC	NC	NC	0,1	0,1	83,3	1	NC	NC	NC	0,0	0,0	83,3

[a] Patients with orbit PN-related morbidity at enrolment.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.1.2.3 Visual Acuity and Exophthalmometry scores and change from baseline over time - PN status at enrol. = Progressive (Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=3) [a]												
		Absolute values						Change from baseline						
Visual Acuity/Exophthalmom-etry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Exophthalmom-etry (mm) - OD	Baseline (n=3)	7,4	7,18	8,0	0	14	0,0							
	Pre-cycle 5 (n=3)	15,3	6,89	14,3	9	23	0,0	3	7,9	12,81	1,0	0	23	0,0
	Pre-cycle 9 (n=3)	15,4	7,20	14,7	9	23	0,0	3	8,0	12,99	0,7	0	23	0,0
	Pre-cycle 13 (n=3)	8,0	7,69	8,7	0	15	0,0	3	0,6	0,51	0,7	0	1	0,0
	Pre-cycle 25 (n=3)	8,1	7,70	9,0	0	15	0,0	3	0,7	0,58	1,0	0	1	0,0
	Pre-cycle 37 (n=1)	NC	NC	NC	13	13	66,7	1	NC	NC	NC	-1	-1	66,7
Exophthalmom-etry (mm) - OS	Baseline (n=3)	7,0	7,00	7,0	0	14	0,0							
	Pre-cycle 5 (n=3)	12,0	2,40	12,7	9	14	0,0	3	5,0	6,74	2,3	0	13	0,0
	Pre-cycle 9 (n=3)	12,1	3,10	13,0	9	15	0,0	3	5,1	6,85	1,7	1	13	0,0
	Pre-cycle 13 (n=3)	12,4	3,53	13,0	9	16	0,0	3	5,4	6,54	1,7	2	13	0,0
	Pre-cycle 25 (n=3)	10,8	1,84	10,7	9	13	0,0	3	3,8	8,15	2,0	-3	13	0,0
	Pre-cycle 37 (n=1)	NC	NC	NC	13	13	66,7	1	NC	NC	NC	-1	-1	66,7
HOTV (logMAR) - OD	Baseline (n=2)	NC	NC	NC	0,1	0,3	33,3							
	Pre-cycle 5 (n=1)	NC	NC	NC	0,0	0,0	66,7	1	NC	NC	NC	-0,1	-0,1	66,7
	Pre-cycle 9 (n=2)	NC	NC	NC	-0,1	0,4	33,3	2	NC	NC	NC	-0,2	0,1	33,3
	Pre-cycle 13 (n=2)	NC	NC	NC	0,0	0,6	33,3	2	NC	NC	NC	-0,1	0,3	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	0,1	0,5	33,3	2	NC	NC	NC	0,0	0,2	33,3
	Pre-cycle 37 (n=1)	NC	NC	NC	0,4	0,4	66,7	1	NC	NC	NC	0,1	0,1	66,7
HOTV(logMAR) - OS	Baseline (n=3)	0,13	0,153	0,10	0,0	0,3	0,0							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	0,6	33,3	2	NC	NC	NC	0,0	0,3	33,3
	Pre-cycle 9 (n=2)	NC	NC	NC	0,1	0,2	33,3	2	NC	NC	NC	0,1	0,1	33,3
	Pre-cycle 13 (n=3)	0,50	0,500	0,50	0,0	1,0	0,0	3	0,37	0,351	0,40	0,0	0,7	0,0
	Pre-cycle 25 (n=3)	0,43	0,513	0,30	0,0	1,0	0,0	3	0,30	0,361	0,20	0,0	0,7	0,0
	Pre-cycle 37 (n=1)	NC	NC	NC	0,1	0,1	66,7	1	NC	NC	NC	0,0	0,0	66,7

[a] Patients with orbit PN-related morbidity at enrolment.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.1.2.4 Visual Acuity and Exophthalmometry scores and change from baseline over time - PN status at enrol. = Non-Progressive (Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=4) [a]												
		Absolute values						Change from baseline						
Visual Acuity/Exophthalmom-etry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Exophthalmom-etry (mm) - OD	Baseline (n=4)	14,3	13,82	12,0	0	33	0,0							
	Pre-cycle 5 (n=2)	NC	NC	NC	16	35	50,0	2	NC	NC	NC	2	6	50,0
	Pre-cycle 9 (n=2)	NC	NC	NC	11	37	50,0	2	NC	NC	NC	1	4	50,0
	Pre-cycle 13 (n=2)	NC	NC	NC	8	37	50,0	2	NC	NC	NC	-2	4	50,0
	Pre-cycle 25 (n=2)	NC	NC	NC	9	36	50,0	2	NC	NC	NC	-1	3	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	11	11	75,0	1	NC	NC	NC	1	1	75,0
Exophthalmom-etry (mm) - OS	Baseline (n=4)	12,4	10,08	12,8	0	24	0,0							
	Pre-cycle 5 (n=2)	NC	NC	NC	14	15	50,0	2	NC	NC	NC	-10	5	50,0
	Pre-cycle 9 (n=2)	NC	NC	NC	20	21	50,0	2	NC	NC	NC	-3	10	50,0
	Pre-cycle 13 (n=2)	NC	NC	NC	0	20	50,0	2	NC	NC	NC	-24	10	50,0
	Pre-cycle 25 (n=2)	NC	NC	NC	18	18	50,0	2	NC	NC	NC	-6	8	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	14	14	75,0	1	NC	NC	NC	-10	-10	75,0
HOTV (logMAR) - OD	Baseline (n=2)	NC	NC	NC	0,0	0,0	50,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	0,0	0,0	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 9 (n=1)	NC	NC	NC	0,0	0,0	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 13 (n=1)	NC	NC	NC	0,0	0,0	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 25 (n=1)	NC	NC	NC	0,0	0,0	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 37 (n=1)	NC	NC	NC	-0,1	-0,1	75,0	1	NC	NC	NC	-0,1	-0,1	75,0
HOTV(logMAR) - OS	Baseline (n=1)	NC	NC	NC	0,5	0,5	75,0							
Teller Acuity Cards (logMAR) - OS	Baseline (n=1)	NC	NC	NC	6,5	6,5	75,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	4,8	4,8	75,0	1	NC	NC	NC	-1,7	-1,7	75,0
	Pre-cycle 9 (n=1)	NC	NC	NC	6,5	6,5	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 13 (n=1)	NC	NC	NC	2,4	2,4	75,0	1	NC	NC	NC	-4,1	-4,1	75,0
	Pre-cycle 25 (n=1)	NC	NC	NC	9,8	9,8	75,0	1	NC	NC	NC	3,3	3,3	75,0

[a] Patients with orbit PN-related morbidity at enrolment.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.1.2.5 Visual Acuity and Exophthalmometry scores and change from baseline over time - PN status at enrol. = Unknown
(Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=3) [a]											
		Absolute values						Change from baseline					
Visual Acuity/Exophthalmom-etry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Exophthalmom-etry (mm) - OD	Baseline (n=2)	NC	NC	NC	0	16	33,3							
	Pre-cycle 5 (n=2)	NC	NC	NC	12	22	33,3	2	NC	NC	NC	-4	22	33,3
	Pre-cycle 9 (n=2)	NC	NC	NC	15	23	33,3	2	NC	NC	NC	-1	23	33,3
	Pre-cycle 13 (n=2)	NC	NC	NC	16	24	33,3	2	NC	NC	NC	0	24	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	0	18	33,3	2	NC	NC	NC	0	2	33,3
Exophthalmom-etry (mm) - OS	Baseline (n=2)	NC	NC	NC	0	12	33,3							
	Pre-cycle 5 (n=2)	NC	NC	NC	12	13	33,3	2	NC	NC	NC	0	13	33,3
	Pre-cycle 9 (n=2)	NC	NC	NC	14	14	33,3	2	NC	NC	NC	2	14	33,3
	Pre-cycle 13 (n=2)	NC	NC	NC	15	15	33,3	2	NC	NC	NC	3	15	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	0	15	33,3	2	NC	NC	NC	0	3	33,3
HOTV (logMAR) - OD	Baseline (n=2)	NC	NC	NC	0,4	1,2	33,3							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,6	1,1	33,3	2	NC	NC	NC	-0,1	0,2	33,3
	Pre-cycle 9 (n=2)	NC	NC	NC	0,5	1,4	33,3	2	NC	NC	NC	0,1	0,2	33,3
	Pre-cycle 13 (n=2)	NC	NC	NC	0,5	1,2	33,3	2	NC	NC	NC	0,0	0,1	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	0,5	1,4	33,3	2	NC	NC	NC	0,1	0,2	33,3
HOTV(logMAR) - OS	Baseline (n=2)	NC	NC	NC	-0,2	0,1	33,3							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	0,2	33,3	2	NC	NC	NC	0,1	0,2	33,3
	Pre-cycle 9 (n=2)	NC	NC	NC	-0,2	0,4	33,3	2	NC	NC	NC	0,0	0,3	33,3
	Pre-cycle 13 (n=2)	NC	NC	NC	0,0	0,1	33,3	2	NC	NC	NC	0,0	0,2	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	0,4	33,3	2	NC	NC	NC	0,2	0,3	33,3

[a] Patients with orbit PN-related morbidity at enrolment.
OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

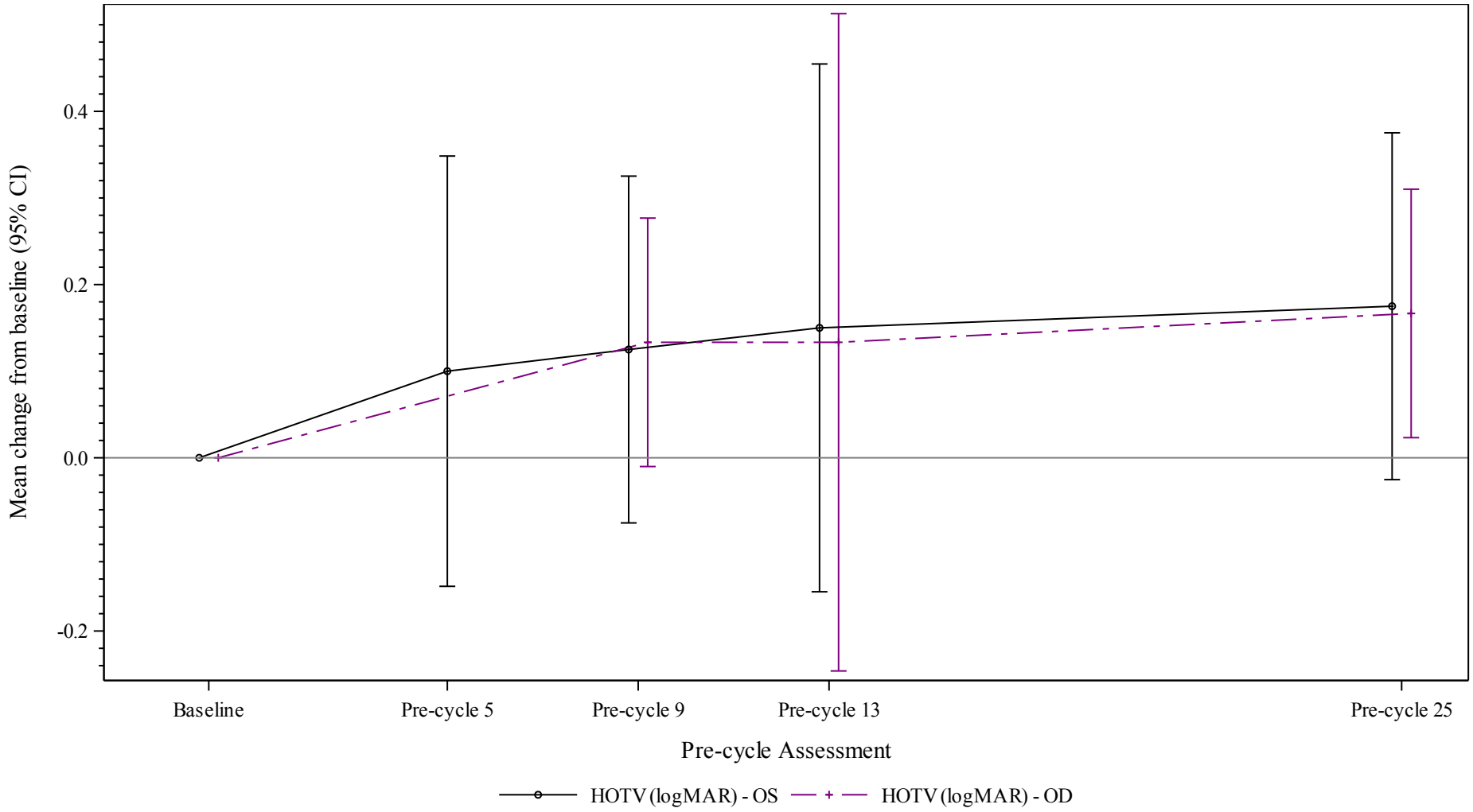
Figure 2.9.1.3.1 Mean change from baseline of Visual Acuity test scores - Gender = Male
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval. OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.

Figure 2.9.1.3.2 Mean change from baseline of Visual Acuity test scores - Gender = Female
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

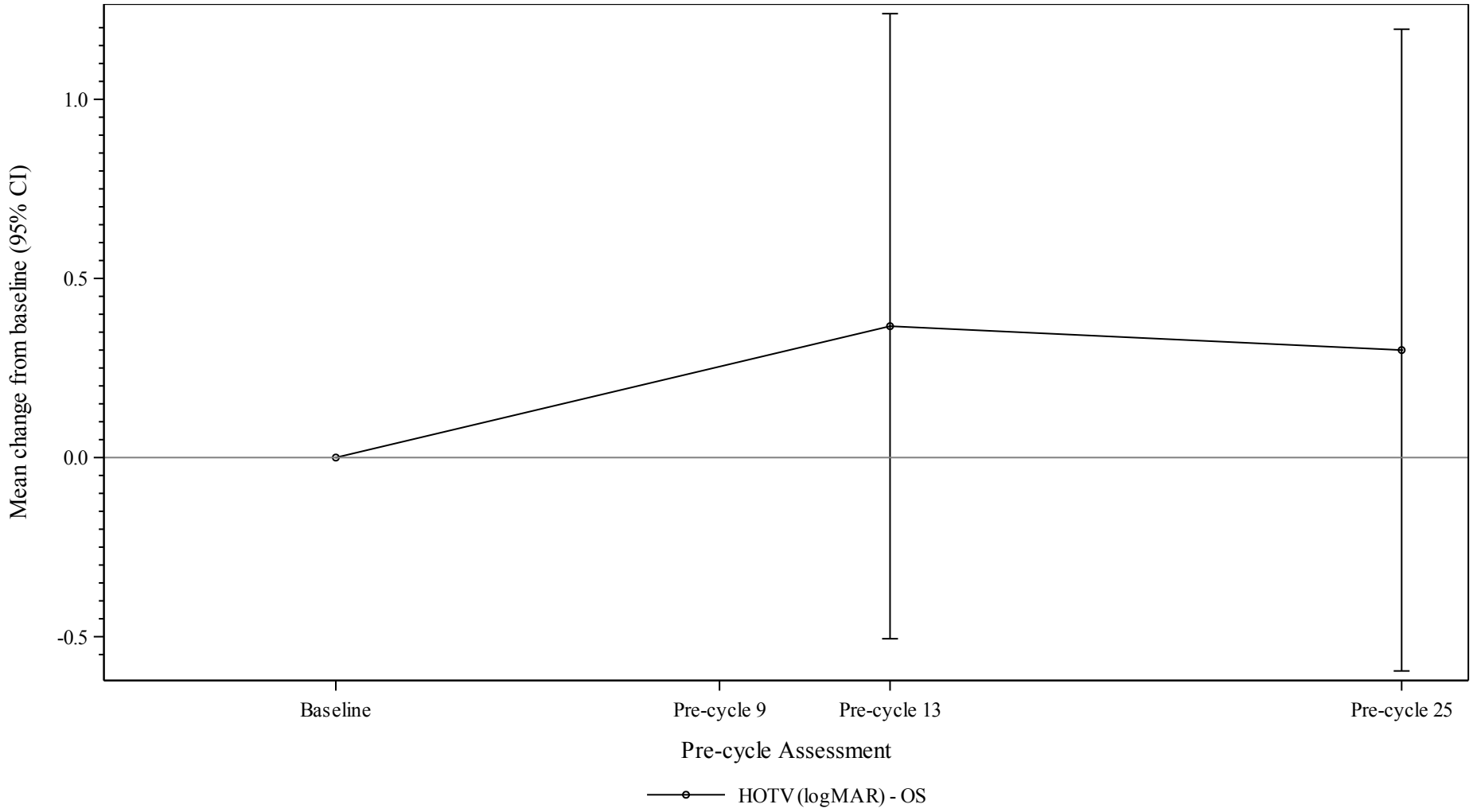
N = 6



CI = Confidence interval. OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.

Figure 2.9.1.3.3 Mean change from baseline of Visual Acuity test scores - PN status at enrollment = Progressive
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 3



CI = Confidence interval. OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.

Figure 2.9.1.3.4 Mean change from baseline of Visual Acuity test scores - PN status at enrollment = Non-progressive (Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval. OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.

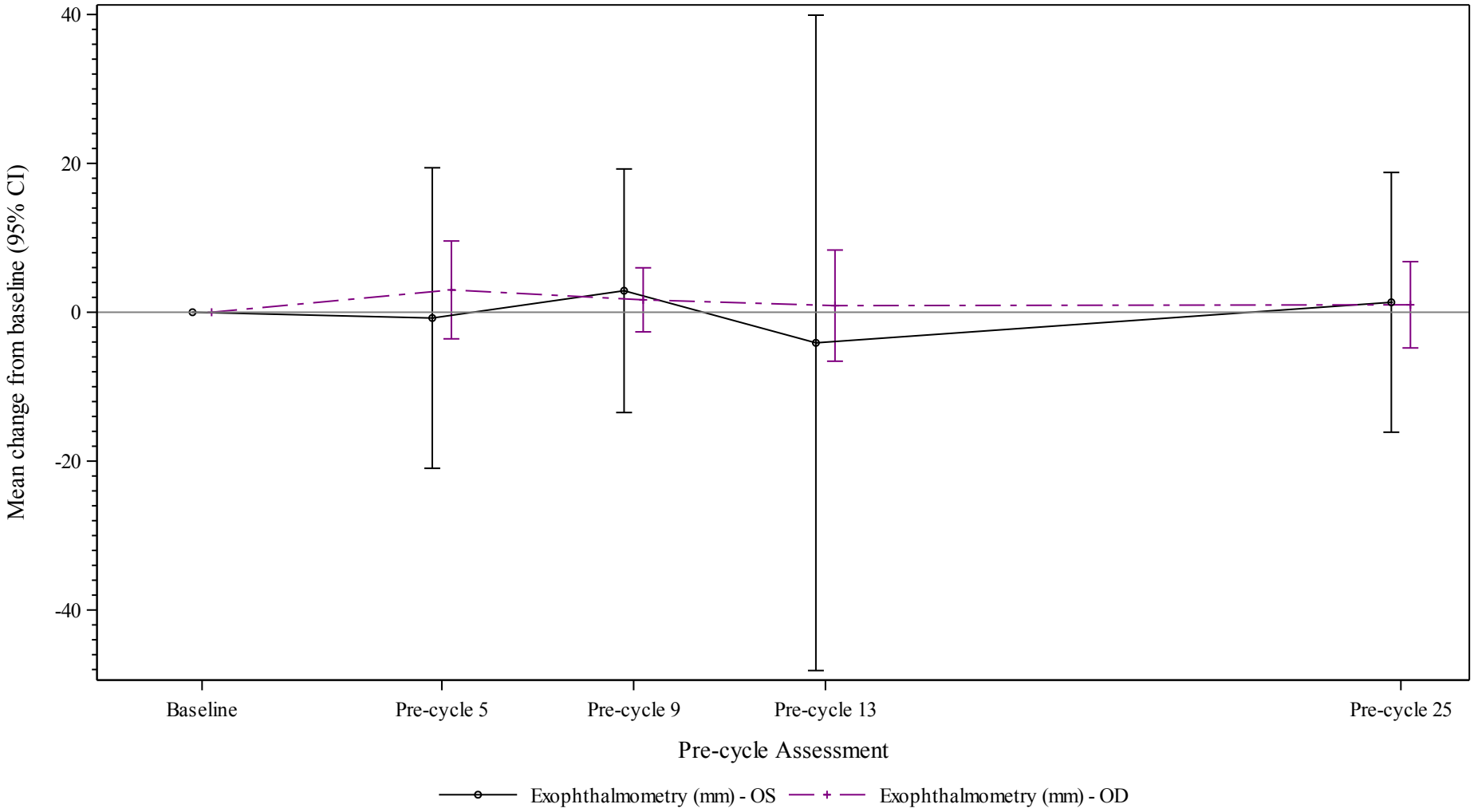
Figure 2.9.1.3.5 Mean change from baseline of Visual Acuity test scores - PN status at enrollment = Unknown
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval. OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.

Table 2.9.1.4.1 Mean change from baseline of Exophthalmometry - Gender = Male
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

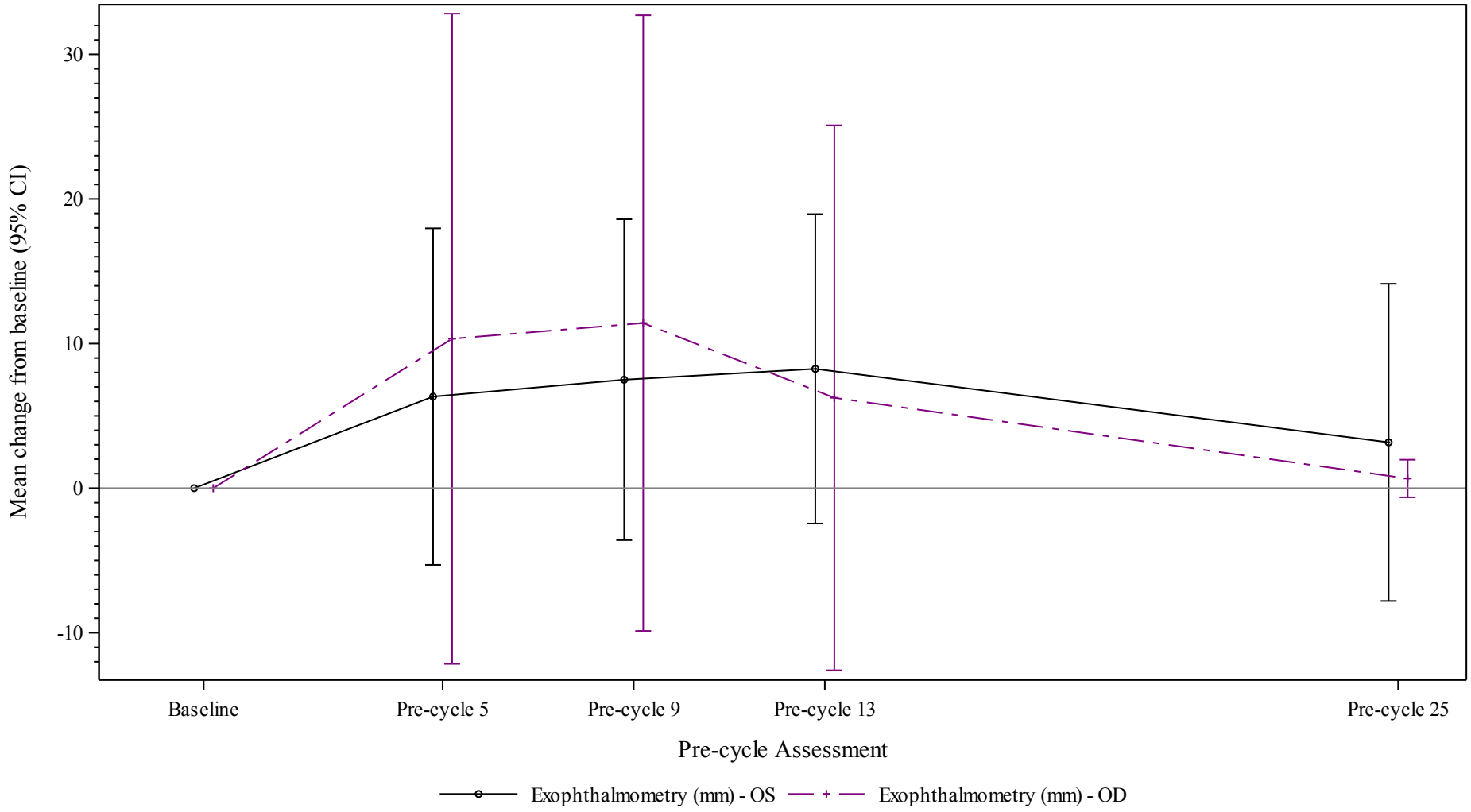
N = 4



CI = Confidence interval. OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.

Table 2.9.1.4.2 Mean change from baseline of Exophthalmometry - Gender = Female
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

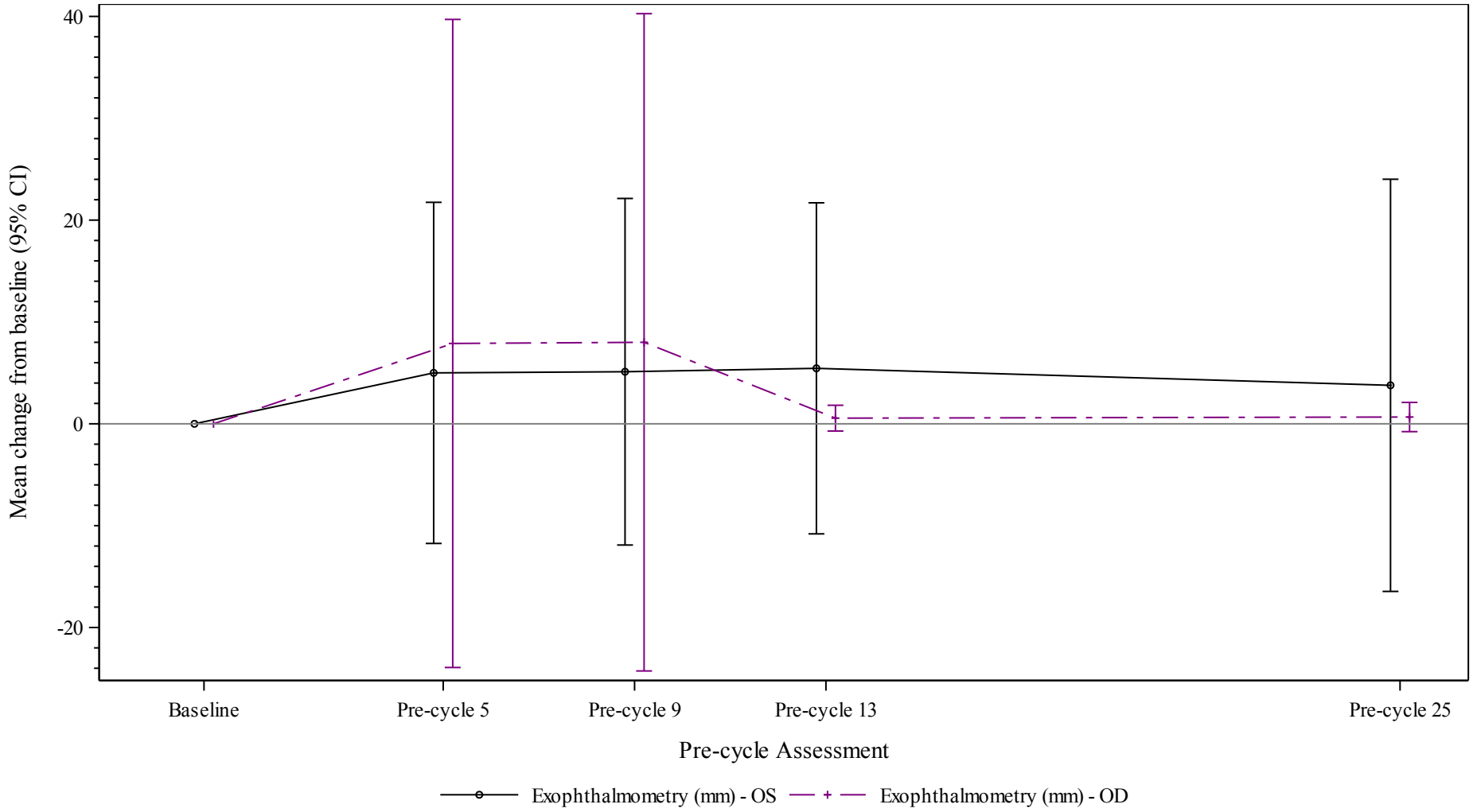
N = 6



CI = Confidence interval. OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.

Table 2.9.1.4.3 Mean change from baseline of Exophthalmometry - PN status at enrollment = Progressive
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 3



CI = Confidence interval. OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.

Table 2.9.1.4.4 Mean change from baseline of Exophthalmometry - PN status at enrollment = Non-progressive
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval. OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.

Table 2.9.1.4.5 Mean change from baseline of Exophthalmometry - PN status at enrollment = Unknown
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval. OS = 'oculus sinister' - left eye; OD = 'oculus dexter' - right eye.

Table 2.9.2 Visual Acuity and Exophthalmometry test score categories of overall change by orbital PN location - percentage of patients with Improvement (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Overall (N=7)	Categories of change [d]			
		Improvement	2	28,6	3,7, 71,0
		No improvement	5	71,4	29,0, 96,3
Exophthalmometry (mm) - non PN-affected side	Overall (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
HOTV (logMAR) - PN-affected side	Overall (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
HOTV (logMAR) - non PN-affected side	Overall (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100
Teller Acuity Cards (logMAR) - non PN-affected side	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV. Teller Acuity Cards.
NC = Not Calculated.

Table 2.9.2.1.1 Visual Acuity and Exophthalmometry test score categories of overall change by orbital PN location - percentage of patients with Improvement - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Overall (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
Exophthalmometry (mm) - non PN-affected side	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
HOTV (logMAR) - PN-affected side	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
HOTV (logMAR) - non PN-affected side	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
Teller Acuity Cards (logMAR) - non PN-affected side	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV. Teller Acuity Cards.
NC = Not Calculated.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.9.2.1.2 Visual Acuity and Exophthalmometry test score categories of overall change by orbital PN location - percentage of patients with Improvement - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Overall (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
Exophthalmometry (mm) - non PN-affected side	Overall (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
HOTV (logMAR) - PN-affected side	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
HOTV (logMAR) - non PN-affected side	Overall (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV. Teller Acuity Cards.
NC = Not Calculated.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.9.2.1.3 Visual Acuity and Exophthalmometry test score categories of overall change by orbital PN location - percentage of patients with Improvement - PN status at enrollment = Progressive (Full analysis set with orbit PN-related morbidit
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=3) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
Exophthalmometry (mm) - non PN-affected side	Overall (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
HOTV (logMAR) - PN-affected side	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
HOTV (logMAR) - non PN-affected side	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV. Teller Acuity Cards.
NC = Not Calculated.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.9.2.1.4 Visual Acuity and Exophthalmometry test score categories of overall change by orbital PN location - percentage of patients with Improvement - PN status at enrollment = Non-progressive (Full analysis set with orbit PN-related morb
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Overall (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
Exophthalmometry (mm) - non PN-affected side	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
HOTV (logMAR) - non PN-affected side	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
Teller Acuity Cards (logMAR) - non PN-affected side	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV. Teller Acuity Cards.
NC = Not Calculated.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.9.2.1.5 Visual Acuity and Exophthalmometry test score categories of overall change by orbital PN location
- percentage of patients with Improvement - PN status at enrollment = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=3) [a] Response category	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Overall (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
Exophthalmometry (mm) - non PN-affected side	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
HOTV (logMAR) - PN-affected side	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
HOTV (logMAR) - non PN-affected side	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV. Teller Acuity Cards.
NC = Not Calculated.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.9.2.2.1 Visual Acuity and Exophthalmometry scores and change from baseline over time - Gender = Male
by orbital PN location ((Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=4) [a]											
		Absolute values						Change from baseline					
Visual Acuity/Exophthalmom-etry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Exophthalmom-etry (mm) - PN-affected side	Baseline (n=3)	21,3	13,20	24,0	7	33	25,0							
	Pre-cycle 5 (n=3)	19,4	13,67	14,0	9	35	25,0	3	-1,9	7,03	2,0	-10	2	25,0
	Pre-cycle 9 (n=3)	22,1	14,03	21,0	9	37	25,0	3	0,8	3,42	1,7	-3	4	25,0
	Pre-cycle 13 (n=3)	15,2	19,35	8,7	0	37	25,0	3	-6,1	15,54	1,7	-24	4	25,0
	Pre-cycle 25 (n=3)	21,1	13,93	18,0	9	36	25,0	3	-0,2	5,05	2,0	-6	3	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	14	14	75,0	1	NC	NC	NC	-10	-10	75,0
Exophthalmom-etry (mm) - non PN-affected side	Baseline (n=5)	5,6	5,18	8,0	0	10	-25,0							
	Pre-cycle 5 (n=3)	13,4	3,86	15,3	9	16	25,0	3	4,1	2,71	5,3	1	6	25,0
	Pre-cycle 9 (n=3)	13,1	6,05	10,7	9	20	25,0	3	3,8	5,39	0,7	1	10	25,0
	Pre-cycle 13 (n=3)	12,2	6,74	8,7	8	20	25,0	3	2,9	6,30	0,7	-2	10	25,0
	Pre-cycle 25 (n=3)	11,9	5,30	9,0	9	18	25,0	3	2,6	4,86	1,0	-1	8	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	11	11	75,0	1	NC	NC	NC	1	1	75,0
HOTV (logMAR) - PN-affected side	Baseline (n=1)	NC	NC	NC	0,3	0,3	75,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	0,6	0,6	75,0	1	NC	NC	NC	0,3	0,3	75,0
	Pre-cycle 13 (n=1)	NC	NC	NC	1,0	1,0	75,0	1	NC	NC	NC	0,7	0,7	75,0
	Pre-cycle 25 (n=1)	NC	NC	NC	1,0	1,0	75,0	1	NC	NC	NC	0,7	0,7	75,0
HOTV (logMAR)- non PN-affected side	Baseline (n=2)	NC	NC	NC	0,0	0,1	50,0							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	0,0	50,0	2	NC	NC	NC	-0,1	0,0	50,0
	Pre-cycle 9 (n=2)	NC	NC	NC	-0,1	0,0	50,0	2	NC	NC	NC	-0,2	0,0	50,0
	Pre-cycle 13 (n=2)	NC	NC	NC	0,0	0,0	50,0	2	NC	NC	NC	-0,1	0,0	50,0
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	0,1	50,0	2	NC	NC	NC	0,0	0,0	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	-0,1	-0,1	75,0	1	NC	NC	NC	-0,1	-0,1	75,0

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.2.2.1 Visual Acuity and Exophthalmometry scores and change from baseline over time - Gender = Male
by orbital PN location ((Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=4) [a]											
		Absolute values						Change from baseline					
Visual Acuity/Exophthalmometry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Teller Acuity Cards(logMAR) - non PN-affected side	Baseline (n=1)	NC	NC	NC	6,5	6,5	75,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	4,8	4,8	75,0	1	NC	NC	NC	-1,7	-1,7	75,0
	Pre-cycle 9 (n=1)	NC	NC	NC	6,5	6,5	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 13 (n=1)	NC	NC	NC	2,4	2,4	75,0	1	NC	NC	NC	-4,1	-4,1	75,0
	Pre-cycle 25 (n=1)	NC	NC	NC	9,8	9,8	75,0	1	NC	NC	NC	3,3	3,3	75,0

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.2.2.2 Visual Acuity and Exophthalmometry scores and change from baseline over time - Gender = Female
by orbital PN location (Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=6) [a]											
		Absolute values						Change from baseline					
Visual Acuity/Exophthalmom-etry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Exophthalmom-etry (mm) - PN-affected side	Baseline (n=5)	9,2	8,42	14,3	0	16	16,7							
	Pre-cycle 5 (n=4)	17,9	5,36	18,3	12	23	33,3	4	10,3	14,13	11,2	-4	23	33,3
	Pre-cycle 9 (n=4)	19,0	4,63	19,2	15	23	33,3	4	11,4	13,38	11,7	-1	23	33,3
	Pre-cycle 13 (n=4)	13,8	10,03	15,7	0	24	33,3	4	6,3	11,84	0,5	0	24	33,3
	Pre-cycle 25 (n=4)	8,2	9,57	7,7	0	18	33,3	4	0,7	0,82	0,5	0	2	33,3
	Pre-cycle 37 (n=1)	NC	NC	NC	13	13	83,3	1	NC	NC	NC	-1	-1	83,3
Exophthalmom-etry (mm) - non PN-affected side	Baseline (n=5)	7,9	7,30	11,7	0	14	16,7							
	Pre-cycle 5 (n=4)	12,8	0,96	12,7	12	14	33,3	4	6,3	7,31	6,3	0	13	33,3
	Pre-cycle 9 (n=4)	13,9	0,69	14,0	13	15	33,3	4	7,5	6,97	7,7	1	14	33,3
	Pre-cycle 13 (n=4)	14,7	1,16	15,0	13	16	33,3	4	8,3	6,72	8,2	2	15	33,3
	Pre-cycle 25 (n=4)	9,6	6,63	11,7	0	15	33,3	4	3,2	6,89	1,7	-3	13	33,3
	Pre-cycle 37 (n=1)	NC	NC	NC	13	13	83,3	1	NC	NC	NC	-1	-1	83,3
HOTV (logMAR) - PN-affected side	Baseline (n=4)	0,60	0,408	0,45	0,3	1,2	33,3							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,6	1,1	66,7	2	NC	NC	NC	-0,1	0,2	66,7
	Pre-cycle 9 (n=3)	0,77	0,551	0,50	0,4	1,4	50,0	3	0,13	0,058	0,10	0,1	0,2	50,0
	Pre-cycle 13 (n=3)	0,77	0,379	0,60	0,5	1,2	50,0	3	0,13	0,153	0,10	0,0	0,3	50,0
	Pre-cycle 25 (n=3)	0,80	0,520	0,50	0,5	1,4	50,0	3	0,17	0,058	0,20	0,1	0,2	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	0,4	0,4	83,3	1	NC	NC	NC	0,1	0,1	83,3

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.2.2.2 Visual Acuity and Exophthalmometry scores and change from baseline over time - Gender = Female
by orbital PN location (Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=6) [a]											
		Absolute values						Change from baseline					
Visual Acuity/Exophthalmometry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
HOTV (logMAR)- non PN-affected side	Baseline (n=5)	0,00	0,122	0,00	-0,2	0,1	16,7							
	Pre-cycle 5 (n=3)	0,07	0,115	0,00	0,0	0,2	50,0	3	0,10	0,100	0,10	0,0	0,2	50,0
	Pre-cycle 9 (n=4)	0,13	0,250	0,15	-0,2	0,4	33,3	4	0,13	0,126	0,10	0,0	0,3	33,3
	Pre-cycle 13 (n=4)	0,15	0,238	0,05	0,0	0,5	33,3	4	0,15	0,191	0,10	0,0	0,4	33,3
	Pre-cycle 25 (n=4)	0,18	0,206	0,15	0,0	0,4	33,3	4	0,18	0,126	0,20	0,0	0,3	33,3
	Pre-cycle 37 (n=1)	NC	NC	NC	0,1	0,1	83,3	1	NC	NC	NC	0,0	0,0	83,3

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.2.2.3 Visual Acuity and Exophthalmometry scores and change from baseline over time - PN status at enrol. = Progressive by orbital PN location (Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=3) [a]											
		Absolute values						Change from baseline					
Visual Acuity/Exophthalmom-etry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Exophthalmom-etry (mm) - PN-affected side	Baseline (n=3)	7,1	7,17	7,0	0	14	0,0							
	Pre-cycle 5 (n=3)	15,4	6,74	14,3	9	23	0,0	3	8,3	12,47	2,3	0	23	0,0
	Pre-cycle 9 (n=3)	15,4	7,20	14,7	9	23	0,0	3	8,3	12,72	1,7	0	23	0,0
	Pre-cycle 13 (n=3)	8,0	7,69	8,7	0	15	0,0	3	0,9	0,84	1,0	0	2	0,0
	Pre-cycle 25 (n=3)	8,1	7,70	9,0	0	15	0,0	3	1,0	1,00	1,0	0	2	0,0
	Pre-cycle 37 (n=1)	NC	NC	NC	13	13	66,7	1	NC	NC	NC	-1	-1	66,7
Exophthalmom-etry (mm) - non PN-affected side	Baseline (n=3)	7,3	7,02	8,0	0	14	0,0							
	Pre-cycle 5 (n=3)	11,9	2,59	12,7	9	14	0,0	3	4,6	7,04	1,0	0	13	0,0
	Pre-cycle 9 (n=3)	12,1	3,10	13,0	9	15	0,0	3	4,8	7,12	0,7	1	13	0,0
	Pre-cycle 13 (n=3)	12,4	3,53	13,0	9	16	0,0	3	5,1	6,85	1,7	1	13	0,0
	Pre-cycle 25 (n=3)	10,8	1,84	10,7	9	13	0,0	3	3,4	8,27	1,0	-3	13	0,0
	Pre-cycle 37 (n=1)	NC	NC	NC	13	13	66,7	1	NC	NC	NC	-1	-1	66,7
HOTV (logMAR) - PN-affected side	Baseline (n=2)	NC	NC	NC	0,3	0,3	33,3							
	Pre-cycle 5 (n=1)	NC	NC	NC	0,6	0,6	66,7	1	NC	NC	NC	0,3	0,3	66,7
	Pre-cycle 9 (n=1)	NC	NC	NC	0,4	0,4	66,7	1	NC	NC	NC	0,1	0,1	66,7
	Pre-cycle 13 (n=2)	NC	NC	NC	0,6	1,0	33,3	2	NC	NC	NC	0,3	0,7	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	0,5	1,0	33,3	2	NC	NC	NC	0,2	0,7	33,3
	Pre-cycle 37 (n=1)	NC	NC	NC	0,4	0,4	66,7	1	NC	NC	NC	0,1	0,1	66,7

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.2.2.3 Visual Acuity and Exophthalmometry scores and change from baseline over time - PN status at enrol. = Progressive by orbital PN location (Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=3) [a]											
		Absolute values						Change from baseline					
Visual Acuity/Exophthalmometry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
HOTV (logMAR)- non PN-affected side	Baseline (n=3)	0,07	0,058	0,10	0,0	0,1	0,0							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	0,0	33,3	2	NC	NC	NC	-0,1	0,0	33,3
	Pre-cycle 9 (n=3)	0,07	0,153	0,10	-0,1	0,2	0,0	3	0,00	0,173	0,10	-0,2	0,1	0,0
	Pre-cycle 13 (n=3)	0,17	0,289	0,00	0,0	0,5	0,0	3	0,10	0,265	0,00	-0,1	0,4	0,0
	Pre-cycle 25 (n=3)	0,13	0,153	0,10	0,0	0,3	0,0	3	0,07	0,115	0,00	0,0	0,2	0,0
	Pre-cycle 37 (n=1)	NC	NC	NC	0,1	0,1	66,7	1	NC	NC	NC	0,0	0,0	66,7

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.2.2.4 Visual Acuity and Exophthalmometry scores and change from baseline over time - PN status at enrol. = Non-Progressive by orbital PN location (Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=4) [a]											
		Absolute values						Change from baseline					
Visual Acuity/Exophthalmom-etry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Exophthalmom-etry (mm) - PN-affected side	Baseline (n=3)	24,2	8,67	24,0	16	33	25,0							
	Pre-cycle 5 (n=2)	NC	NC	NC	14	35	50,0	2	NC	NC	NC	-10	2	50,0
	Pre-cycle 9 (n=2)	NC	NC	NC	21	37	50,0	2	NC	NC	NC	-3	4	50,0
	Pre-cycle 13 (n=2)	NC	NC	NC	0	37	50,0	2	NC	NC	NC	-24	4	50,0
	Pre-cycle 25 (n=2)	NC	NC	NC	18	36	50,0	2	NC	NC	NC	-6	3	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	14	14	75,0	1	NC	NC	NC	-10	-10	75,0
Exophthalmom-etry (mm) - non PN-affected side	Baseline (n=5)	6,8	6,42	10,0	0	14	-25,0							
	Pre-cycle 5 (n=2)	NC	NC	NC	15	16	50,0	2	NC	NC	NC	5	6	50,0
	Pre-cycle 9 (n=2)	NC	NC	NC	11	20	50,0	2	NC	NC	NC	1	10	50,0
	Pre-cycle 13 (n=2)	NC	NC	NC	8	20	50,0	2	NC	NC	NC	-2	10	50,0
	Pre-cycle 25 (n=2)	NC	NC	NC	9	18	50,0	2	NC	NC	NC	-1	8	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	11	11	75,0	1	NC	NC	NC	1	1	75,0
HOTV (logMAR) - PN-affected side	Baseline (n=1)	NC	NC	NC	0,5	0,5	75,0							
HOTV (logMAR)- non PN-affected side	Baseline (n=2)	NC	NC	NC	0,0	0,0	50,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	0,0	0,0	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 9 (n=1)	NC	NC	NC	0,0	0,0	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 13 (n=1)	NC	NC	NC	0,0	0,0	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 25 (n=1)	NC	NC	NC	0,0	0,0	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 37 (n=1)	NC	NC	NC	-0,1	-0,1	75,0	1	NC	NC	NC	-0,1	-0,1	75,0

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.2.2.4 Visual Acuity and Exophthalmometry scores and change from baseline over time - PN status at enrol. = Non-Progressive by orbital PN location (Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=4) [a]											
		Absolute values						Change from baseline					
Visual Acuity/Exophthalmometry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Teller Acuity Cards(logMAR) - non PN-affected side	Baseline (n=1)	NC	NC	NC	6,5	6,5	75,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	4,8	4,8	75,0	1	NC	NC	NC	-1,7	-1,7	75,0
	Pre-cycle 9 (n=1)	NC	NC	NC	6,5	6,5	75,0	1	NC	NC	NC	0,0	0,0	75,0
	Pre-cycle 13 (n=1)	NC	NC	NC	2,4	2,4	75,0	1	NC	NC	NC	-4,1	-4,1	75,0
	Pre-cycle 25 (n=1)	NC	NC	NC	9,8	9,8	75,0	1	NC	NC	NC	3,3	3,3	75,0

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.9.2.2.5 Visual Acuity and Exophthalmometry scores and change from baseline over time - PN status at enrol. = Unknown by orbital PN location (Full analysis set with orbit PN-related morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=3) [a]											
		Absolute values						Change from baseline					
Visual Acuity/Exophthalmom-etry test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Exophthalmom-etry (mm) - PN-affected side	Baseline (n=2)	NC	NC	NC	0	16	33,3							
	Pre-cycle 5 (n=2)	NC	NC	NC	12	22	33,3	2	NC	NC	NC	-4	22	33,3
	Pre-cycle 9 (n=2)	NC	NC	NC	15	23	33,3	2	NC	NC	NC	-1	23	33,3
	Pre-cycle 13 (n=2)	NC	NC	NC	16	24	33,3	2	NC	NC	NC	0	24	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	0	18	33,3	2	NC	NC	NC	0	2	33,3
Exophthalmom-etry (mm) - non PN-affected side	Baseline (n=2)	NC	NC	NC	0	12	33,3							
	Pre-cycle 5 (n=2)	NC	NC	NC	12	13	33,3	2	NC	NC	NC	0	13	33,3
	Pre-cycle 9 (n=2)	NC	NC	NC	14	14	33,3	2	NC	NC	NC	2	14	33,3
	Pre-cycle 13 (n=2)	NC	NC	NC	15	15	33,3	2	NC	NC	NC	3	15	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	0	15	33,3	2	NC	NC	NC	0	3	33,3
HOTV (logMAR) - PN-affected side	Baseline (n=2)	NC	NC	NC	0,4	1,2	33,3							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,6	1,1	33,3	2	NC	NC	NC	-0,1	0,2	33,3
	Pre-cycle 9 (n=2)	NC	NC	NC	0,5	1,4	33,3	2	NC	NC	NC	0,1	0,2	33,3
	Pre-cycle 13 (n=2)	NC	NC	NC	0,5	1,2	33,3	2	NC	NC	NC	0,0	0,1	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	0,5	1,4	33,3	2	NC	NC	NC	0,1	0,2	33,3
HOTV (logMAR)- non PN-affected side	Baseline (n=2)	NC	NC	NC	-0,2	0,1	33,3							
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	0,2	33,3	2	NC	NC	NC	0,1	0,2	33,3
	Pre-cycle 9 (n=2)	NC	NC	NC	-0,2	0,4	33,3	2	NC	NC	NC	0,0	0,3	33,3
	Pre-cycle 13 (n=2)	NC	NC	NC	0,0	0,1	33,3	2	NC	NC	NC	0,0	0,2	33,3
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	0,4	33,3	2	NC	NC	NC	0,2	0,3	33,3

[a] Patients with orbit PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

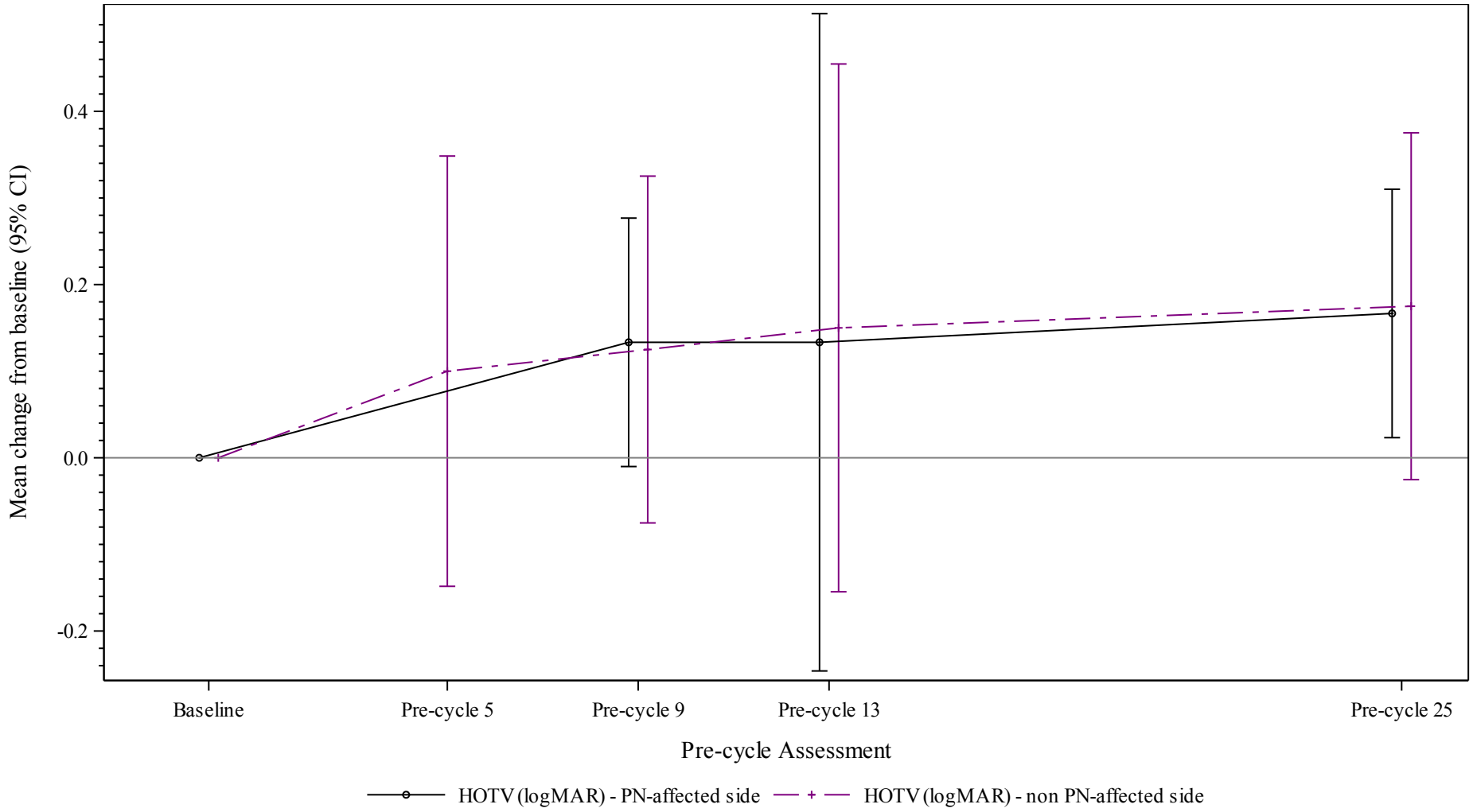
Figure 2.9.2.3.1 Mean change from baseline of Visual Acuity test scores by orbital PN location - Gender = Male
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

Figure 2.9.2.3.2 Mean change from baseline of Visual Acuity test scores by orbital PN location - Gender = Female
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

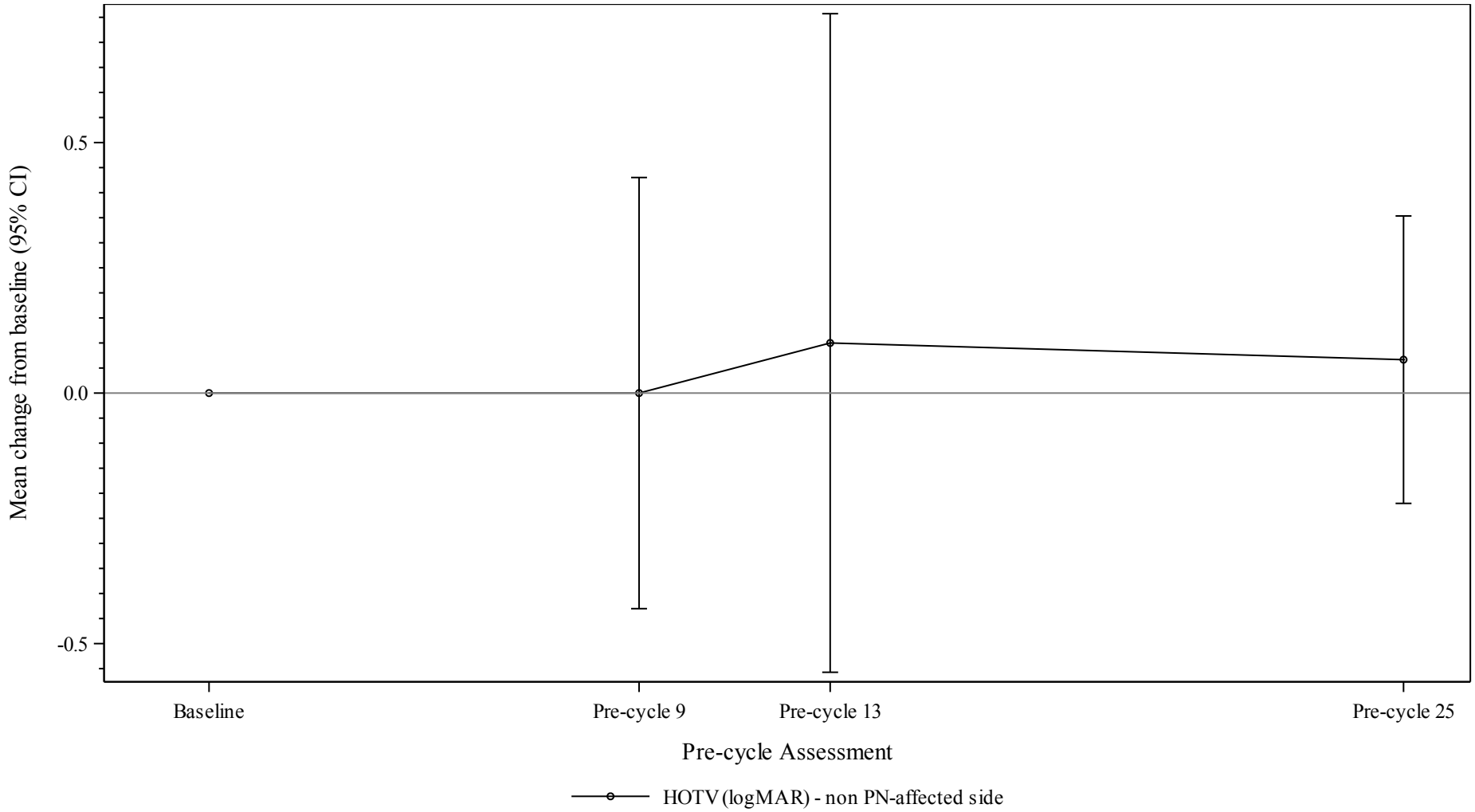
N = 6



CI = Confidence interval.

Figure 2.9.2.3.3 Mean change from baseline of Visual Acuity test scores by orbital PN location - PN status at enrol. = Progressive (Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 3



CI = Confidence interval.

Figure 2.9.2.3.4 Mean change from baseline of Visual Acuity test scores by orbital PN location- PN status at enrol. = Non-progressiv
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

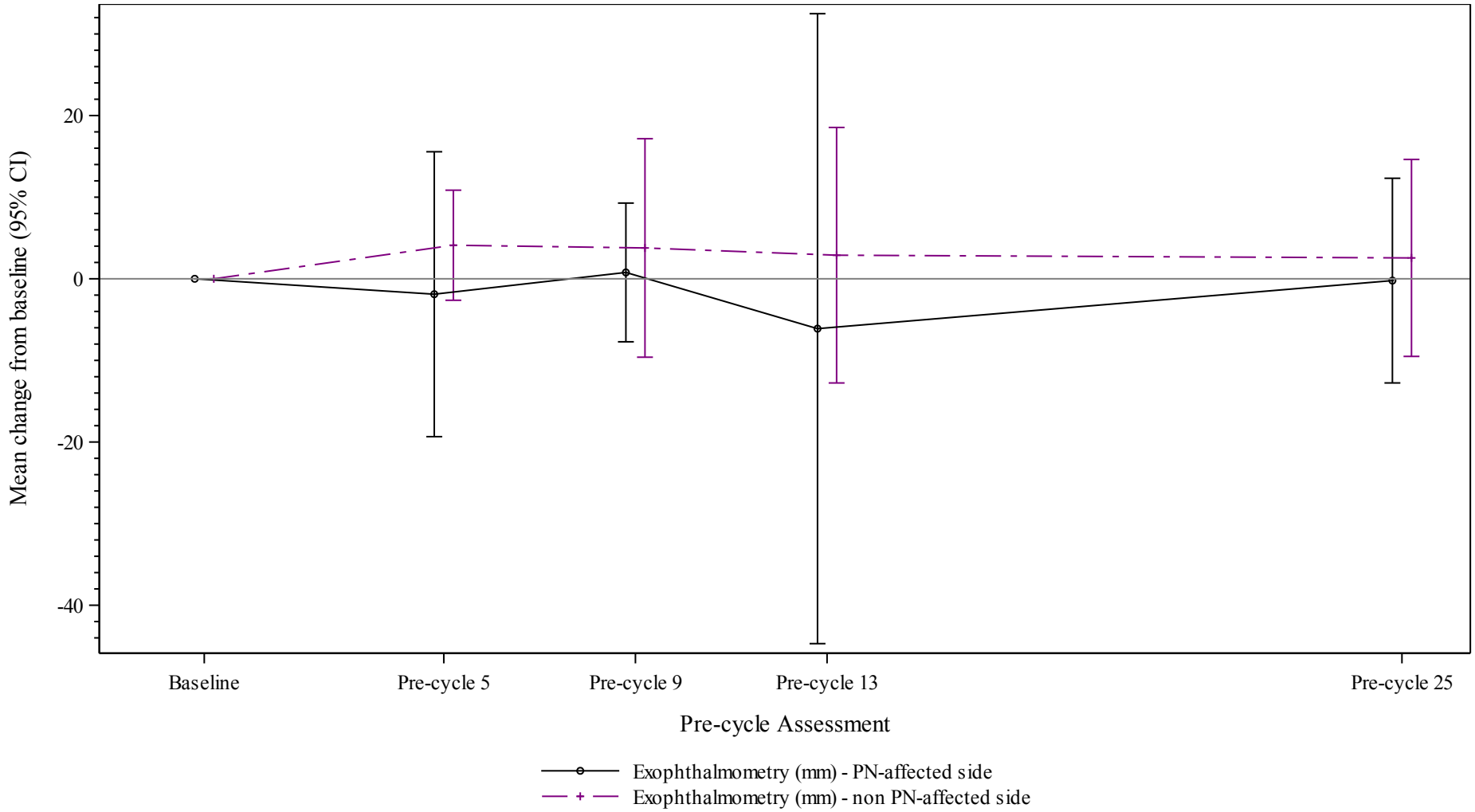
Figure 2.9.2.3.5 Mean change from baseline of Visual Acuity test scores by orbital PN location - PN status at enrollment = Unknown
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

Table 2.9.2.4.1 Mean change from baseline of Exophthalmometry by orbital PN location - Gender = Male
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

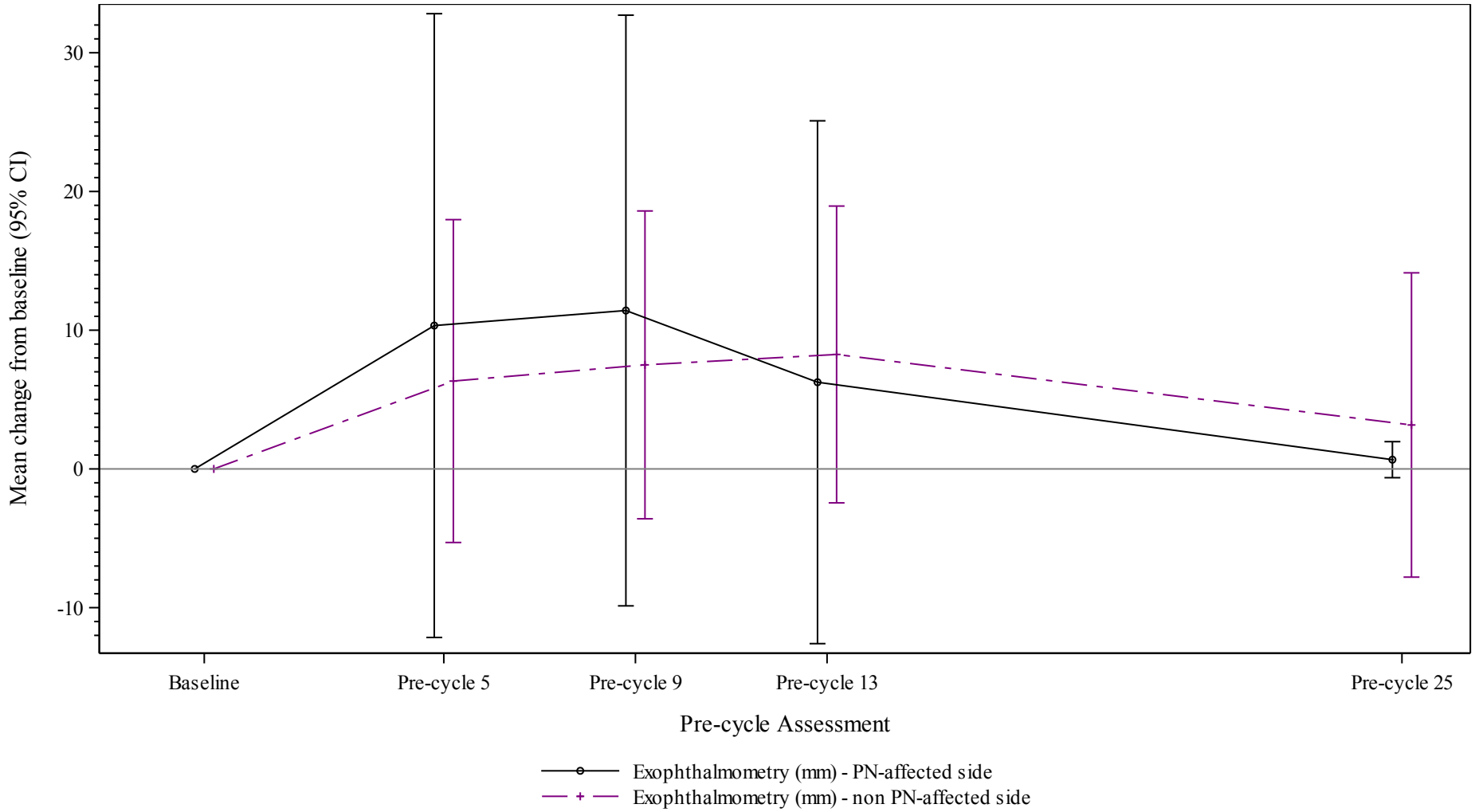
N = 4



CI = Confidence interval.

Table 2.9.2.4.2 Mean change from baseline of Exophthalmometry by orbital PN location - Gender = Female
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

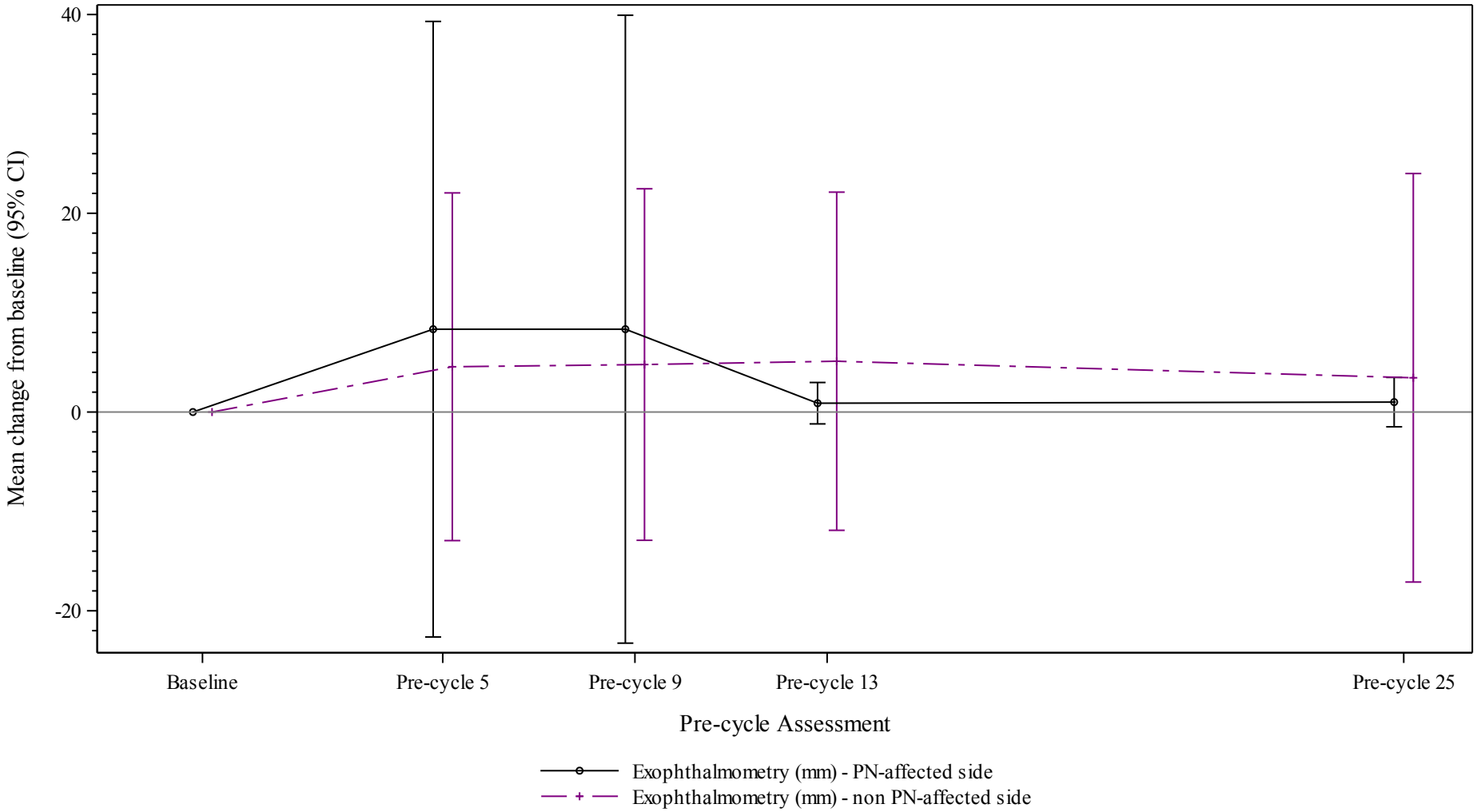
N = 6



CI = Confidence interval.

Table 2.9.2.4.3 Mean change from baseline of Exophthalmometry by orbital PN location - PN status at enrollment = Progressive (Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 3



CI = Confidence interval.

Table 2.9.2.4.4 Mean change from baseline of Exophthalmometry by orbital PN location - PN status at enrollment = Non-progressive (Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

Table 2.9.2.4.5 Mean change from baseline of Exophthalmometry by orbital PN location - PN status at enrollment = Unknown
(Full analysis set with a vision related-PN morbidity) Phase II Stratum 1, Data cut-off: 29th June 2018

INSUFFICIENT DATA

CI = Confidence interval.

Table 2.10.1.1 Distribution of Global Impression of Change self-report item responses over time
Patients with much or very much improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=34) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=26)	1 = Much or Very Much Improved	12/26 (46,2)
		2 = Not Much or Very Much Improved	14/26 (53,8)
	Pre-cycle 5 (N=30)	1 = Much or Very Much Improved	14/30 (46,7)
		2 = Not Much or Very Much Improved	16/30 (53,3)
	Pre-cycle 9 (N=30)	1 = Much or Very Much Improved	16/30 (53,3)
		2 = Not Much or Very Much Improved	14/30 (46,7)
	Pre-cycle 13 (N=29)	1 = Much or Very Much Improved	15/29 (51,7)
		2 = Not Much or Very Much Improved	14/29 (48,3)
	Pre-cycle 25 (N=23)	1 = Much or Very Much Improved	16/23 (69,6)
		2 = Not Much or Very Much Improved	7/23 (30,4)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	1/ 4 (25,0)
		2 = Not Much or Very Much Improved	3/ 4 (75,0)
	Overall (N=31)	1 = Much or Very Much Improved	24/31 (77,4)
		2 = Not Much or Very Much Improved	7/31 (22,6)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=30)	1 = Much or Very Much Improved	9/30 (30,0)
		2 = Not Much or Very Much Improved	21/30 (70,0)
	Pre-cycle 5 (N=30)	1 = Much or Very Much Improved	12/30 (40,0)
		2 = Not Much or Very Much Improved	18/30 (60,0)
	Pre-cycle 9 (N=30)	1 = Much or Very Much Improved	10/30 (33,3)
		2 = Not Much or Very Much Improved	20/30 (66,7)
	Pre-cycle 13 (N=29)	1 = Much or Very Much Improved	12/29 (41,4)
		2 = Not Much or Very Much Improved	17/29 (58,6)
	Pre-cycle 25 (N=23)	1 = Much or Very Much Improved	9/23 (39,1)
		2 = Not Much or Very Much Improved	14/23 (60,9)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	1/ 4 (25,0)
		2 = Not Much or Very Much Improved	3/ 4 (75,0)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1 Distribution of Global Impression of Change self-report item responses over time
Patients with much or very much improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=34) [a] n/N (%) [b]
	Overall (N=31)	1 = Much or Very Much Improved	21/31 (67,7)
		2 = Not Much or Very Much Improved	10/31 (32,3)
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=23)	1 = Much or Very Much Improved	9/23 (39,1)
		2 = Not Much or Very Much Improved	14/23 (60,9)
	Pre-cycle 5 (N=29)	1 = Much or Very Much Improved	14/29 (48,3)
		2 = Not Much or Very Much Improved	15/29 (51,7)
	Pre-cycle 9 (N=30)	1 = Much or Very Much Improved	13/30 (43,3)
		2 = Not Much or Very Much Improved	17/30 (56,7)
	Pre-cycle 13 (N=29)	1 = Much or Very Much Improved	17/29 (58,6)
		2 = Not Much or Very Much Improved	12/29 (41,4)
	Pre-cycle 25 (N=23)	1 = Much or Very Much Improved	16/23 (69,6)
		2 = Not Much or Very Much Improved	7/23 (30,4)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	4/ 4 (100,0)
		2 = Not Much or Very Much Improved	0
	Overall (N=31)	1 = Much or Very Much Improved	26/31 (83,9)
		2 = Not Much or Very Much Improved	5/31 (16,1)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.1 Distribution of Global Impression of Change self-report item responses - Gender = Male
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=14)	1 = Much or Very Much Improved	9/14 (64,3)
		2 = Not Much or Very Much Improved	5/14 (35,7)
	Pre-cycle 5 (N=18)	1 = Much or Very Much Improved	11/18 (61,1)
		2 = Not Much or Very Much Improved	7/18 (38,9)
	Pre-cycle 9 (N=18)	1 = Much or Very Much Improved	12/18 (66,7)
		2 = Not Much or Very Much Improved	6/18 (33,3)
	Pre-cycle 13 (N=18)	1 = Much or Very Much Improved	10/18 (55,6)
		2 = Not Much or Very Much Improved	8/18 (44,4)
	Pre-cycle 25 (N=14)	1 = Much or Very Much Improved	9/14 (64,3)
		2 = Not Much or Very Much Improved	5/14 (35,7)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	1/ 4 (25,0)
		2 = Not Much or Very Much Improved	3/ 4 (75,0)
	Overall (N=19)	1 = Much or Very Much Improved	16/19 (84,2)
		2 = Not Much or Very Much Improved	3/19 (15,8)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=18)	1 = Much or Very Much Improved	7/18 (38,9)
		2 = Not Much or Very Much Improved	11/18 (61,1)
	Pre-cycle 5 (N=18)	1 = Much or Very Much Improved	8/18 (44,4)
		2 = Not Much or Very Much Improved	10/18 (55,6)
	Pre-cycle 9 (N=18)	1 = Much or Very Much Improved	6/18 (33,3)
		2 = Not Much or Very Much Improved	12/18 (66,7)
	Pre-cycle 13 (N=18)	1 = Much or Very Much Improved	8/18 (44,4)
		2 = Not Much or Very Much Improved	10/18 (55,6)
	Pre-cycle 25 (N=14)	1 = Much or Very Much Improved	5/14 (35,7)
		2 = Not Much or Very Much Improved	9/14 (64,3)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	1/ 4 (25,0)
		2 = Not Much or Very Much Improved	3/ 4 (75,0)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.1 Distribution of Global Impression of Change self-report item responses - Gender = Male
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a] n/N (%) [b]
	Overall (N=19)	1 = Much or Very Much Improved	13/19 (68,4)
		2 = Not Much or Very Much Improved	6/19 (31,6)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.1 Distribution of Global Impression of Change self-report item responses - Gender = Male
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a] n/N (%) [b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=12)	1 = Much or Very Much Improved	7/12 (58,3)
		2 = Not Much or Very Much Improved	5/12 (41,7)
	Pre-cycle 5 (N=17)	1 = Much or Very Much Improved	10/17 (58,8)
		2 = Not Much or Very Much Improved	7/17 (41,2)
	Pre-cycle 9 (N=18)	1 = Much or Very Much Improved	9/18 (50,0)
		2 = Not Much or Very Much Improved	9/18 (50,0)
	Pre-cycle 13 (N=18)	1 = Much or Very Much Improved	13/18 (72,2)
		2 = Not Much or Very Much Improved	5/18 (27,8)
	Pre-cycle 25 (N=14)	1 = Much or Very Much Improved	10/14 (71,4)
		2 = Not Much or Very Much Improved	4/14 (28,6)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	4/ 4 (100,0)
		2 = Not Much or Very Much Improved	0
	Overall (N=19)	1 = Much or Very Much Improved	16/19 (84,2)
		2 = Not Much or Very Much Improved	3/19 (15,8)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.2 Distribution of Global Impression of Change self-report item responses - Gender = Female
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=13) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=12)	1 = Much or Very Much Improved	3/12 (25,0)
		2 = Not Much or Very Much Improved	9/12 (75,0)
	Pre-cycle 5 (N=12)	1 = Much or Very Much Improved	3/12 (25,0)
		2 = Not Much or Very Much Improved	9/12 (75,0)
	Pre-cycle 9 (N=12)	1 = Much or Very Much Improved	4/12 (33,3)
		2 = Not Much or Very Much Improved	8/12 (66,7)
	Pre-cycle 13 (N=11)	1 = Much or Very Much Improved	5/11 (45,5)
		2 = Not Much or Very Much Improved	6/11 (54,5)
	Pre-cycle 25 (N=9)	1 = Much or Very Much Improved	7/ 9 (77,8)
		2 = Not Much or Very Much Improved	2/ 9 (22,2)
	Overall (N=12)	1 = Much or Very Much Improved	8/12 (66,7)
		2 = Not Much or Very Much Improved	4/12 (33,3)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=12)	1 = Much or Very Much Improved	2/12 (16,7)
		2 = Not Much or Very Much Improved	10/12 (83,3)
	Pre-cycle 5 (N=12)	1 = Much or Very Much Improved	4/12 (33,3)
		2 = Not Much or Very Much Improved	8/12 (66,7)
	Pre-cycle 9 (N=12)	1 = Much or Very Much Improved	4/12 (33,3)
		2 = Not Much or Very Much Improved	8/12 (66,7)
	Pre-cycle 13 (N=11)	1 = Much or Very Much Improved	4/11 (36,4)
		2 = Not Much or Very Much Improved	7/11 (63,6)
	Pre-cycle 25 (N=9)	1 = Much or Very Much Improved	4/ 9 (44,4)
		2 = Not Much or Very Much Improved	5/ 9 (55,6)
	Overall (N=12)	1 = Much or Very Much Improved	8/12 (66,7)
		2 = Not Much or Very Much Improved	4/12 (33,3)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.2 Distribution of Global Impression of Change self-report item responses - Gender = Female
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=13) [a] n/N (%) [b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=11)	1 = Much or Very Much Improved	2/11 (18,2)
		2 = Not Much or Very Much Improved	9/11 (81,8)
	Pre-cycle 5 (N=12)	1 = Much or Very Much Improved	4/12 (33,3)
		2 = Not Much or Very Much Improved	8/12 (66,7)
	Pre-cycle 9 (N=12)	1 = Much or Very Much Improved	4/12 (33,3)
		2 = Not Much or Very Much Improved	8/12 (66,7)
	Pre-cycle 13 (N=11)	1 = Much or Very Much Improved	4/11 (36,4)
		2 = Not Much or Very Much Improved	7/11 (63,6)
	Pre-cycle 25 (N=9)	1 = Much or Very Much Improved	6/ 9 (66,7)
		2 = Not Much or Very Much Improved	3/ 9 (33,3)
	Overall (N=12)	1 = Much or Very Much Improved	10/12 (83,3)
		2 = Not Much or Very Much Improved	2/12 (16,7)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.3 Distribution of Global Impression of Change self-report item responses - PN status at enrollment = Progressive Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=8)	1 = Much or Very Much Improved	3/ 8 (37,5)
		2 = Not Much or Very Much Improved	5/ 8 (62,5)
	Pre-cycle 5 (N=10)	1 = Much or Very Much Improved	4/10 (40,0)
		2 = Not Much or Very Much Improved	6/10 (60,0)
	Pre-cycle 9 (N=11)	1 = Much or Very Much Improved	6/11 (54,5)
		2 = Not Much or Very Much Improved	5/11 (45,5)
	Pre-cycle 13 (N=10)	1 = Much or Very Much Improved	5/10 (50,0)
		2 = Not Much or Very Much Improved	5/10 (50,0)
	Pre-cycle 25 (N=6)	1 = Much or Very Much Improved	5/ 6 (83,3)
		2 = Not Much or Very Much Improved	1/ 6 (16,7)
	Pre-cycle 37 (N=3)	1 = Much or Very Much Improved	1/ 3 (33,3)
		2 = Not Much or Very Much Improved	2/ 3 (66,7)
	Overall (N=11)	1 = Much or Very Much Improved	9/11 (81,8)
		2 = Not Much or Very Much Improved	2/11 (18,2)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=10)	1 = Much or Very Much Improved	4/10 (40,0)
		2 = Not Much or Very Much Improved	6/10 (60,0)
	Pre-cycle 5 (N=10)	1 = Much or Very Much Improved	3/10 (30,0)
		2 = Not Much or Very Much Improved	7/10 (70,0)
	Pre-cycle 9 (N=11)	1 = Much or Very Much Improved	4/11 (36,4)
		2 = Not Much or Very Much Improved	7/11 (63,6)
	Pre-cycle 13 (N=10)	1 = Much or Very Much Improved	4/10 (40,0)
		2 = Not Much or Very Much Improved	6/10 (60,0)
	Pre-cycle 25 (N=6)	1 = Much or Very Much Improved	3/ 6 (50,0)
		2 = Not Much or Very Much Improved	3/ 6 (50,0)
	Pre-cycle 37 (N=3)	1 = Much or Very Much Improved	1/ 3 (33,3)
		2 = Not Much or Very Much Improved	2/ 3 (66,7)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit. Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.3 Distribution of Global Impression of Change self-report item responses - PN status at enrollment = Progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a] n/N (%) [b]
	Overall (N=11)	1 = Much or Very Much Improved	8/11 (72,7)
		2 = Not Much or Very Much Improved	3/11 (27,3)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.3 Distribution of Global Impression of Change self-report item responses - PN status at enrollment = Progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a] n/N (%) [b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=5)	1 = Much or Very Much Improved	3/ 5 (60,0)
		2 = Not Much or Very Much Improved	2/ 5 (40,0)
	Pre-cycle 5 (N=10)	1 = Much or Very Much Improved	6/10 (60,0)
		2 = Not Much or Very Much Improved	4/10 (40,0)
	Pre-cycle 9 (N=11)	1 = Much or Very Much Improved	6/11 (54,5)
		2 = Not Much or Very Much Improved	5/11 (45,5)
	Pre-cycle 13 (N=10)	1 = Much or Very Much Improved	7/10 (70,0)
		2 = Not Much or Very Much Improved	3/10 (30,0)
	Pre-cycle 25 (N=6)	1 = Much or Very Much Improved	6/ 6 (100,0)
		2 = Not Much or Very Much Improved	0
	Pre-cycle 37 (N=3)	1 = Much or Very Much Improved	3/ 3 (100,0)
		2 = Not Much or Very Much Improved	0
	Overall (N=11)	1 = Much or Very Much Improved	10/11 (90,9)
		2 = Not Much or Very Much Improved	1/11 (9,1)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.4 Distribution of Global Impression of Change self-report item responses - PN status at enrol. = Non-progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=9)	1 = Much or Very Much Improved	6/ 9 (66,7)
		2 = Not Much or Very Much Improved	3/ 9 (33,3)
	Pre-cycle 5 (N=10)	1 = Much or Very Much Improved	6/10 (60,0)
		2 = Not Much or Very Much Improved	4/10 (40,0)
	Pre-cycle 9 (N=9)	1 = Much or Very Much Improved	5/ 9 (55,6)
		2 = Not Much or Very Much Improved	4/ 9 (44,4)
	Pre-cycle 13 (N=9)	1 = Much or Very Much Improved	4/ 9 (44,4)
		2 = Not Much or Very Much Improved	5/ 9 (55,6)
	Pre-cycle 25 (N=9)	1 = Much or Very Much Improved	5/ 9 (55,6)
		2 = Not Much or Very Much Improved	4/ 9 (44,4)
	Pre-cycle 37 (N=1)	1 = Much or Very Much Improved	0
		2 = Not Much or Very Much Improved	1/ 1 (100,0)
	Overall (N=10)	1 = Much or Very Much Improved	7/10 (70,0)
		2 = Not Much or Very Much Improved	3/10 (30,0)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=10)	1 = Much or Very Much Improved	2/10 (20,0)
		2 = Not Much or Very Much Improved	8/10 (80,0)
	Pre-cycle 5 (N=10)	1 = Much or Very Much Improved	5/10 (50,0)
		2 = Not Much or Very Much Improved	5/10 (50,0)
	Pre-cycle 9 (N=9)	1 = Much or Very Much Improved	1/ 9 (11,1)
		2 = Not Much or Very Much Improved	8/ 9 (88,9)
	Pre-cycle 13 (N=9)	1 = Much or Very Much Improved	3/ 9 (33,3)
		2 = Not Much or Very Much Improved	6/ 9 (66,7)
	Pre-cycle 25 (N=9)	1 = Much or Very Much Improved	2/ 9 (22,2)
		2 = Not Much or Very Much Improved	7/ 9 (77,8)
	Pre-cycle 37 (N=1)	1 = Much or Very Much Improved	0
		2 = Not Much or Very Much Improved	1/ 1 (100,0)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.4 Distribution of Global Impression of Change self-report item responses - PN status at enrol. = Non-progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a] n/N (%) [b]
	Overall (N=10)	1 = Much or Very Much Improved	5/10 (50,0)
		2 = Not Much or Very Much Improved	5/10 (50,0)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.4 Distribution of Global Impression of Change self-report item responses - PN status at enrol. = Non-progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a] n/N (%) [b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=9)	1 = Much or Very Much Improved	3/ 9 (33,3)
		2 = Not Much or Very Much Improved	6/ 9 (66,7)
	Pre-cycle 5 (N=10)	1 = Much or Very Much Improved	4/10 (40,0)
		2 = Not Much or Very Much Improved	6/10 (60,0)
	Pre-cycle 9 (N=9)	1 = Much or Very Much Improved	4/ 9 (44,4)
		2 = Not Much or Very Much Improved	5/ 9 (55,6)
	Pre-cycle 13 (N=9)	1 = Much or Very Much Improved	6/ 9 (66,7)
		2 = Not Much or Very Much Improved	3/ 9 (33,3)
	Pre-cycle 25 (N=9)	1 = Much or Very Much Improved	4/ 9 (44,4)
		2 = Not Much or Very Much Improved	5/ 9 (55,6)
	Pre-cycle 37 (N=1)	1 = Much or Very Much Improved	1/ 1 (100,0)
		2 = Not Much or Very Much Improved	0
	Overall (N=10)	1 = Much or Very Much Improved	8/10 (80,0)
		2 = Not Much or Very Much Improved	2/10 (20,0)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.5 Distribution of Global Impression of Change self-report item responses - PN status at enrollment = Unknown
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=12) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=9)	1 = Much or Very Much Improved	3/ 9 (33,3)
		2 = Not Much or Very Much Improved	6/ 9 (66,7)
	Pre-cycle 5 (N=10)	1 = Much or Very Much Improved	4/10 (40,0)
		2 = Not Much or Very Much Improved	6/10 (60,0)
	Pre-cycle 9 (N=10)	1 = Much or Very Much Improved	5/10 (50,0)
		2 = Not Much or Very Much Improved	5/10 (50,0)
	Pre-cycle 13 (N=10)	1 = Much or Very Much Improved	6/10 (60,0)
		2 = Not Much or Very Much Improved	4/10 (40,0)
	Pre-cycle 25 (N=8)	1 = Much or Very Much Improved	6/ 8 (75,0)
		2 = Not Much or Very Much Improved	2/ 8 (25,0)
	Overall (N=10)	1 = Much or Very Much Improved	8/10 (80,0)
		2 = Not Much or Very Much Improved	2/10 (20,0)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=10)	1 = Much or Very Much Improved	3/10 (30,0)
		2 = Not Much or Very Much Improved	7/10 (70,0)
	Pre-cycle 5 (N=10)	1 = Much or Very Much Improved	4/10 (40,0)
		2 = Not Much or Very Much Improved	6/10 (60,0)
	Pre-cycle 9 (N=10)	1 = Much or Very Much Improved	5/10 (50,0)
		2 = Not Much or Very Much Improved	5/10 (50,0)
	Pre-cycle 13 (N=10)	1 = Much or Very Much Improved	5/10 (50,0)
		2 = Not Much or Very Much Improved	5/10 (50,0)
	Pre-cycle 25 (N=8)	1 = Much or Very Much Improved	4/ 8 (50,0)
		2 = Not Much or Very Much Improved	4/ 8 (50,0)
	Overall (N=10)	1 = Much or Very Much Improved	8/10 (80,0)
		2 = Not Much or Very Much Improved	2/10 (20,0)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.1.5 Distribution of Global Impression of Change self-report item responses - PN status at enrollment = Unknown
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=12) [a] n/N (%) [b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=9)	1 = Much or Very Much Improved	3/ 9 (33,3)
		2 = Not Much or Very Much Improved	6/ 9 (66,7)
	Pre-cycle 5 (N=9)	1 = Much or Very Much Improved	4/ 9 (44,4)
		2 = Not Much or Very Much Improved	5/ 9 (55,6)
	Pre-cycle 9 (N=10)	1 = Much or Very Much Improved	3/10 (30,0)
		2 = Not Much or Very Much Improved	7/10 (70,0)
	Pre-cycle 13 (N=10)	1 = Much or Very Much Improved	4/10 (40,0)
		2 = Not Much or Very Much Improved	6/10 (60,0)
	Pre-cycle 25 (N=8)	1 = Much or Very Much Improved	6/ 8 (75,0)
		2 = Not Much or Very Much Improved	2/ 8 (25,0)
	Overall (N=10)	1 = Much or Very Much Improved	8/10 (80,0)
		2 = Not Much or Very Much Improved	2/10 (20,0)

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.1.2.1 Distribution of Global Impression of Change self-report responses over time - Gender = Male
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=14)	1 = Very Much Improved	6/14 (42,9)
		2 = Much Improved	3/14 (21,4)
		3 = Minimally Improved	3/14 (21,4)
		4 = No Change	2/14 (14,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=18)	1 = Very Much Improved	6/18 (33,3)
		2 = Much Improved	5/18 (27,8)
		3 = Minimally Improved	2/18 (11,1)
		4 = No Change	4/18 (22,2)
		5 = Minimally Worse	1/18 (5,6)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=18)	1 = Very Much Improved	10/18 (55,6)
		2 = Much Improved	2/18 (11,1)
		3 = Minimally Improved	2/18 (11,1)
		4 = No Change	3/18 (16,7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	1/18 (5,6)
	Pre-cycle 13 (n=18)	1 = Very Much Improved	7/18 (38,9)
		2 = Much Improved	3/18 (16,7)
		3 = Minimally Improved	3/18 (16,7)
		4 = No Change	5/18 (27,8)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=14)	1 = Very Much Improved	7/14 (50,0)
		2 = Much Improved	2/14 (14,3)
		3 = Minimally Improved	0
		4 = No Change	5/14 (35,7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=4)	1 = Very Much Improved	1/ 4 (25,0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	3/ 4 (75,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.1 Distribution of Global Impression of Change self-report responses over time - Gender = Male
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=18)	1 = Very Much Improved	6/18 (33,3)
		2 = Much Improved	1/18 (5,6)
		3 = Minimally Improved	2/18 (11,1)
		4 = No Change	7/18 (38,9)
		5 = Minimally Worse	2/18 (11,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=18)	1 = Very Much Improved	5/18 (27,8)
		2 = Much Improved	3/18 (16,7)
		3 = Minimally Improved	2/18 (11,1)
		4 = No Change	6/18 (33,3)
		5 = Minimally Worse	1/18 (5,6)
		6 = Much Worse	1/18 (5,6)
		7 = Very Much Worse	0
	Pre-cycle 9 (n=18)	1 = Very Much Improved	4/18 (22,2)
		2 = Much Improved	2/18 (11,1)
		3 = Minimally Improved	6/18 (33,3)
		4 = No Change	4/18 (22,2)
		5 = Minimally Worse	2/18 (11,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=18)	1 = Very Much Improved	6/18 (33,3)
		2 = Much Improved	2/18 (11,1)
		3 = Minimally Improved	1/18 (5,6)
		4 = No Change	9/18 (50,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=14)	1 = Very Much Improved	4/14 (28,6)
		2 = Much Improved	1/14 (7,1)
		3 = Minimally Improved	4/14 (28,6)
		4 = No Change	5/14 (35,7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=4)	1 = Very Much Improved	1/ 4 (25,0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	2/ 4 (50,0)
		5 = Minimally Worse	1/ 4 (25,0)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.1 Distribution of Global Impression of Change self-report responses over time - Gender = Male
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=12)	1 = Very Much Improved	3/12 (25,0)
		2 = Much Improved	4/12 (33,3)
		3 = Minimally Improved	2/12 (16,7)
		4 = No Change	2/12 (16,7)
		5 = Minimally Worse	1/12 (8,3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=17)	1 = Very Much Improved	6/17 (35,3)
		2 = Much Improved	4/17 (23,5)
		3 = Minimally Improved	4/17 (23,5)
		4 = No Change	3/17 (17,6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=18)	1 = Very Much Improved	7/18 (38,9)
		2 = Much Improved	2/18 (11,1)
		3 = Minimally Improved	4/18 (22,2)
		4 = No Change	5/18 (27,8)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=18)	1 = Very Much Improved	9/18 (50,0)
		2 = Much Improved	4/18 (22,2)
		3 = Minimally Improved	1/18 (5,6)
		4 = No Change	3/18 (16,7)
		5 = Minimally Worse	1/18 (5,6)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=14)	1 = Very Much Improved	6/14 (42,9)
		2 = Much Improved	4/14 (28,6)
		3 = Minimally Improved	2/14 (14,3)
		4 = No Change	2/14 (14,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=4)	1 = Very Much Improved	4/ 4 (100,0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.2 Distribution of Global Impression of Change self-report responses over time - Gender = Female
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=13) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=12)	1 = Very Much Improved	1/12 (8,3)
		2 = Much Improved	2/12 (16,7)
		3 = Minimally Improved	3/12 (25,0)
		4 = No Change	5/12 (41,7)
		5 = Minimally Worse	1/12 (8,3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=12)	1 = Very Much Improved	0
		2 = Much Improved	3/12 (25,0)
		3 = Minimally Improved	3/12 (25,0)
		4 = No Change	6/12 (50,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=12)	1 = Very Much Improved	3/12 (25,0)
		2 = Much Improved	1/12 (8,3)
		3 = Minimally Improved	2/12 (16,7)
		4 = No Change	6/12 (50,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=11)	1 = Very Much Improved	3/11 (27,3)
		2 = Much Improved	2/11 (18,2)
		3 = Minimally Improved	4/11 (36,4)
		4 = No Change	1/11 (9,1)
		5 = Minimally Worse	1/11 (9,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=9)	1 = Very Much Improved	4/ 9 (44,4)
		2 = Much Improved	3/ 9 (33,3)
		3 = Minimally Improved	1/ 9 (11,1)
		4 = No Change	1/ 9 (11,1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.2 Distribution of Global Impression of Change self-report responses over time - Gender = Female
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=13) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=12)	1 = Very Much Improved	0
		2 = Much Improved	2/12 (16,7)
		3 = Minimally Improved	4/12 (33,3)
		4 = No Change	5/12 (41,7)
		5 = Minimally Worse	1/12 (8,3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=12)	1 = Very Much Improved	1/12 (8,3)
		2 = Much Improved	3/12 (25,0)
		3 = Minimally Improved	2/12 (16,7)
		4 = No Change	6/12 (50,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=12)	1 = Very Much Improved	0
		2 = Much Improved	4/12 (33,3)
		3 = Minimally Improved	3/12 (25,0)
		4 = No Change	4/12 (33,3)
		5 = Minimally Worse	1/12 (8,3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=11)	1 = Very Much Improved	0
		2 = Much Improved	4/11 (36,4)
		3 = Minimally Improved	4/11 (36,4)
		4 = No Change	3/11 (27,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=9)	1 = Very Much Improved	2/ 9 (22,2)
		2 = Much Improved	2/ 9 (22,2)
		3 = Minimally Improved	2/ 9 (22,2)
		4 = No Change	3/ 9 (33,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.2 Distribution of Global Impression of Change self-report responses over time - Gender = Female
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=13) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=11)	1 = Very Much Improved	1/11 (9,1)
		2 = Much Improved	1/11 (9,1)
		3 = Minimally Improved	5/11 (45,5)
		4 = No Change	4/11 (36,4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=12)	1 = Very Much Improved	1/12 (8,3)
		2 = Much Improved	3/12 (25,0)
		3 = Minimally Improved	4/12 (33,3)
		4 = No Change	4/12 (33,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=12)	1 = Very Much Improved	1/12 (8,3)
		2 = Much Improved	3/12 (25,0)
		3 = Minimally Improved	4/12 (33,3)
		4 = No Change	4/12 (33,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=11)	1 = Very Much Improved	1/11 (9,1)
		2 = Much Improved	3/11 (27,3)
		3 = Minimally Improved	3/11 (27,3)
		4 = No Change	4/11 (36,4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=9)	1 = Very Much Improved	2/ 9 (22,2)
		2 = Much Improved	4/ 9 (44,4)
		3 = Minimally Improved	1/ 9 (11,1)
		4 = No Change	2/ 9 (22,2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.3 Distribution of Global Impression of Change self-report responses over time PN status at enrol. = Progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=8)	1 = Very Much Improved	1/ 8 (12,5)
		2 = Much Improved	2/ 8 (25,0)
		3 = Minimally Improved	2/ 8 (25,0)
		4 = No Change	3/ 8 (37,5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	2/10 (20,0)
		2 = Much Improved	2/10 (20,0)
		3 = Minimally Improved	1/10 (10,0)
		4 = No Change	4/10 (40,0)
		5 = Minimally Worse	1/10 (10,0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=11)	1 = Very Much Improved	4/11 (36,4)
		2 = Much Improved	2/11 (18,2)
		3 = Minimally Improved	1/11 (9,1)
		4 = No Change	3/11 (27,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	1/11 (9,1)
	Pre-cycle 13 (n=10)	1 = Very Much Improved	3/10 (30,0)
		2 = Much Improved	2/10 (20,0)
		3 = Minimally Improved	4/10 (40,0)
		4 = No Change	1/10 (10,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=6)	1 = Very Much Improved	4/ 6 (66,7)
		2 = Much Improved	1/ 6 (16,7)
		3 = Minimally Improved	0
		4 = No Change	1/ 6 (16,7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=3)	1 = Very Much Improved	1/ 3 (33,3)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	2/ 3 (66,7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.3 Distribution of Global Impression of Change self-report responses over time PN status at enrol. = Progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Very Much Improved	2/10 (20,0)
		2 = Much Improved	2/10 (20,0)
		3 = Minimally Improved	0
		4 = No Change	5/10 (50,0)
		5 = Minimally Worse	1/10 (10,0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	2/10 (20,0)
		2 = Much Improved	1/10 (10,0)
		3 = Minimally Improved	1/10 (10,0)
		4 = No Change	5/10 (50,0)
		5 = Minimally Worse	0
		6 = Much Worse	1/10 (10,0)
		7 = Very Much Worse	0
	Pre-cycle 9 (n=11)	1 = Very Much Improved	2/11 (18,2)
		2 = Much Improved	2/11 (18,2)
		3 = Minimally Improved	3/11 (27,3)
		4 = No Change	3/11 (27,3)
		5 = Minimally Worse	1/11 (9,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=10)	1 = Very Much Improved	2/10 (20,0)
		2 = Much Improved	2/10 (20,0)
		3 = Minimally Improved	2/10 (20,0)
		4 = No Change	4/10 (40,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=6)	1 = Very Much Improved	2/ 6 (33,3)
		2 = Much Improved	1/ 6 (16,7)
		3 = Minimally Improved	1/ 6 (16,7)
		4 = No Change	2/ 6 (33,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=3)	1 = Very Much Improved	1/ 3 (33,3)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1/ 3 (33,3)
		5 = Minimally Worse	1/ 3 (33,3)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.3 Distribution of Global Impression of Change self-report responses over time PN status at enrol. = Progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=5)	1 = Very Much Improved	1/ 5 (20,0)
		2 = Much Improved	2/ 5 (40,0)
		3 = Minimally Improved	0
		4 = No Change	1/ 5 (20,0)
		5 = Minimally Worse	1/ 5 (20,0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	5/10 (50,0)
		2 = Much Improved	1/10 (10,0)
		3 = Minimally Improved	2/10 (20,0)
		4 = No Change	2/10 (20,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=11)	1 = Very Much Improved	4/11 (36,4)
		2 = Much Improved	2/11 (18,2)
		3 = Minimally Improved	2/11 (18,2)
		4 = No Change	3/11 (27,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=10)	1 = Very Much Improved	5/10 (50,0)
		2 = Much Improved	2/10 (20,0)
		3 = Minimally Improved	1/10 (10,0)
		4 = No Change	1/10 (10,0)
		5 = Minimally Worse	1/10 (10,0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=6)	1 = Very Much Improved	4/ 6 (66,7)
		2 = Much Improved	2/ 6 (33,3)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=3)	1 = Very Much Improved	3/ 3 (100,0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.4 Distribution of Global Impression of Change self-report responses over time PN status at enrol. = Non-progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=9)	1 = Very Much Improved	3/ 9 (33,3)
		2 = Much Improved	3/ 9 (33,3)
		3 = Minimally Improved	1/ 9 (11,1)
		4 = No Change	2/ 9 (22,2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	3/10 (30,0)
		2 = Much Improved	3/10 (30,0)
		3 = Minimally Improved	2/10 (20,0)
		4 = No Change	2/10 (20,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=9)	1 = Very Much Improved	4/ 9 (44,4)
		2 = Much Improved	1/ 9 (11,1)
		3 = Minimally Improved	2/ 9 (22,2)
		4 = No Change	2/ 9 (22,2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=9)	1 = Very Much Improved	2/ 9 (22,2)
		2 = Much Improved	2/ 9 (22,2)
		3 = Minimally Improved	0
		4 = No Change	4/ 9 (44,4)
		5 = Minimally Worse	1/ 9 (11,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=9)	1 = Very Much Improved	3/ 9 (33,3)
		2 = Much Improved	2/ 9 (22,2)
		3 = Minimally Improved	0
		4 = No Change	4/ 9 (44,4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=1)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1/ 1 (100,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.4 Distribution of Global Impression of Change self-report responses over time PN status at enrol. = Non-progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Very Much Improved	2/10 (20,0)
		2 = Much Improved	0
		3 = Minimally Improved	3/10 (30,0)
		4 = No Change	4/10 (40,0)
		5 = Minimally Worse	1/10 (10,0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	1/10 (10,0)
		2 = Much Improved	4/10 (40,0)
		3 = Minimally Improved	1/10 (10,0)
		4 = No Change	3/10 (30,0)
		5 = Minimally Worse	1/10 (10,0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=9)	1 = Very Much Improved	1/ 9 (11,1)
		2 = Much Improved	0
		3 = Minimally Improved	4/ 9 (44,4)
		4 = No Change	2/ 9 (22,2)
		5 = Minimally Worse	2/ 9 (22,2)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=9)	1 = Very Much Improved	2/ 9 (22,2)
		2 = Much Improved	1/ 9 (11,1)
		3 = Minimally Improved	1/ 9 (11,1)
		4 = No Change	5/ 9 (55,6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=9)	1 = Very Much Improved	2/ 9 (22,2)
		2 = Much Improved	0
		3 = Minimally Improved	2/ 9 (22,2)
		4 = No Change	5/ 9 (55,6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=1)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1/ 1 (100,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.4 Distribution of Global Impression of Change self-report responses over time PN status at enrol. = Non-progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=9)	1 = Very Much Improved	1/ 9 (11,1)
		2 = Much Improved	2/ 9 (22,2)
		3 = Minimally Improved	4/ 9 (44,4)
		4 = No Change	2/ 9 (22,2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	1/10 (10,0)
		2 = Much Improved	3/10 (30,0)
		3 = Minimally Improved	3/10 (30,0)
		4 = No Change	3/10 (30,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=9)	1 = Very Much Improved	2/ 9 (22,2)
		2 = Much Improved	2/ 9 (22,2)
		3 = Minimally Improved	4/ 9 (44,4)
		4 = No Change	1/ 9 (11,1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=9)	1 = Very Much Improved	3/ 9 (33,3)
		2 = Much Improved	3/ 9 (33,3)
		3 = Minimally Improved	0
		4 = No Change	3/ 9 (33,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=9)	1 = Very Much Improved	2/ 9 (22,2)
		2 = Much Improved	2/ 9 (22,2)
		3 = Minimally Improved	3/ 9 (33,3)
		4 = No Change	2/ 9 (22,2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=1)	1 = Very Much Improved	1/ 1 (100,0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.5 Distribution of Global Impression of Change self-report responses over time PN status at enrol. = Unknown
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=12) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=9)	1 = Very Much Improved	3/ 9 (33,3)
		2 = Much Improved	0
		3 = Minimally Improved	3/ 9 (33,3)
		4 = No Change	2/ 9 (22,2)
		5 = Minimally Worse	1/ 9 (11,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	1/10 (10,0)
		2 = Much Improved	3/10 (30,0)
		3 = Minimally Improved	2/10 (20,0)
		4 = No Change	4/10 (40,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=10)	1 = Very Much Improved	5/10 (50,0)
		2 = Much Improved	0
		3 = Minimally Improved	1/10 (10,0)
		4 = No Change	4/10 (40,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=10)	1 = Very Much Improved	5/10 (50,0)
		2 = Much Improved	1/10 (10,0)
		3 = Minimally Improved	3/10 (30,0)
		4 = No Change	1/10 (10,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=8)	1 = Very Much Improved	4/ 8 (50,0)
		2 = Much Improved	2/ 8 (25,0)
		3 = Minimally Improved	1/ 8 (12,5)
		4 = No Change	1/ 8 (12,5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.5 Distribution of Global Impression of Change self-report responses over time PN status at enrol. = Unknown
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=12) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Very Much Improved	2/10 (20,0)
		2 = Much Improved	1/10 (10,0)
		3 = Minimally Improved	3/10 (30,0)
		4 = No Change	3/10 (30,0)
		5 = Minimally Worse	1/10 (10,0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	3/10 (30,0)
		2 = Much Improved	1/10 (10,0)
		3 = Minimally Improved	2/10 (20,0)
		4 = No Change	4/10 (40,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=10)	1 = Very Much Improved	1/10 (10,0)
		2 = Much Improved	4/10 (40,0)
		3 = Minimally Improved	2/10 (20,0)
		4 = No Change	3/10 (30,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=10)	1 = Very Much Improved	2/10 (20,0)
		2 = Much Improved	3/10 (30,0)
		3 = Minimally Improved	2/10 (20,0)
		4 = No Change	3/10 (30,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=8)	1 = Very Much Improved	2/ 8 (25,0)
		2 = Much Improved	2/ 8 (25,0)
		3 = Minimally Improved	3/ 8 (37,5)
		4 = No Change	1/ 8 (12,5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.1.2.5 Distribution of Global Impression of Change self-report responses over time PN status at enrol. = Unknown
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=12) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=9)	1 = Very Much Improved	2/ 9 (22,2)
		2 = Much Improved	1/ 9 (11,1)
		3 = Minimally Improved	3/ 9 (33,3)
		4 = No Change	3/ 9 (33,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=9)	1 = Very Much Improved	1/ 9 (11,1)
		2 = Much Improved	3/ 9 (33,3)
		3 = Minimally Improved	3/ 9 (33,3)
		4 = No Change	2/ 9 (22,2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=10)	1 = Very Much Improved	2/10 (20,0)
		2 = Much Improved	1/10 (10,0)
		3 = Minimally Improved	2/10 (20,0)
		4 = No Change	5/10 (50,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=10)	1 = Very Much Improved	2/10 (20,0)
		2 = Much Improved	2/10 (20,0)
		3 = Minimally Improved	3/10 (30,0)
		4 = No Change	3/10 (30,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=8)	1 = Very Much Improved	2/ 8 (25,0)
		2 = Much Improved	4/ 8 (50,0)
		3 = Minimally Improved	0
		4 = No Change	2/ 8 (25,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.1.2 Distribution of Global Impression of Change parent-report item responses over time
Patients with much or very much improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=48) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=38)	1 = Much or Very Much Improved	9/38 (23,7)
		2 = Not Much or Very Much Improved	29/38 (76,3)
	Pre-cycle 5 (N=44)	1 = Much or Very Much Improved	16/44 (36,4)
		2 = Not Much or Very Much Improved	28/44 (63,6)
	Pre-cycle 9 (N=45)	1 = Much or Very Much Improved	23/45 (51,1)
		2 = Not Much or Very Much Improved	22/45 (48,9)
	Pre-cycle 13 (N=43)	1 = Much or Very Much Improved	25/43 (58,1)
		2 = Not Much or Very Much Improved	18/43 (41,9)
	Pre-cycle 25 (N=34)	1 = Much or Very Much Improved	20/34 (58,8)
		2 = Not Much or Very Much Improved	14/34 (41,2)
	Pre-cycle 37 (N=5)	1 = Much or Very Much Improved	2/ 5 (40,0)
		2 = Not Much or Very Much Improved	3/ 5 (60,0)
	Overall (N=46)	1 = Much or Very Much Improved	32/46 (69,6)
		2 = Not Much or Very Much Improved	14/46 (30,4)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=44)	1 = Much or Very Much Improved	10/44 (22,7)
		2 = Not Much or Very Much Improved	34/44 (77,3)
	Pre-cycle 5 (N=44)	1 = Much or Very Much Improved	17/44 (38,6)
		2 = Not Much or Very Much Improved	27/44 (61,4)
	Pre-cycle 9 (N=45)	1 = Much or Very Much Improved	21/45 (46,7)
		2 = Not Much or Very Much Improved	24/45 (53,3)
	Pre-cycle 13 (N=43)	1 = Much or Very Much Improved	22/43 (51,2)
		2 = Not Much or Very Much Improved	21/43 (48,8)
	Pre-cycle 25 (N=34)	1 = Much or Very Much Improved	18/34 (52,9)
		2 = Not Much or Very Much Improved	16/34 (47,1)
	Pre-cycle 37 (N=5)	1 = Much or Very Much Improved	3/ 5 (60,0)
		2 = Not Much or Very Much Improved	2/ 5 (40,0)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2 Distribution of Global Impression of Change parent-report item responses over time
Patients with much or very much improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=48) [a] n/N (%) [b]
	Overall (N=46)	1 = Much or Very Much Improved	30/46 (65,2)
		2 = Not Much or Very Much Improved	16/46 (34,8)
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=34)	1 = Much or Very Much Improved	6/34 (17,6)
		2 = Not Much or Very Much Improved	28/34 (82,4)
	Pre-cycle 5 (N=43)	1 = Much or Very Much Improved	15/43 (34,9)
		2 = Not Much or Very Much Improved	28/43 (65,1)
	Pre-cycle 9 (N=45)	1 = Much or Very Much Improved	28/45 (62,2)
		2 = Not Much or Very Much Improved	17/45 (37,8)
	Pre-cycle 13 (N=43)	1 = Much or Very Much Improved	31/43 (72,1)
		2 = Not Much or Very Much Improved	12/43 (27,9)
	Pre-cycle 25 (N=34)	1 = Much or Very Much Improved	24/34 (70,6)
		2 = Not Much or Very Much Improved	10/34 (29,4)
	Pre-cycle 37 (N=5)	1 = Much or Very Much Improved	5/ 5 (100,0)
		2 = Not Much or Very Much Improved	0
	Overall (N=46)	1 = Much or Very Much Improved	36/46 (78,3)
		2 = Not Much or Very Much Improved	10/46 (21,7)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.1 Distribution of Global Impression of Change parent-report item responses - Gender = Male
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=28) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=20)	1 = Much or Very Much Improved	6/20 (30,0)
		2 = Not Much or Very Much Improved	14/20 (70,0)
	Pre-cycle 5 (N=26)	1 = Much or Very Much Improved	10/26 (38,5)
		2 = Not Much or Very Much Improved	16/26 (61,5)
	Pre-cycle 9 (N=26)	1 = Much or Very Much Improved	12/26 (46,2)
		2 = Not Much or Very Much Improved	14/26 (53,8)
	Pre-cycle 13 (N=26)	1 = Much or Very Much Improved	13/26 (50,0)
		2 = Not Much or Very Much Improved	13/26 (50,0)
	Pre-cycle 25 (N=19)	1 = Much or Very Much Improved	11/19 (57,9)
		2 = Not Much or Very Much Improved	8/19 (42,1)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	2/ 4 (50,0)
		2 = Not Much or Very Much Improved	2/ 4 (50,0)
	Overall (N=27)	1 = Much or Very Much Improved	18/27 (66,7)
		2 = Not Much or Very Much Improved	9/27 (33,3)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=25)	1 = Much or Very Much Improved	7/25 (28,0)
		2 = Not Much or Very Much Improved	18/25 (72,0)
	Pre-cycle 5 (N=26)	1 = Much or Very Much Improved	10/26 (38,5)
		2 = Not Much or Very Much Improved	16/26 (61,5)
	Pre-cycle 9 (N=26)	1 = Much or Very Much Improved	12/26 (46,2)
		2 = Not Much or Very Much Improved	14/26 (53,8)
	Pre-cycle 13 (N=26)	1 = Much or Very Much Improved	10/26 (38,5)
		2 = Not Much or Very Much Improved	16/26 (61,5)
	Pre-cycle 25 (N=19)	1 = Much or Very Much Improved	9/19 (47,4)
		2 = Not Much or Very Much Improved	10/19 (52,6)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	3/ 4 (75,0)
		2 = Not Much or Very Much Improved	1/ 4 (25,0)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.1 Distribution of Global Impression of Change parent-report item responses - Gender = Male
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=28) [a] n/N (%) [b]
	Overall (N=27)	1 = Much or Very Much Improved	16/27 (59,3)
		2 = Not Much or Very Much Improved	11/27 (40,7)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.1 Distribution of Global Impression of Change parent-report item responses - Gender = Male
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=28) [a] n/N (%) [b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=18)	1 = Much or Very Much Improved	5/18 (27,8)
		2 = Not Much or Very Much Improved	13/18 (72,2)
	Pre-cycle 5 (N=25)	1 = Much or Very Much Improved	11/25 (44,0)
		2 = Not Much or Very Much Improved	14/25 (56,0)
	Pre-cycle 9 (N=26)	1 = Much or Very Much Improved	19/26 (73,1)
		2 = Not Much or Very Much Improved	7/26 (26,9)
	Pre-cycle 13 (N=26)	1 = Much or Very Much Improved	19/26 (73,1)
		2 = Not Much or Very Much Improved	7/26 (26,9)
	Pre-cycle 25 (N=19)	1 = Much or Very Much Improved	14/19 (73,7)
		2 = Not Much or Very Much Improved	5/19 (26,3)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	4/ 4 (100,0)
		2 = Not Much or Very Much Improved	0
	Overall (N=27)	1 = Much or Very Much Improved	22/27 (81,5)
		2 = Not Much or Very Much Improved	5/27 (18,5)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.2 Distribution of Global Impression of Change parent-report item responses - Gender = Female
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=18)	1 = Much or Very Much Improved	3/18 (16,7)
		2 = Not Much or Very Much Improved	15/18 (83,3)
	Pre-cycle 5 (N=18)	1 = Much or Very Much Improved	6/18 (33,3)
		2 = Not Much or Very Much Improved	12/18 (66,7)
	Pre-cycle 9 (N=19)	1 = Much or Very Much Improved	11/19 (57,9)
		2 = Not Much or Very Much Improved	8/19 (42,1)
	Pre-cycle 13 (N=17)	1 = Much or Very Much Improved	12/17 (70,6)
		2 = Not Much or Very Much Improved	5/17 (29,4)
	Pre-cycle 25 (N=15)	1 = Much or Very Much Improved	9/15 (60,0)
		2 = Not Much or Very Much Improved	6/15 (40,0)
	Pre-cycle 37 (N=1)	1 = Much or Very Much Improved	0
		2 = Not Much or Very Much Improved	1/ 1 (100,0)
	Overall (N=19)	1 = Much or Very Much Improved	14/19 (73,7)
		2 = Not Much or Very Much Improved	5/19 (26,3)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=19)	1 = Much or Very Much Improved	3/19 (15,8)
		2 = Not Much or Very Much Improved	16/19 (84,2)
	Pre-cycle 5 (N=18)	1 = Much or Very Much Improved	7/18 (38,9)
		2 = Not Much or Very Much Improved	11/18 (61,1)
	Pre-cycle 9 (N=19)	1 = Much or Very Much Improved	9/19 (47,4)
		2 = Not Much or Very Much Improved	10/19 (52,6)
	Pre-cycle 13 (N=17)	1 = Much or Very Much Improved	12/17 (70,6)
		2 = Not Much or Very Much Improved	5/17 (29,4)
	Pre-cycle 25 (N=15)	1 = Much or Very Much Improved	9/15 (60,0)
		2 = Not Much or Very Much Improved	6/15 (40,0)
	Pre-cycle 37 (N=1)	1 = Much or Very Much Improved	0
		2 = Not Much or Very Much Improved	1/ 1 (100,0)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.2 Distribution of Global Impression of Change parent-report item responses - Gender = Female
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a] n/N (%) [b]
	Overall (N=19)	1 = Much or Very Much Improved	14/19 (73,7)
		2 = Not Much or Very Much Improved	5/19 (26,3)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.2 Distribution of Global Impression of Change parent-report item responses - Gender = Female
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a] n/N (%) [b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=16)	1 = Much or Very Much Improved	1/16 (6,3)
		2 = Not Much or Very Much Improved	15/16 (93,8)
	Pre-cycle 5 (N=18)	1 = Much or Very Much Improved	4/18 (22,2)
		2 = Not Much or Very Much Improved	14/18 (77,8)
	Pre-cycle 9 (N=19)	1 = Much or Very Much Improved	9/19 (47,4)
		2 = Not Much or Very Much Improved	10/19 (52,6)
	Pre-cycle 13 (N=17)	1 = Much or Very Much Improved	12/17 (70,6)
		2 = Not Much or Very Much Improved	5/17 (29,4)
	Pre-cycle 25 (N=15)	1 = Much or Very Much Improved	10/15 (66,7)
		2 = Not Much or Very Much Improved	5/15 (33,3)
	Pre-cycle 37 (N=1)	1 = Much or Very Much Improved	1/ 1 (100,0)
		2 = Not Much or Very Much Improved	0
	Overall (N=19)	1 = Much or Very Much Improved	14/19 (73,7)
		2 = Not Much or Very Much Improved	5/19 (26,3)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.3 Distribution of Global Impression of Change parent-report item responses - PN status at enrol. = Progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=15)	1 = Much or Very Much Improved	3/15 (20,0)
		2 = Not Much or Very Much Improved	12/15 (80,0)
	Pre-cycle 5 (N=18)	1 = Much or Very Much Improved	6/18 (33,3)
		2 = Not Much or Very Much Improved	12/18 (66,7)
	Pre-cycle 9 (N=20)	1 = Much or Very Much Improved	8/20 (40,0)
		2 = Not Much or Very Much Improved	12/20 (60,0)
	Pre-cycle 13 (N=19)	1 = Much or Very Much Improved	9/19 (47,4)
		2 = Not Much or Very Much Improved	10/19 (52,6)
	Pre-cycle 25 (N=13)	1 = Much or Very Much Improved	8/13 (61,5)
		2 = Not Much or Very Much Improved	5/13 (38,5)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	2/ 4 (50,0)
		2 = Not Much or Very Much Improved	2/ 4 (50,0)
	Overall (N=20)	1 = Much or Very Much Improved	14/20 (70,0)
		2 = Not Much or Very Much Improved	6/20 (30,0)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=19)	1 = Much or Very Much Improved	4/19 (21,1)
		2 = Not Much or Very Much Improved	15/19 (78,9)
	Pre-cycle 5 (N=18)	1 = Much or Very Much Improved	6/18 (33,3)
		2 = Not Much or Very Much Improved	12/18 (66,7)
	Pre-cycle 9 (N=20)	1 = Much or Very Much Improved	7/20 (35,0)
		2 = Not Much or Very Much Improved	13/20 (65,0)
	Pre-cycle 13 (N=19)	1 = Much or Very Much Improved	7/19 (36,8)
		2 = Not Much or Very Much Improved	12/19 (63,2)
	Pre-cycle 25 (N=13)	1 = Much or Very Much Improved	6/13 (46,2)
		2 = Not Much or Very Much Improved	7/13 (53,8)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	3/ 4 (75,0)
		2 = Not Much or Very Much Improved	1/ 4 (25,0)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.3 Distribution of Global Impression of Change parent-report item responses - PN status at enrol. = Progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a] n/N (%) [b]
	Overall (N=20)	1 = Much or Very Much Improved	12/20 (60,0)
		2 = Not Much or Very Much Improved	8/20 (40,0)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.3 Distribution of Global Impression of Change parent-report item responses - PN status at enrol. = Progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a] n/N (%) [b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=11)	1 = Much or Very Much Improved	2/11 (18,2)
		2 = Not Much or Very Much Improved	9/11 (81,8)
	Pre-cycle 5 (N=18)	1 = Much or Very Much Improved	7/18 (38,9)
		2 = Not Much or Very Much Improved	11/18 (61,1)
	Pre-cycle 9 (N=20)	1 = Much or Very Much Improved	14/20 (70,0)
		2 = Not Much or Very Much Improved	6/20 (30,0)
	Pre-cycle 13 (N=19)	1 = Much or Very Much Improved	15/19 (78,9)
		2 = Not Much or Very Much Improved	4/19 (21,1)
	Pre-cycle 25 (N=13)	1 = Much or Very Much Improved	11/13 (84,6)
		2 = Not Much or Very Much Improved	2/13 (15,4)
	Pre-cycle 37 (N=4)	1 = Much or Very Much Improved	4/ 4 (100,0)
		2 = Not Much or Very Much Improved	0
	Overall (N=20)	1 = Much or Very Much Improved	17/20 (85,0)
		2 = Not Much or Very Much Improved	3/20 (15,0)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.4 Distribution of Global Impression of Change parent-report item responses - PN status at enrol. = Non-progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=12)	1 = Much or Very Much Improved	3/12 (25,0)
		2 = Not Much or Very Much Improved	9/12 (75,0)
	Pre-cycle 5 (N=13)	1 = Much or Very Much Improved	6/13 (46,2)
		2 = Not Much or Very Much Improved	7/13 (53,8)
	Pre-cycle 9 (N=12)	1 = Much or Very Much Improved	7/12 (58,3)
		2 = Not Much or Very Much Improved	5/12 (41,7)
	Pre-cycle 13 (N=11)	1 = Much or Very Much Improved	7/11 (63,6)
		2 = Not Much or Very Much Improved	4/11 (36,4)
	Pre-cycle 25 (N=11)	1 = Much or Very Much Improved	6/11 (54,5)
		2 = Not Much or Very Much Improved	5/11 (45,5)
	Pre-cycle 37 (N=1)	1 = Much or Very Much Improved	0
		2 = Not Much or Very Much Improved	1/ 1 (100,0)
	Overall (N=13)	1 = Much or Very Much Improved	8/13 (61,5)
		2 = Not Much or Very Much Improved	5/13 (38,5)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=13)	1 = Much or Very Much Improved	3/13 (23,1)
		2 = Not Much or Very Much Improved	10/13 (76,9)
	Pre-cycle 5 (N=13)	1 = Much or Very Much Improved	6/13 (46,2)
		2 = Not Much or Very Much Improved	7/13 (53,8)
	Pre-cycle 9 (N=12)	1 = Much or Very Much Improved	5/12 (41,7)
		2 = Not Much or Very Much Improved	7/12 (58,3)
	Pre-cycle 13 (N=11)	1 = Much or Very Much Improved	6/11 (54,5)
		2 = Not Much or Very Much Improved	5/11 (45,5)
	Pre-cycle 25 (N=11)	1 = Much or Very Much Improved	6/11 (54,5)
		2 = Not Much or Very Much Improved	5/11 (45,5)
	Pre-cycle 37 (N=1)	1 = Much or Very Much Improved	0
		2 = Not Much or Very Much Improved	1/ 1 (100,0)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.4 Distribution of Global Impression of Change parent-report item responses - PN status at enrol. = Non-progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a] n/N (%) [b]
	Overall (N=13)	1 = Much or Very Much Improved	8/13 (61,5)
		2 = Not Much or Very Much Improved	5/13 (38,5)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.4 Distribution of Global Impression of Change parent-report item responses - PN status at enrol. = Non-progressive
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a] n/N (%) [b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=12)	1 = Much or Very Much Improved	1/12 (8,3)
		2 = Not Much or Very Much Improved	11/12 (91,7)
	Pre-cycle 5 (N=13)	1 = Much or Very Much Improved	4/13 (30,8)
		2 = Not Much or Very Much Improved	9/13 (69,2)
	Pre-cycle 9 (N=12)	1 = Much or Very Much Improved	8/12 (66,7)
		2 = Not Much or Very Much Improved	4/12 (33,3)
	Pre-cycle 13 (N=11)	1 = Much or Very Much Improved	8/11 (72,7)
		2 = Not Much or Very Much Improved	3/11 (27,3)
	Pre-cycle 25 (N=11)	1 = Much or Very Much Improved	8/11 (72,7)
		2 = Not Much or Very Much Improved	3/11 (27,3)
	Pre-cycle 37 (N=1)	1 = Much or Very Much Improved	1/ 1 (100,0)
		2 = Not Much or Very Much Improved	0
	Overall (N=13)	1 = Much or Very Much Improved	11/13 (84,6)
		2 = Not Much or Very Much Improved	2/13 (15,4)

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.5 Distribution of Global Impression of Change parent-report item responses - PN status at enrol. = Unknown
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a] n/N (%) [b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (N=11)	1 = Much or Very Much Improved	3/11 (27,3)
		2 = Not Much or Very Much Improved	8/11 (72,7)
	Pre-cycle 5 (N=13)	1 = Much or Very Much Improved	4/13 (30,8)
		2 = Not Much or Very Much Improved	9/13 (69,2)
	Pre-cycle 9 (N=13)	1 = Much or Very Much Improved	8/13 (61,5)
		2 = Not Much or Very Much Improved	5/13 (38,5)
	Pre-cycle 13 (N=13)	1 = Much or Very Much Improved	9/13 (69,2)
		2 = Not Much or Very Much Improved	4/13 (30,8)
	Pre-cycle 25 (N=10)	1 = Much or Very Much Improved	6/10 (60,0)
		2 = Not Much or Very Much Improved	4/10 (40,0)
	Overall (N=13)	1 = Much or Very Much Improved	10/13 (76,9)
		2 = Not Much or Very Much Improved	3/13 (23,1)
Item 2: Overall Pain, n (%)	Pre-cycle 3 (N=12)	1 = Much or Very Much Improved	3/12 (25,0)
		2 = Not Much or Very Much Improved	9/12 (75,0)
	Pre-cycle 5 (N=13)	1 = Much or Very Much Improved	5/13 (38,5)
		2 = Not Much or Very Much Improved	8/13 (61,5)
	Pre-cycle 9 (N=13)	1 = Much or Very Much Improved	9/13 (69,2)
		2 = Not Much or Very Much Improved	4/13 (30,8)
	Pre-cycle 13 (N=13)	1 = Much or Very Much Improved	9/13 (69,2)
		2 = Not Much or Very Much Improved	4/13 (30,8)
	Pre-cycle 25 (N=10)	1 = Much or Very Much Improved	6/10 (60,0)
		2 = Not Much or Very Much Improved	4/10 (40,0)
	Overall (N=13)	1 = Much or Very Much Improved	10/13 (76,9)
		2 = Not Much or Very Much Improved	3/13 (23,1)

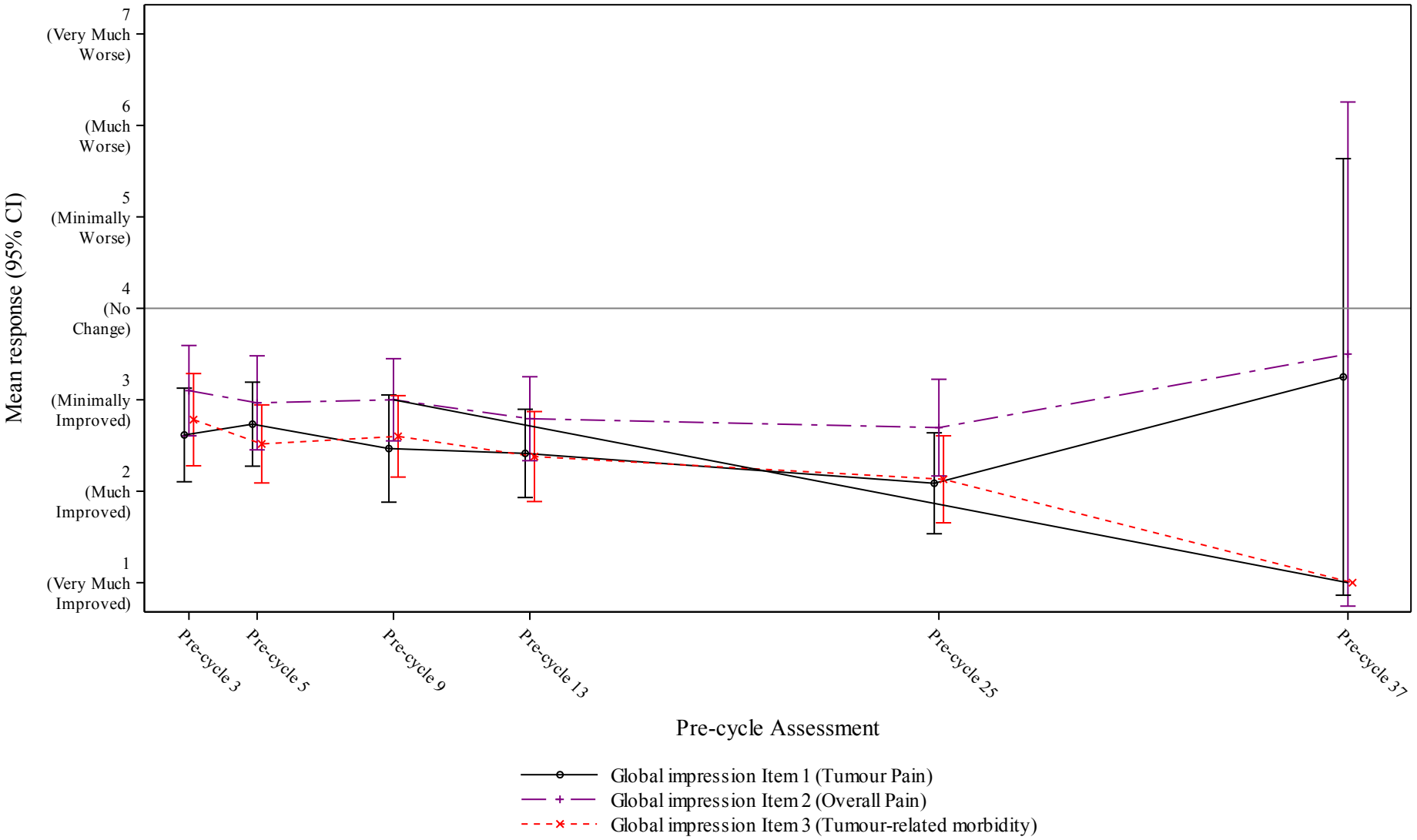
[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Table 2.10.1.2.1.5 Distribution of Global Impression of Change parent-report item responses - PN status at enrol. = Unknown
Patients with much or very much improvement (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a] n/N (%) [b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (N=11)	1 = Much or Very Much Improved	3/11 (27,3)
		2 = Not Much or Very Much Improved	8/11 (72,7)
	Pre-cycle 5 (N=12)	1 = Much or Very Much Improved	4/12 (33,3)
		2 = Not Much or Very Much Improved	8/12 (66,7)
	Pre-cycle 9 (N=13)	1 = Much or Very Much Improved	6/13 (46,2)
		2 = Not Much or Very Much Improved	7/13 (53,8)
	Pre-cycle 13 (N=13)	1 = Much or Very Much Improved	8/13 (61,5)
		2 = Not Much or Very Much Improved	5/13 (38,5)
	Pre-cycle 25 (N=10)	1 = Much or Very Much Improved	5/10 (50,0)
		2 = Not Much or Very Much Improved	5/10 (50,0)
	Overall (N=13)	1 = Much or Very Much Improved	8/13 (61,5)
		2 = Not Much or Very Much Improved	5/13 (38,5)

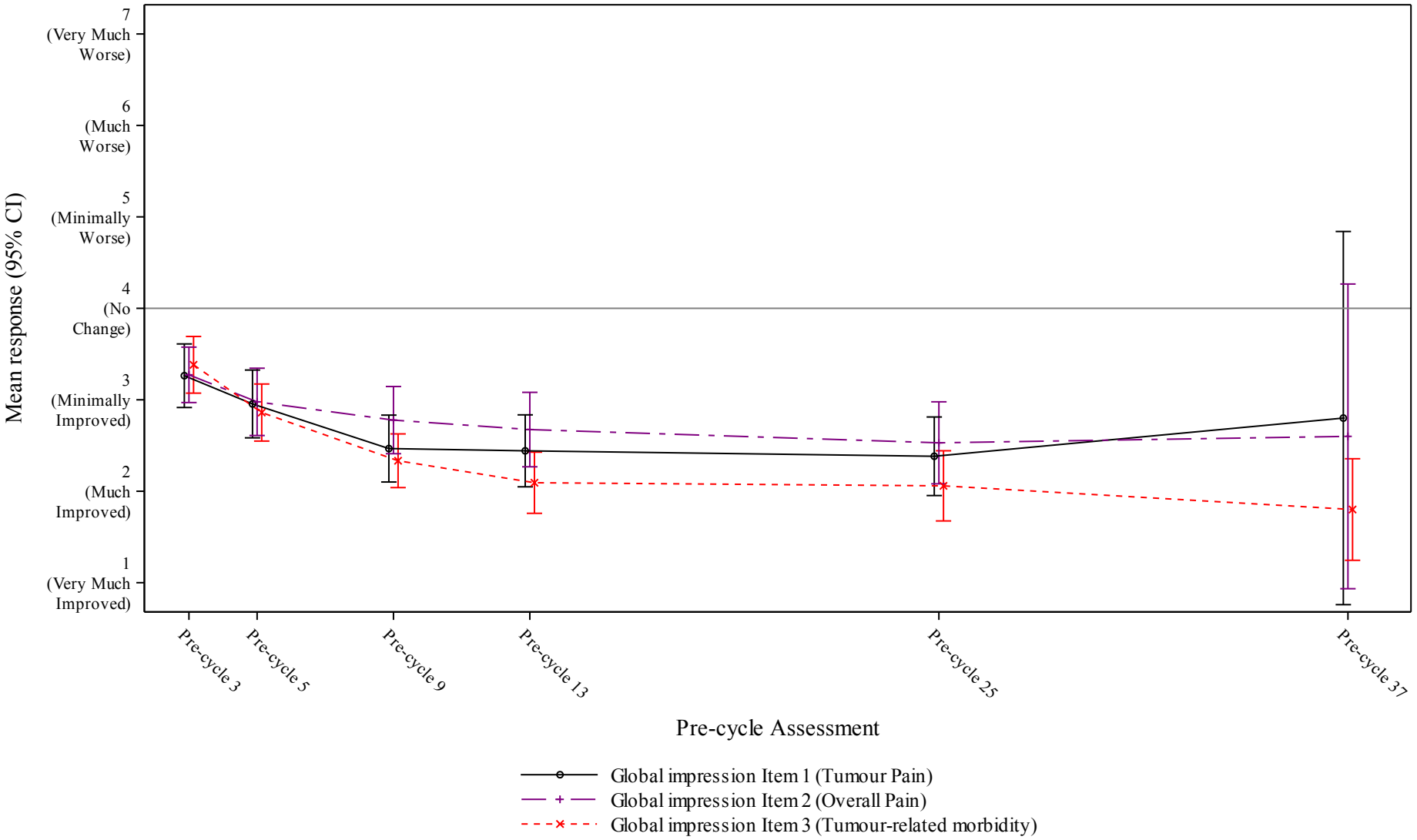
[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
Improvement category includes patients with much or very much improvement.

Figure 2.10.1.3 Global Impression of Change self-report item responses over time
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 34



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Note: Children, ages 8 to 18 years of age at enrolment completed self-report measures of the GIC.

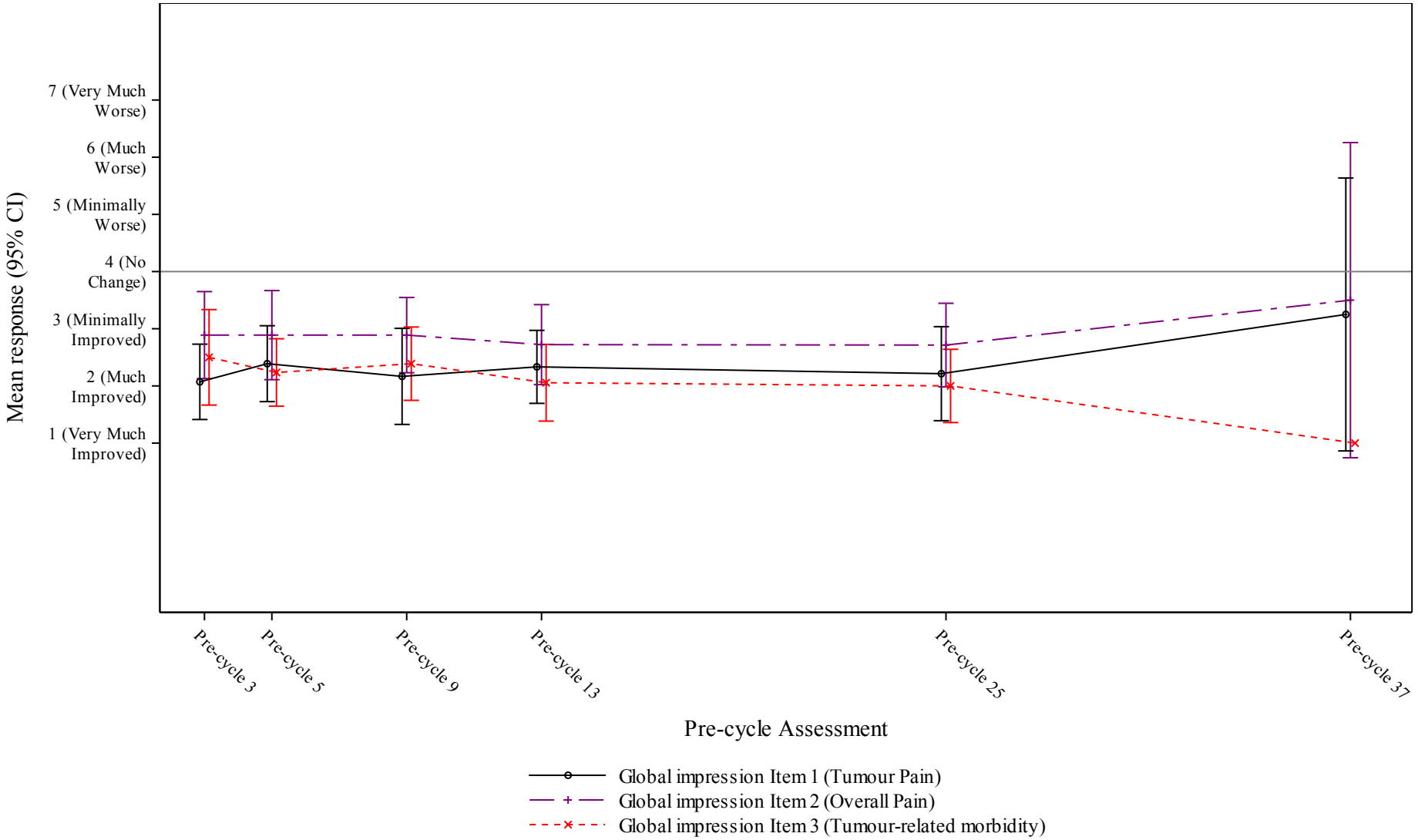
Figure 2.10.1.4 Global Impression of Change parent-report item responses over time
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 48



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy measures.

Figure 2.10.1.5 Global Impression of Change self-report item responses over time by subgroups
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

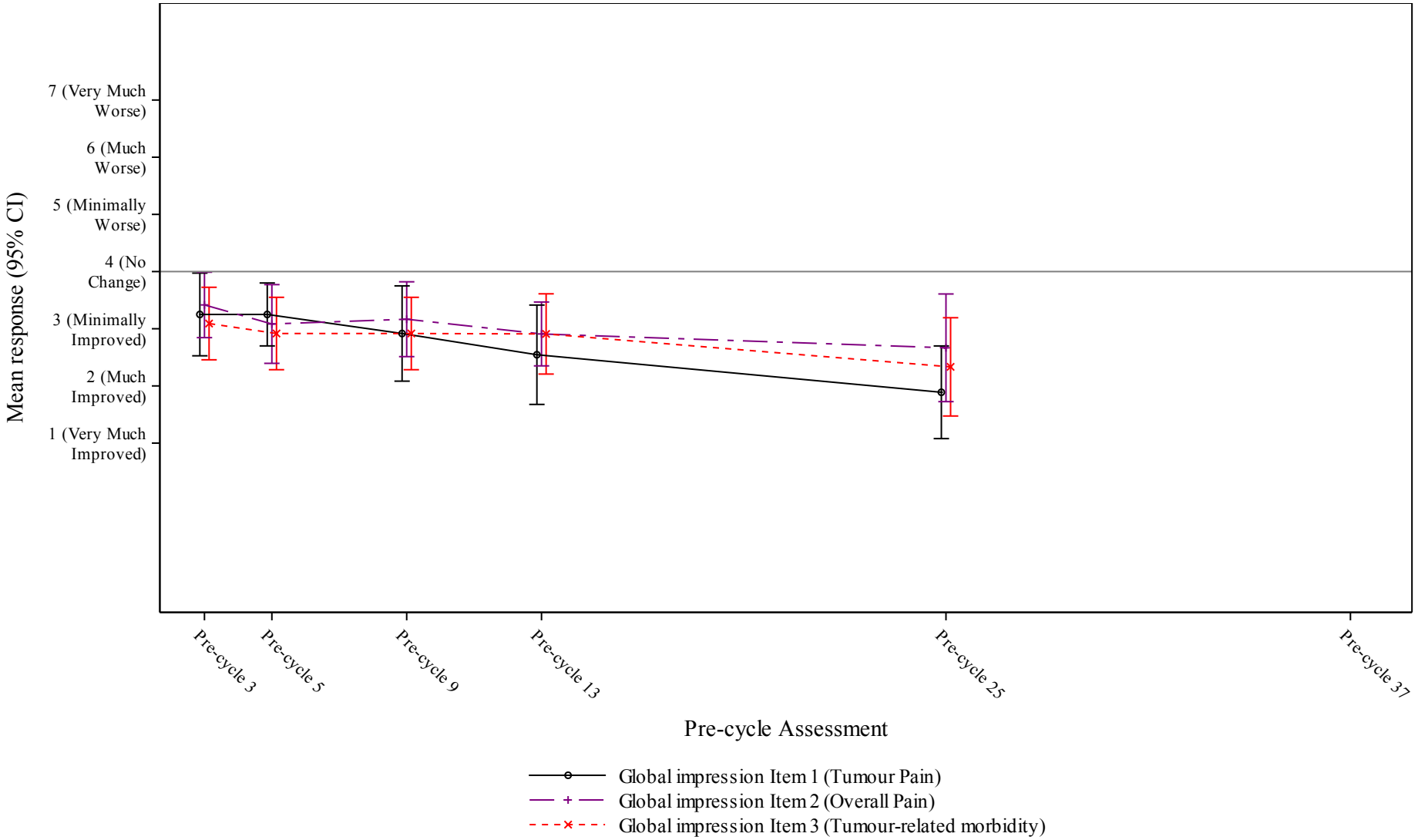
Gender = Male (N=21)



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Timepoints with <3 patients are omitted.
Note: Children, ages 8 to 18 years of age at enrolment completed self-report measures of the GIC.

Figure 2.10.1.5 Global Impression of Change self-report item responses over time by subgroups
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

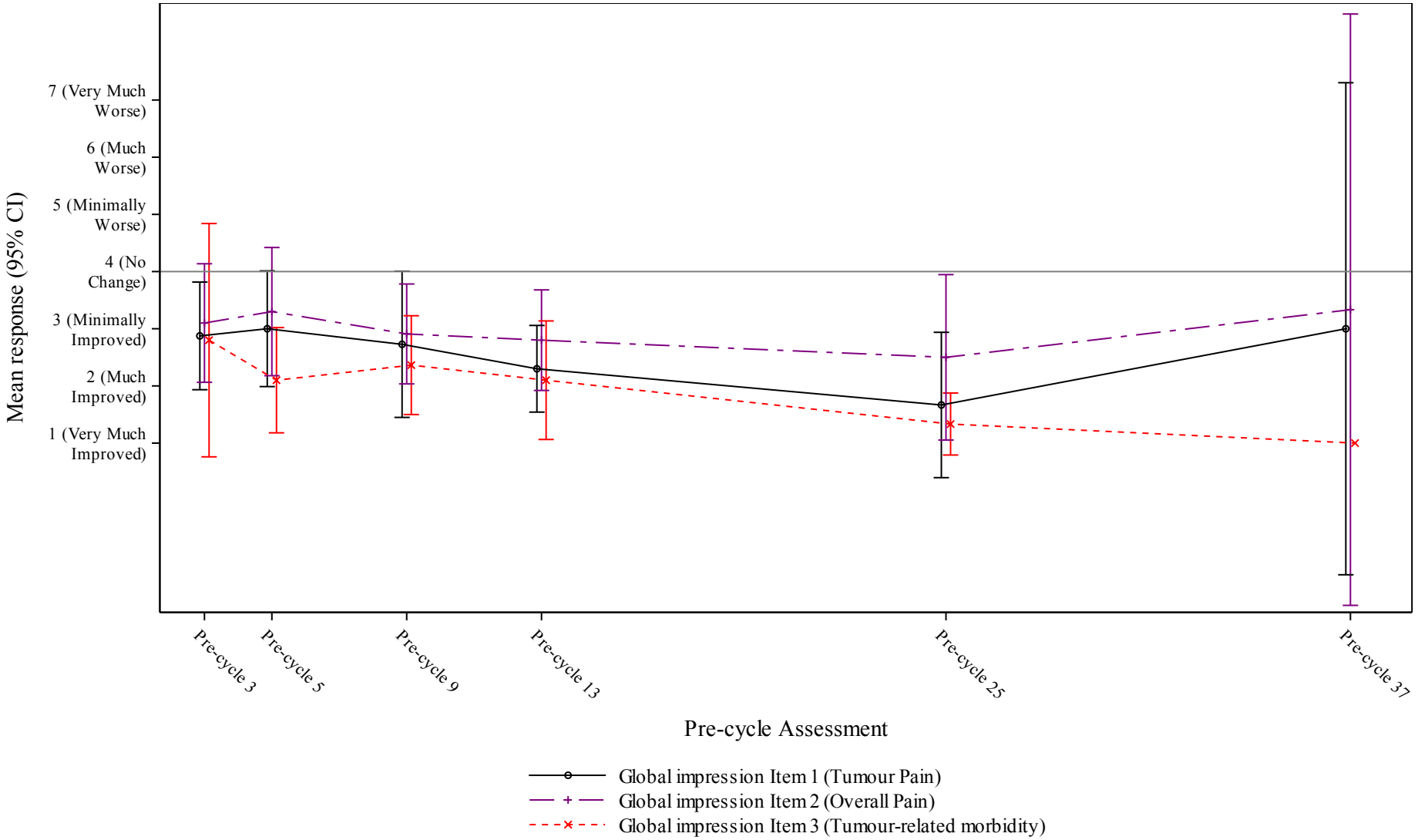
Gender = Female (N=13)



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Timepoints with <3 patients are omitted.
Note: Children, ages 8 to 18 years of age at enrolment completed self-report measures of the GIC.

Figure 2.10.1.5 Global Impression of Change self-report item responses over time by subgroups
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

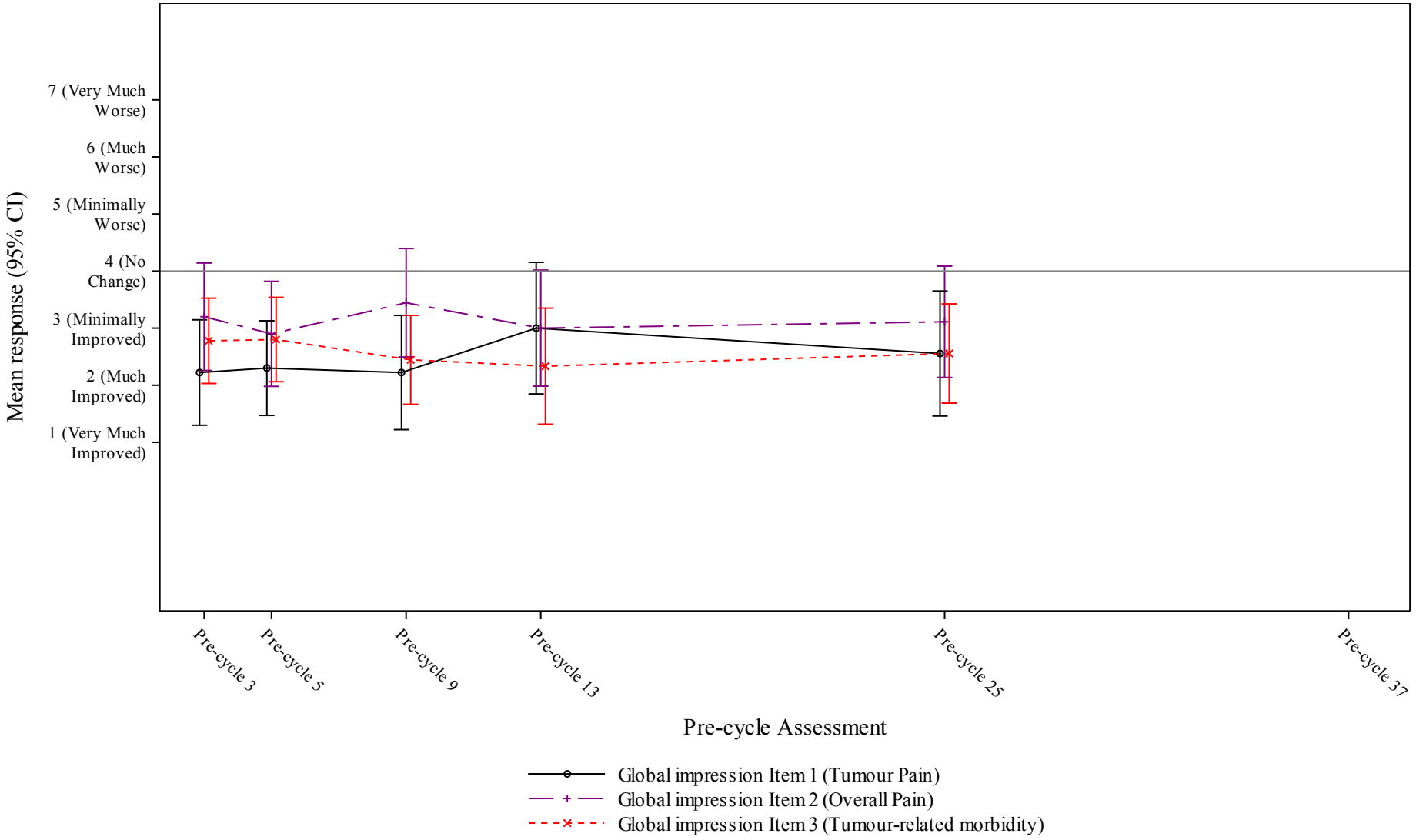
PN status at enrollment = Progressive (N=11)



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Timepoints with <3 patients are omitted.
Note: Children, ages 8 to 18 years of age at enrolment completed self-report measures of the GIC.

Figure 2.10.1.5 Global Impression of Change self-report item responses over time by subgroups
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

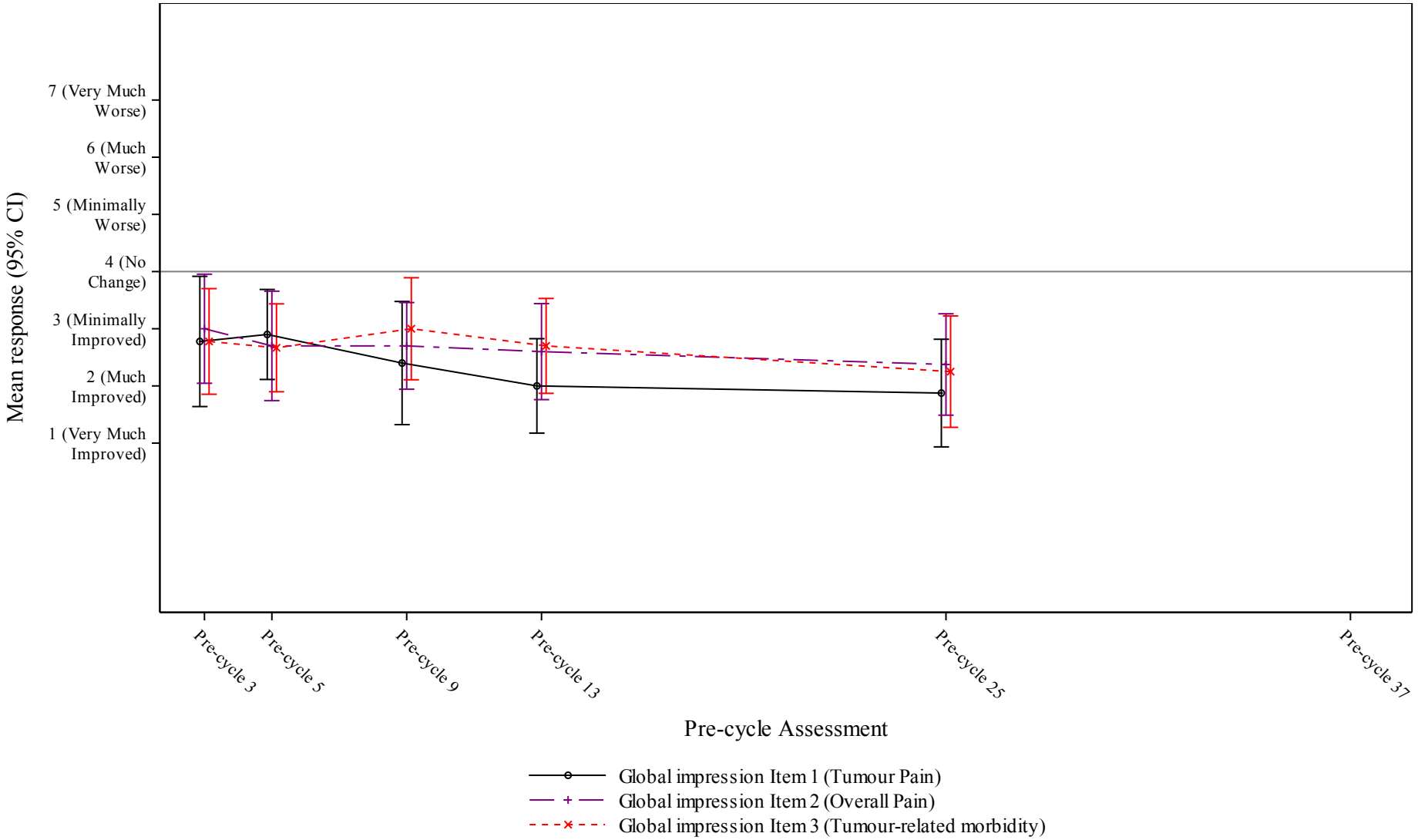
PN status at enrollment = Non-progressive (N=11)



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Timepoints with <3 patients are omitted.
Note: Children, ages 8 to 18 years of age at enrolment completed self-report measures of the GIC.

Figure 2.10.1.5 Global Impression of Change self-report item responses over time by subgroups
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

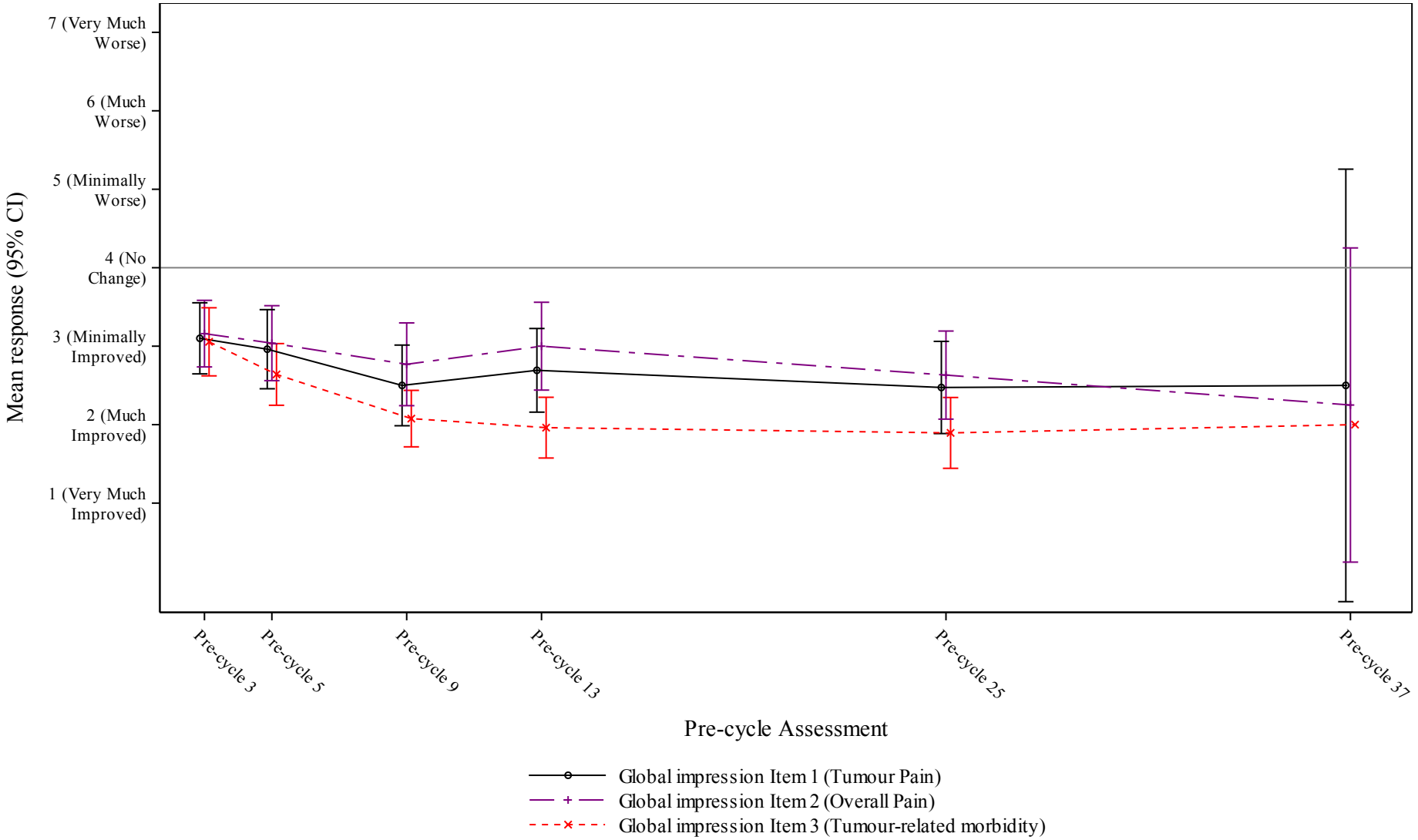
PN status at enrollment = Unknown (N=12)



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Timepoints with <3 patients are omitted.
Note: Children, ages 8 to 18 years of age at enrolment completed self-report measures of the GIC.

Figure 2.10.1.6 Global Impression of Change parent-report item responses over time by subgroups
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

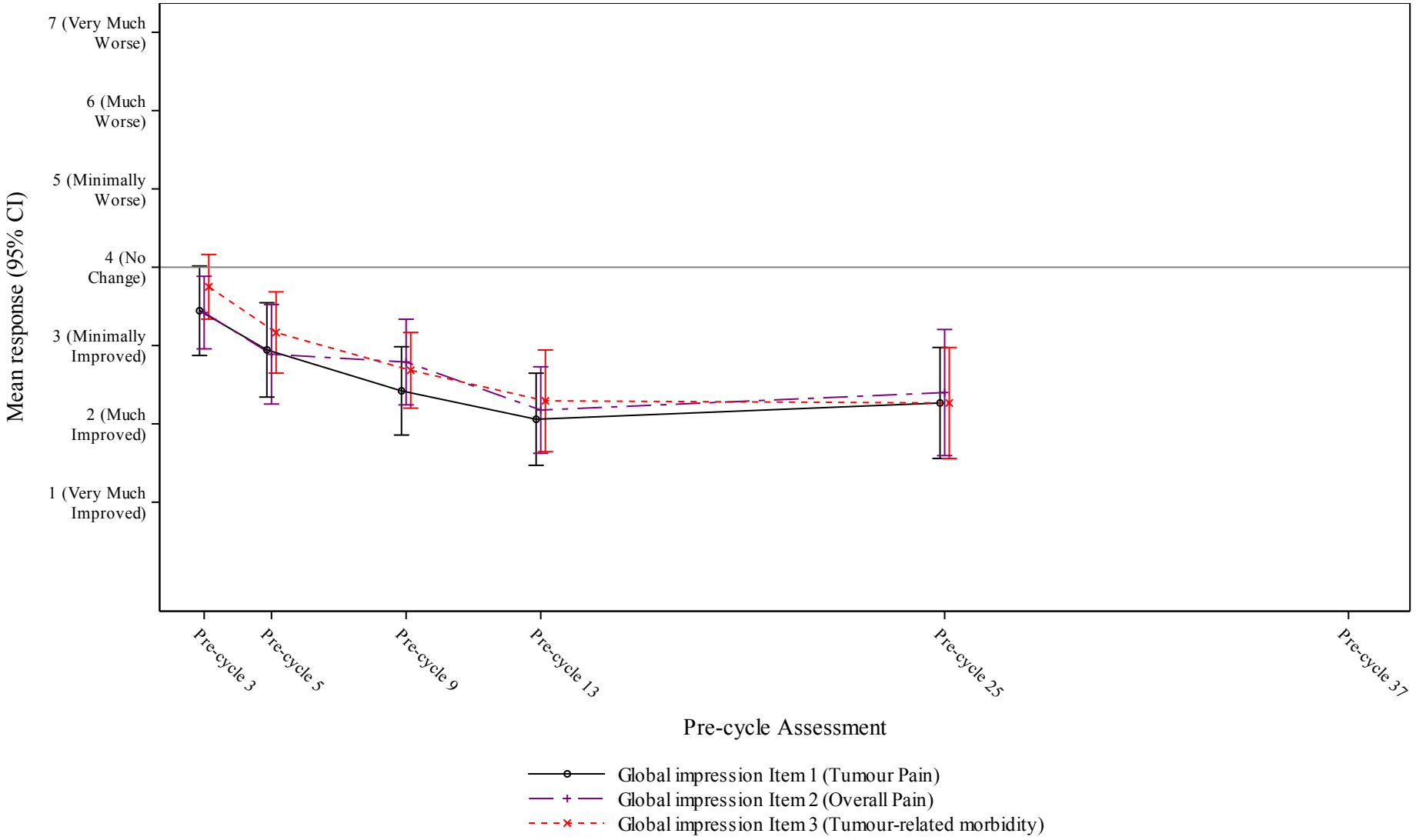
Gender = Male (N=28)



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Timepoints with <3 patients are omitted.
Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy measures.

Figure 2.10.1.6 Global Impression of Change parent-report item responses over time by subgroups
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

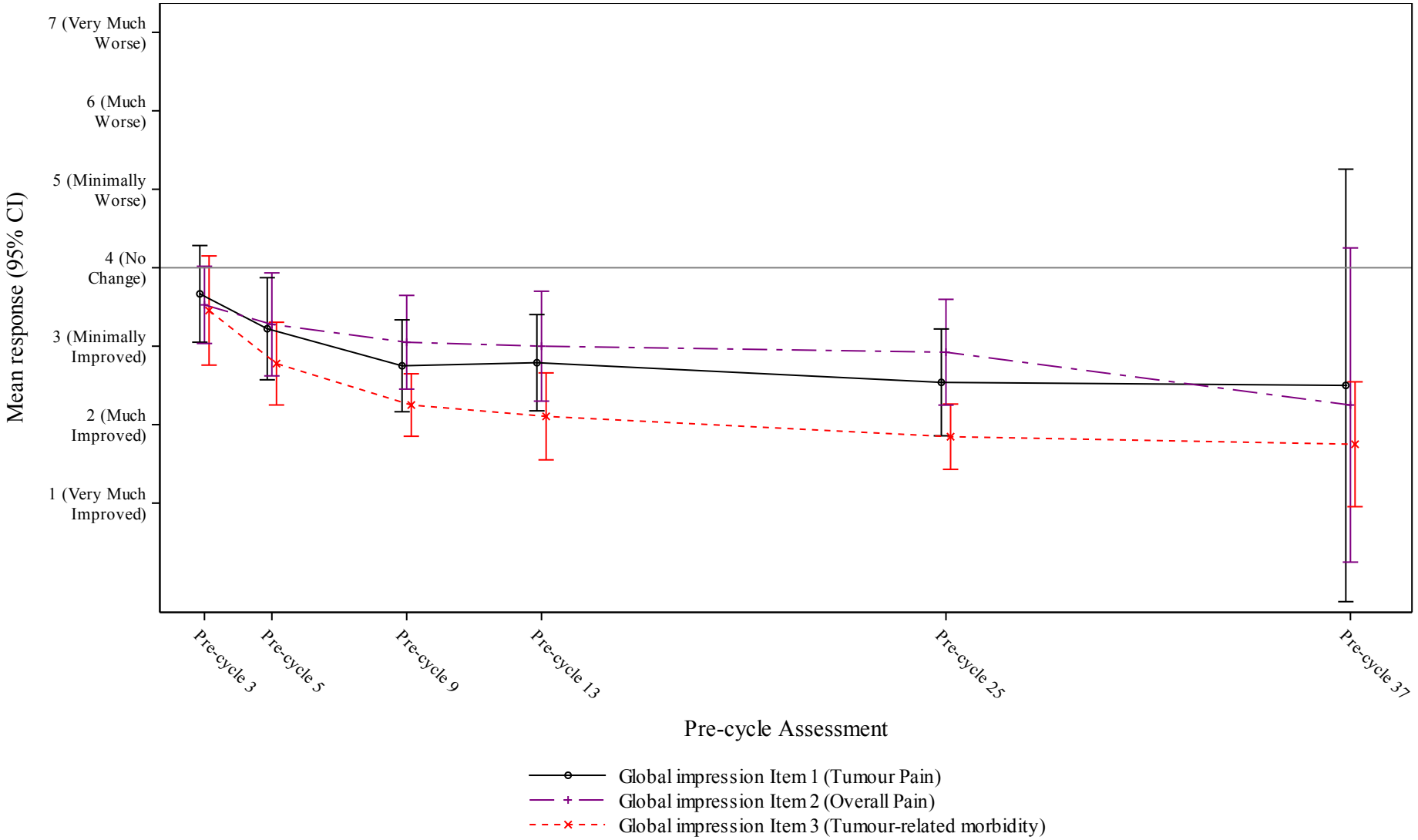
Gender = Female (N=20)



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Timepoints with <3 patients are omitted.
Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy measures.

Figure 2.10.1.6 Global Impression of Change parent-report item responses over time by subgroups
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

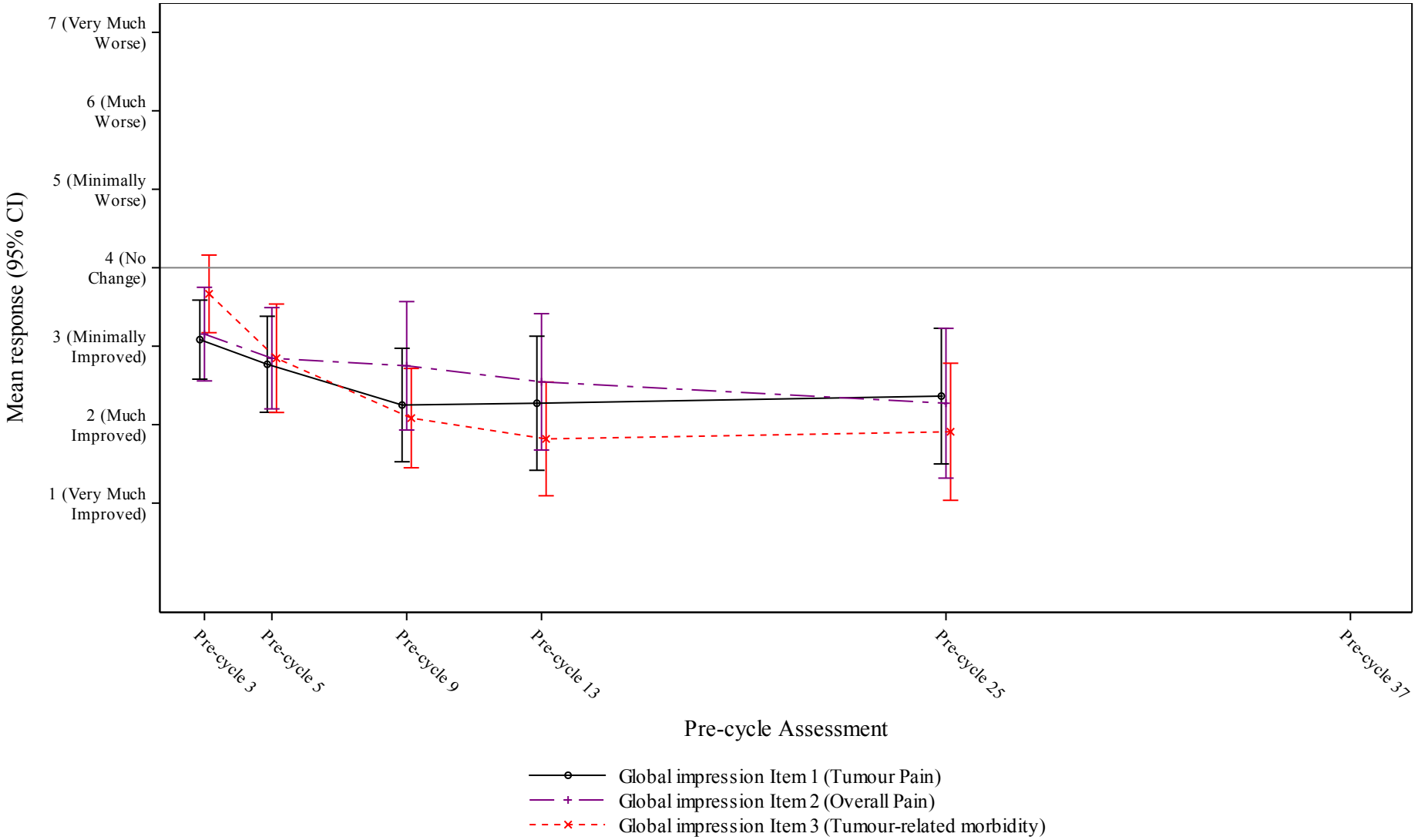
PN status at enrollment = Progressive (N=20)



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Timepoints with <3 patients are omitted.
Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy measures.

Figure 2.10.1.6 Global Impression of Change parent-report item responses over time by subgroups
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

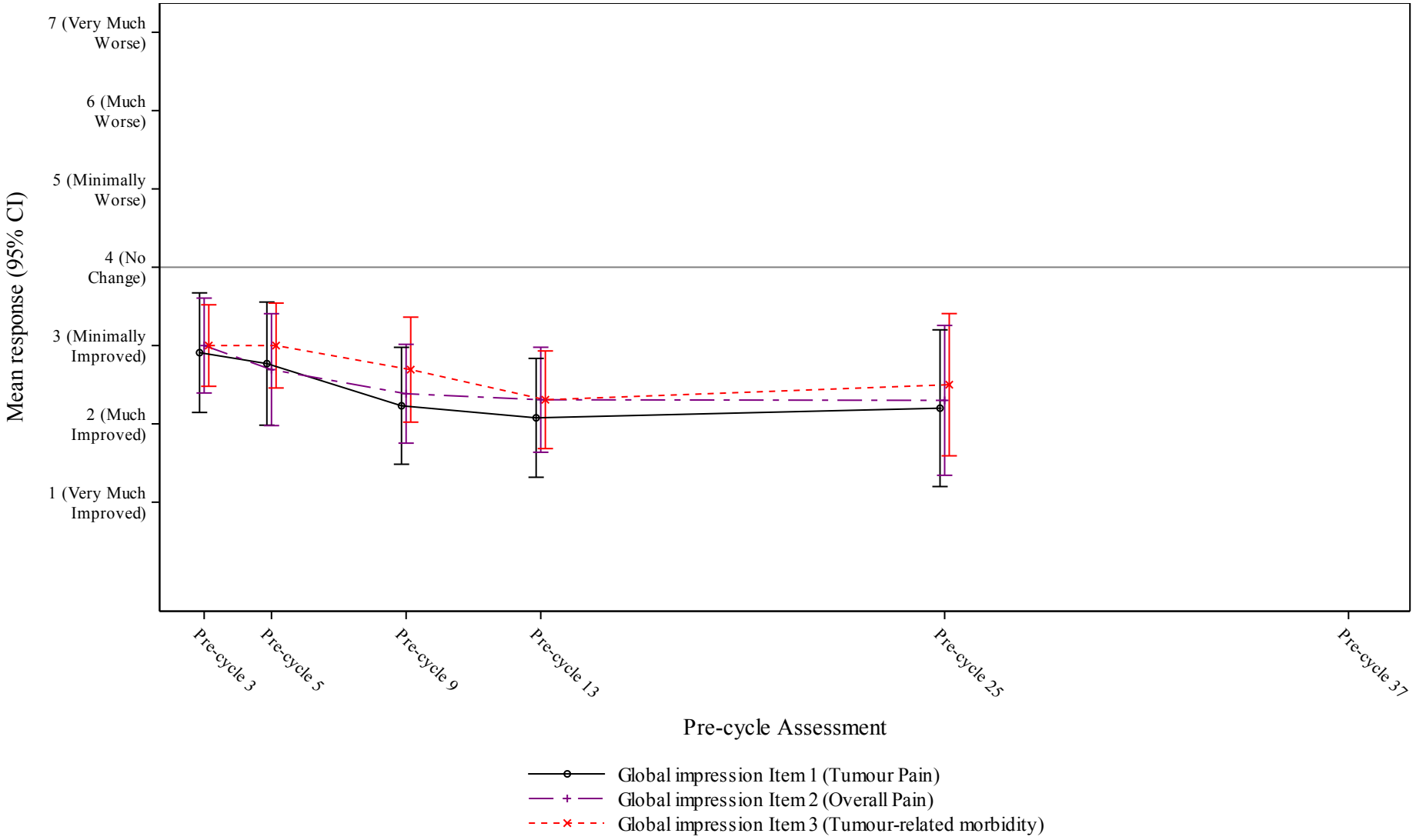
PN status at enrollment = Non-progressive (N=14)



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Timepoints with <3 patients are omitted.
Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy measures.

Figure 2.10.1.6 Global Impression of Change parent-report item responses over time by subgroups
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

PN status at enrollment = Unknown (N=14)



CI = Confidence interval. Mean and CI response are calculated using the numeric value of the response category (1 to 7).
Timepoints with <3 patients are omitted.
Note: Parents or legal guardians of children from 5 to 18 years of age at enrolment completed the parent proxy measures.

Table 2.10.2.1.1 Distribution of Global Impression of Change parent-report responses over time - Gender = Male
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=28) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=20)	1 = Very Much Improved	1/20 (5,0)
		2 = Much Improved	5/20 (25,0)
		3 = Minimally Improved	5/20 (25,0)
		4 = No Change	9/20 (45,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=26)	1 = Very Much Improved	5/26 (19,2)
		2 = Much Improved	5/26 (19,2)
		3 = Minimally Improved	2/26 (7,7)
		4 = No Change	14/26 (53,8)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=26)	1 = Very Much Improved	9/26 (34,6)
		2 = Much Improved	3/26 (11,5)
		3 = Minimally Improved	6/26 (23,1)
		4 = No Change	8/26 (30,8)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=26)	1 = Very Much Improved	7/26 (26,9)
		2 = Much Improved	6/26 (23,1)
		3 = Minimally Improved	1/26 (3,8)
		4 = No Change	12/26 (46,2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=19)	1 = Very Much Improved	5/19 (26,3)
		2 = Much Improved	6/19 (31,6)
		3 = Minimally Improved	2/19 (10,5)
		4 = No Change	6/19 (31,6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=4)	1 = Very Much Improved	2/ 4 (50,0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	2/ 4 (50,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.1 Distribution of Global Impression of Change parent-report responses over time - Gender = Male
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=28) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=25)	1 = Very Much Improved	2/25 (8,0)
		2 = Much Improved	5/25 (20,0)
		3 = Minimally Improved	5/25 (20,0)
		4 = No Change	13/25 (52,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=26)	1 = Very Much Improved	3/26 (11,5)
		2 = Much Improved	7/26 (26,9)
		3 = Minimally Improved	3/26 (11,5)
		4 = No Change	12/26 (46,2)
		5 = Minimally Worse	1/26 (3,8)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=26)	1 = Very Much Improved	6/26 (23,1)
		2 = Much Improved	6/26 (23,1)
		3 = Minimally Improved	3/26 (11,5)
		4 = No Change	10/26 (38,5)
		5 = Minimally Worse	1/26 (3,8)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=26)	1 = Very Much Improved	5/26 (19,2)
		2 = Much Improved	5/26 (19,2)
		3 = Minimally Improved	4/26 (15,4)
		4 = No Change	10/26 (38,5)
		5 = Minimally Worse	1/26 (3,8)
		6 = Much Worse	1/26 (3,8)
		7 = Very Much Worse	0
	Pre-cycle 25 (n=19)	1 = Very Much Improved	4/19 (21,1)
		2 = Much Improved	5/19 (26,3)
		3 = Minimally Improved	4/19 (21,1)
		4 = No Change	6/19 (31,6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=4)	1 = Very Much Improved	1/ 4 (25,0)
		2 = Much Improved	2/ 4 (50,0)
		3 = Minimally Improved	0
		4 = No Change	1/ 4 (25,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.1 Distribution of Global Impression of Change parent-report responses over time - Gender = Male
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=28) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=18)	1 = Very Much Improved	0
		2 = Much Improved	5/18 (27,8)
		3 = Minimally Improved	8/18 (44,4)
		4 = No Change	4/18 (22,2)
		5 = Minimally Worse	1/18 (5,6)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=25)	1 = Very Much Improved	3/25 (12,0)
		2 = Much Improved	8/25 (32,0)
		3 = Minimally Improved	9/25 (36,0)
		4 = No Change	5/25 (20,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=26)	1 = Very Much Improved	7/26 (26,9)
		2 = Much Improved	12/26 (46,2)
		3 = Minimally Improved	5/26 (19,2)
		4 = No Change	2/26 (7,7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=26)	1 = Very Much Improved	10/26 (38,5)
		2 = Much Improved	9/26 (34,6)
		3 = Minimally Improved	5/26 (19,2)
		4 = No Change	2/26 (7,7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=19)	1 = Very Much Improved	8/19 (42,1)
		2 = Much Improved	6/19 (31,6)
		3 = Minimally Improved	4/19 (21,1)
		4 = No Change	1/19 (5,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=4)	1 = Very Much Improved	0
		2 = Much Improved	4/ 4 (100,0)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.2 Distribution of Global Impression of Change parent-report responses over time - Gender = Female
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=18)	1 = Very Much Improved	1/18 (5,6)
		2 = Much Improved	2/18 (11,1)
		3 = Minimally Improved	6/18 (33,3)
		4 = No Change	7/18 (38,9)
		5 = Minimally Worse	1/18 (5,6)
		6 = Much Worse	1/18 (5,6)
		7 = Very Much Worse	0
	Pre-cycle 5 (n=18)	1 = Very Much Improved	3/18 (16,7)
		2 = Much Improved	3/18 (16,7)
		3 = Minimally Improved	5/18 (27,8)
		4 = No Change	6/18 (33,3)
		5 = Minimally Worse	1/18 (5,6)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=19)	1 = Very Much Improved	5/19 (26,3)
		2 = Much Improved	6/19 (31,6)
		3 = Minimally Improved	3/19 (15,8)
		4 = No Change	5/19 (26,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=17)	1 = Very Much Improved	7/17 (41,2)
		2 = Much Improved	5/17 (29,4)
		3 = Minimally Improved	2/17 (11,8)
		4 = No Change	3/17 (17,6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=15)	1 = Very Much Improved	6/15 (40,0)
		2 = Much Improved	3/15 (20,0)
		3 = Minimally Improved	2/15 (13,3)
		4 = No Change	4/15 (26,7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=1)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1/ 1 (100,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.2 Distribution of Global Impression of Change parent-report responses over time - Gender = Female
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=19)	1 = Very Much Improved	0
		2 = Much Improved	3/19 (15,8)
		3 = Minimally Improved	7/19 (36,8)
		4 = No Change	8/19 (42,1)
		5 = Minimally Worse	0
		6 = Much Worse	1/19 (5,3)
		7 = Very Much Worse	0
	Pre-cycle 5 (n=18)	1 = Very Much Improved	3/18 (16,7)
		2 = Much Improved	4/18 (22,2)
		3 = Minimally Improved	5/18 (27,8)
		4 = No Change	4/18 (22,2)
		5 = Minimally Worse	2/18 (11,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=19)	1 = Very Much Improved	2/19 (10,5)
		2 = Much Improved	7/19 (36,8)
		3 = Minimally Improved	4/19 (21,1)
		4 = No Change	5/19 (26,3)
		5 = Minimally Worse	1/19 (5,3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=17)	1 = Very Much Improved	5/17 (29,4)
		2 = Much Improved	7/17 (41,2)
		3 = Minimally Improved	2/17 (11,8)
		4 = No Change	3/17 (17,6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=15)	1 = Very Much Improved	6/15 (40,0)
		2 = Much Improved	3/15 (20,0)
		3 = Minimally Improved	1/15 (6,7)
		4 = No Change	4/15 (26,7)
		5 = Minimally Worse	1/15 (6,7)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=1)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1/ 1 (100,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.2 Distribution of Global Impression of Change parent-report responses over time - Gender = Female
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=16)	1 = Very Much Improved	0
		2 = Much Improved	1/16 (6,3)
		3 = Minimally Improved	4/16 (25,0)
		4 = No Change	9/16 (56,3)
		5 = Minimally Worse	2/16 (12,5)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=18)	1 = Very Much Improved	1/18 (5,6)
		2 = Much Improved	3/18 (16,7)
		3 = Minimally Improved	8/18 (44,4)
		4 = No Change	4/18 (22,2)
		5 = Minimally Worse	2/18 (11,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=19)	1 = Very Much Improved	2/19 (10,5)
		2 = Much Improved	7/19 (36,8)
		3 = Minimally Improved	5/19 (26,3)
		4 = No Change	5/19 (26,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=17)	1 = Very Much Improved	5/17 (29,4)
		2 = Much Improved	7/17 (41,2)
		3 = Minimally Improved	1/17 (5,9)
		4 = No Change	3/17 (17,6)
		5 = Minimally Worse	1/17 (5,9)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=15)	1 = Very Much Improved	5/15 (33,3)
		2 = Much Improved	5/15 (33,3)
		3 = Minimally Improved	2/15 (13,3)
		4 = No Change	2/15 (13,3)
		5 = Minimally Worse	1/15 (6,7)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=1)	1 = Very Much Improved	1/ 1 (100,0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.3 Distribution of Global Impression of Change parent-report responses over time PN status at enrol. = Progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=15)	1 = Very Much Improved	0
		2 = Much Improved	3/15 (20,0)
		3 = Minimally Improved	2/15 (13,3)
		4 = No Change	8/15 (53,3)
		5 = Minimally Worse	1/15 (6,7)
		6 = Much Worse	1/15 (6,7)
		7 = Very Much Worse	0
	Pre-cycle 5 (n=18)	1 = Very Much Improved	3/18 (16,7)
		2 = Much Improved	3/18 (16,7)
		3 = Minimally Improved	0
		4 = No Change	11/18 (61,1)
		5 = Minimally Worse	1/18 (5,6)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=20)	1 = Very Much Improved	5/20 (25,0)
		2 = Much Improved	3/20 (15,0)
		3 = Minimally Improved	4/20 (20,0)
		4 = No Change	8/20 (40,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=19)	1 = Very Much Improved	4/19 (21,1)
		2 = Much Improved	5/19 (26,3)
		3 = Minimally Improved	1/19 (5,3)
		4 = No Change	9/19 (47,4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=13)	1 = Very Much Improved	2/13 (15,4)
		2 = Much Improved	6/13 (46,2)
		3 = Minimally Improved	1/13 (7,7)
		4 = No Change	4/13 (30,8)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=4)	1 = Very Much Improved	2/ 4 (50,0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	2/ 4 (50,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.3 Distribution of Global Impression of Change parent-report responses over time PN status at enrol. = Progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=19)	1 = Very Much Improved	0
		2 = Much Improved	4/19 (21,1)
		3 = Minimally Improved	3/19 (15,8)
		4 = No Change	11/19 (57,9)
		5 = Minimally Worse	0
		6 = Much Worse	1/19 (5,3)
		7 = Very Much Worse	0
	Pre-cycle 5 (n=18)	1 = Very Much Improved	2/18 (11,1)
		2 = Much Improved	4/18 (22,2)
		3 = Minimally Improved	2/18 (11,1)
		4 = No Change	7/18 (38,9)
		5 = Minimally Worse	3/18 (16,7)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=20)	1 = Very Much Improved	3/20 (15,0)
		2 = Much Improved	4/20 (20,0)
		3 = Minimally Improved	4/20 (20,0)
		4 = No Change	7/20 (35,0)
		5 = Minimally Worse	2/20 (10,0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=19)	1 = Very Much Improved	4/19 (21,1)
		2 = Much Improved	3/19 (15,8)
		3 = Minimally Improved	4/19 (21,1)
		4 = No Change	6/19 (31,6)
		5 = Minimally Worse	1/19 (5,3)
		6 = Much Worse	1/19 (5,3)
		7 = Very Much Worse	0
	Pre-cycle 25 (n=13)	1 = Very Much Improved	1/13 (7,7)
		2 = Much Improved	5/13 (38,5)
		3 = Minimally Improved	1/13 (7,7)
		4 = No Change	6/13 (46,2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=4)	1 = Very Much Improved	1/ 4 (25,0)
		2 = Much Improved	2/ 4 (50,0)
		3 = Minimally Improved	0
		4 = No Change	1/ 4 (25,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.3 Distribution of Global Impression of Change parent-report responses over time PN status at enrol. = Progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=11)	1 = Very Much Improved	0
		2 = Much Improved	2/11 (18,2)
		3 = Minimally Improved	4/11 (36,4)
		4 = No Change	3/11 (27,3)
		5 = Minimally Worse	2/11 (18,2)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=18)	1 = Very Much Improved	2/18 (11,1)
		2 = Much Improved	5/18 (27,8)
		3 = Minimally Improved	7/18 (38,9)
		4 = No Change	3/18 (16,7)
		5 = Minimally Worse	1/18 (5,6)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=20)	1 = Very Much Improved	3/20 (15,0)
		2 = Much Improved	11/20 (55,0)
		3 = Minimally Improved	4/20 (20,0)
		4 = No Change	2/20 (10,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=19)	1 = Very Much Improved	6/19 (31,6)
		2 = Much Improved	9/19 (47,4)
		3 = Minimally Improved	1/19 (5,3)
		4 = No Change	2/19 (10,5)
		5 = Minimally Worse	1/19 (5,3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=13)	1 = Very Much Improved	4/13 (30,8)
		2 = Much Improved	7/13 (53,8)
		3 = Minimally Improved	2/13 (15,4)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=4)	1 = Very Much Improved	1/ 4 (25,0)
		2 = Much Improved	3/ 4 (75,0)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.4 Distribution of Global Impression of Change parent-report responses over time PN status at enrol. = Non-progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=12)	1 = Very Much Improved	0
		2 = Much Improved	3/12 (25,0)
		3 = Minimally Improved	5/12 (41,7)
		4 = No Change	4/12 (33,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=13)	1 = Very Much Improved	1/13 (7,7)
		2 = Much Improved	5/13 (38,5)
		3 = Minimally Improved	3/13 (23,1)
		4 = No Change	4/13 (30,8)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=12)	1 = Very Much Improved	4/12 (33,3)
		2 = Much Improved	3/12 (25,0)
		3 = Minimally Improved	3/12 (25,0)
		4 = No Change	2/12 (16,7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=11)	1 = Very Much Improved	4/11 (36,4)
		2 = Much Improved	3/11 (27,3)
		3 = Minimally Improved	1/11 (9,1)
		4 = No Change	3/11 (27,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=11)	1 = Very Much Improved	4/11 (36,4)
		2 = Much Improved	2/11 (18,2)
		3 = Minimally Improved	2/11 (18,2)
		4 = No Change	3/11 (27,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=1)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1/ 1 (100,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.4 Distribution of Global Impression of Change parent-report responses over time PN status at enrol. = Non-progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=13)	1 = Very Much Improved	1/13 (7,7)
		2 = Much Improved	2/13 (15,4)
		3 = Minimally Improved	4/13 (30,8)
		4 = No Change	6/13 (46,2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=13)	1 = Very Much Improved	1/13 (7,7)
		2 = Much Improved	5/13 (38,5)
		3 = Minimally Improved	2/13 (15,4)
		4 = No Change	5/13 (38,5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=12)	1 = Very Much Improved	3/12 (25,0)
		2 = Much Improved	2/12 (16,7)
		3 = Minimally Improved	2/12 (16,7)
		4 = No Change	5/12 (41,7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=11)	1 = Very Much Improved	3/11 (27,3)
		2 = Much Improved	3/11 (27,3)
		3 = Minimally Improved	1/11 (9,1)
		4 = No Change	4/11 (36,4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=11)	1 = Very Much Improved	5/11 (45,5)
		2 = Much Improved	1/11 (9,1)
		3 = Minimally Improved	3/11 (27,3)
		4 = No Change	1/11 (9,1)
		5 = Minimally Worse	1/11 (9,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=1)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1/ 1 (100,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.4 Distribution of Global Impression of Change parent-report responses over time PN status at enrol. = Non-progressive
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=12)	1 = Very Much Improved	0
		2 = Much Improved	1/12 (8,3)
		3 = Minimally Improved	3/12 (25,0)
		4 = No Change	7/12 (58,3)
		5 = Minimally Worse	1/12 (8,3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=13)	1 = Very Much Improved	2/13 (15,4)
		2 = Much Improved	2/13 (15,4)
		3 = Minimally Improved	6/13 (46,2)
		4 = No Change	2/13 (15,4)
		5 = Minimally Worse	1/13 (7,7)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=12)	1 = Very Much Improved	4/12 (33,3)
		2 = Much Improved	4/12 (33,3)
		3 = Minimally Improved	3/12 (25,0)
		4 = No Change	1/12 (8,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=11)	1 = Very Much Improved	6/11 (54,5)
		2 = Much Improved	2/11 (18,2)
		3 = Minimally Improved	2/11 (18,2)
		4 = No Change	1/11 (9,1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=11)	1 = Very Much Improved	6/11 (54,5)
		2 = Much Improved	2/11 (18,2)
		3 = Minimally Improved	2/11 (18,2)
		4 = No Change	0
		5 = Minimally Worse	1/11 (9,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=1)	1 = Very Much Improved	0
		2 = Much Improved	1/ 1 (100,0)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.5 Distribution of Global Impression of Change parent-report responses over time PN status at enrol. = Unknown
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=11)	1 = Very Much Improved	2/11 (18,2)
		2 = Much Improved	1/11 (9,1)
		3 = Minimally Improved	4/11 (36,4)
		4 = No Change	4/11 (36,4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=13)	1 = Very Much Improved	4/13 (30,8)
		2 = Much Improved	0
		3 = Minimally Improved	4/13 (30,8)
		4 = No Change	5/13 (38,5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=13)	1 = Very Much Improved	5/13 (38,5)
		2 = Much Improved	3/13 (23,1)
		3 = Minimally Improved	2/13 (15,4)
		4 = No Change	3/13 (23,1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=13)	1 = Very Much Improved	6/13 (46,2)
		2 = Much Improved	3/13 (23,1)
		3 = Minimally Improved	1/13 (7,7)
		4 = No Change	3/13 (23,1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=10)	1 = Very Much Improved	5/10 (50,0)
		2 = Much Improved	1/10 (10,0)
		3 = Minimally Improved	1/10 (10,0)
		4 = No Change	3/10 (30,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.5 Distribution of Global Impression of Change parent-report responses over time PN status at enrol. = Unknown
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=12)	1 = Very Much Improved	1/12 (8,3)
		2 = Much Improved	2/12 (16,7)
		3 = Minimally Improved	5/12 (41,7)
		4 = No Change	4/12 (33,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=13)	1 = Very Much Improved	3/13 (23,1)
		2 = Much Improved	2/13 (15,4)
		3 = Minimally Improved	4/13 (30,8)
		4 = No Change	4/13 (30,8)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=13)	1 = Very Much Improved	2/13 (15,4)
		2 = Much Improved	7/13 (53,8)
		3 = Minimally Improved	1/13 (7,7)
		4 = No Change	3/13 (23,1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=13)	1 = Very Much Improved	3/13 (23,1)
		2 = Much Improved	6/13 (46,2)
		3 = Minimally Improved	1/13 (7,7)
		4 = No Change	3/13 (23,1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=10)	1 = Very Much Improved	4/10 (40,0)
		2 = Much Improved	2/10 (20,0)
		3 = Minimally Improved	1/10 (10,0)
		4 = No Change	3/10 (30,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.10.2.1.5 Distribution of Global Impression of Change parent-report responses over time PN status at enrol. = Unknown
All categories (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=14) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=11)	1 = Very Much Improved	0
		2 = Much Improved	3/11 (27,3)
		3 = Minimally Improved	5/11 (45,5)
		4 = No Change	3/11 (27,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=12)	1 = Very Much Improved	0
		2 = Much Improved	4/12 (33,3)
		3 = Minimally Improved	4/12 (33,3)
		4 = No Change	4/12 (33,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=13)	1 = Very Much Improved	2/13 (15,4)
		2 = Much Improved	4/13 (30,8)
		3 = Minimally Improved	3/13 (23,1)
		4 = No Change	4/13 (30,8)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=13)	1 = Very Much Improved	3/13 (23,1)
		2 = Much Improved	5/13 (38,5)
		3 = Minimally Improved	3/13 (23,1)
		4 = No Change	2/13 (15,4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=10)	1 = Very Much Improved	3/10 (30,0)
		2 = Much Improved	2/10 (20,0)
		3 = Minimally Improved	2/10 (20,0)
		4 = No Change	3/10 (30,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 18 years of age at enrolment completed the parent proxy measures of the GIC.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.

Table 2.11.1.1 Motor function secondary outcomes test score categories of overall change by PN Quadrant - percentage of patients with Improvement (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=33) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=24)	Categories of change [d]			
		Improvement	11	45,8	25,6, 67,2
		No improvement	13	54,2	32,8, 74,4
6-minute walk test distance achieved (m) - Unilateral Upper	Overall (N=8)	Categories of change [d]			
		Improvement	4	50,0	15,7, 84,3
		No improvement	4	50,0	15,7, 84,3
6-minute walk test distance achieved (m) - Unilateral Lower	Overall (N=10)	Categories of change [d]			
		Improvement	5	50,0	18,7, 81,3
		No improvement	5	50,0	18,7, 81,3
6-minute walk test distance achieved (m) - Bilateral Upper	Overall (N=5)	Categories of change [d]			
		Improvement	1	20,0	0,5, 71,6
		No improvement	4	80,0	28,4, 99,5
6-minute walk test distance achieved (m) - Bilateral Lower	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.

Table 2.11.1.1.1 Motor function secondary outcomes test score categories of overall change by PN Quadrant - percentage of patients with Improvement - Gender = Male (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=19) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=12)	Categories of change [d]			
		Improvement	6	50,0	21,1, 78,9
		No improvement	6	50,0	21,1, 78,9
6-minute walk test distance achieved (m) - Unilateral Upper	Overall (N=4)	Categories of change [d]			
		Improvement	2	50,0	6,8, 93,2
		No improvement	2	50,0	6,8, 93,2
6-minute walk test distance achieved (m) - Unilateral Lower	Overall (N=3)	Categories of change [d]			
		Improvement	2	66,7	9,4, 99,2
		No improvement	1	33,3	0,8, 90,6
6-minute walk test distance achieved (m) - Bilateral Upper	Overall (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
6-minute walk test distance achieved (m) - Bilateral Lower	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
% and 95% CI not calculated for timepoints with <3 patients.

Table 2.11.1.1.2 Motor function secondary outcomes test score categories of overall change by PN Quadrant - percentage of patients with Improvement - Gender = Female (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=14) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8
6-minute walk test distance achieved (m) - Unilateral Upper	Overall (N=4)	Categories of change [d]			
		Improvement	2	50,0	6,8, 93,2
		No improvement	2	50,0	6,8, 93,2
6-minute walk test distance achieved (m) - Unilateral Lower	Overall (N=7)	Categories of change [d]			
		Improvement	3	42,9	9,9, 81,6
		No improvement	4	57,1	18,4, 90,1
6-minute walk test distance achieved (m) - Bilateral Upper	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC

[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
% and 95% CI not calculated for timepoints with <3 patients.
Bilateral Lower parameter omitted owing to insufficient data.

Table 2.11.1.1.3 Motor function secondary outcomes test score categories of overall change by PN Quadrant - percentage of patients with Improvement - PN status at enrollment = Progressive (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=9)	Categories of change [d]			
		Improvement	6	66,7	29,9, 92,5
		No improvement	3	33,3	7,5, 70,1
6-minute walk test distance achieved (m) - Unilateral Upper	Overall (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
6-minute walk test distance achieved (m) - Unilateral Lower	Overall (N=6)	Categories of change [d]			
		Improvement	4	66,7	22,3, 95,7
		No improvement	2	33,3	4,3, 77,7
6-minute walk test distance achieved (m) - Bilateral Lower	Overall (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC

[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
% and 95% CI not calculated for timepoints with <3 patients.
Bilateral Upper parameter omitted owing to insufficient data.

Table 2.11.1.1.4 Motor function secondary outcomes test score categories of overall change by PN Quadrant - percentage of patients with Improvement - PN status at enrollment = Non-progressive (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8
6-minute walk test distance achieved (m) - Unilateral Upper	Overall (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
6-minute walk test distance achieved (m) - Unilateral Lower	Overall (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
6-minute walk test distance achieved (m) - Bilateral Upper	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC

[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
% and 95% CI not calculated for timepoints with <3 patients.
Bilateral Lower parameter omitted owing to insufficient data.

Table 2.11.1.1.5 Motor function secondary outcomes test score categories of overall change by PN Quadrant - percentage of patients with Improvement - PN status at enrollment = Unknown (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=7)	Categories of change [d]			
		Improvement	3	42,9	9,9, 81,6
		No improvement	4	57,1	18,4, 90,1
6-minute walk test distance achieved (m) - Unilateral Upper	Overall (N=3)	Categories of change [d]			
		Improvement	2	66,7	9,4, 99,2
		No improvement	1	33,3	0,8, 90,6
6-minute walk test distance achieved (m) - Bilateral Upper	Overall (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4

[a] Patients with motor PN-related morbidity at enrolment.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
% and 95% CI not calculated for timepoints with <3 patients.
Unilateral Lower and Bilateral Lower parameters omitted owing to insufficient data.

Table 2.11.1.2 Motor function secondary outcomes test score mean change from baseline
(Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=33) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - all	Baseline (n=25)	509,19	165,813	467,00	135,0	836,0	24,2							
	Pre-cycle 5 (n=26)	504,12	145,939	483,00	186,6	860,0	21,2	23	22,96	74,681	22,00	-117,0	236,2	30,3
	Pre-cycle 9 (n=26)	507,07	126,724	502,50	263,0	845,0	21,2	24	22,83	91,001	4,50	-117,0	297,2	27,3
	Pre-cycle 13 (n=24)	471,86	158,741	475,50	101,0	861,0	27,3	21	-1,83	115,656	-3,00	-174,0	281,9	36,4
	Pre-cycle 25 (n=18)	495,20	177,216	553,00	45,5	770,0	45,5	16	0,89	134,419	-2,00	-317,0	265,2	51,5
6-minute walk test % normal distance achieved - all	Baseline (n=24)	75,32	19,872	75,50	20,5	114,4	27,3							
	Pre-cycle 5 (n=25)	75,33	16,399	78,26	28,2	97,5	24,2	23	3,54	11,213	1,70	-16,1	35,4	30,3
	Pre-cycle 9 (n=25)	74,99	14,402	77,10	36,6	92,1	24,2	23	3,02	13,614	0,70	-13,3	44,0	30,3
	Pre-cycle 13 (n=23)	71,39	17,589	71,65	30,8	107,2	30,3	21	-1,39	17,649	-2,04	-32,6	40,7	36,4
	Pre-cycle 25 (n=16)	79,18	15,869	83,20	54,4	109,7	51,5	14	1,58	15,482	1,70	-19,6	36,6	57,6
6-minute walk test velocity achieved (m/min) - all	Baseline (n=25)	84,86	27,635	77,83	22,5	139,3	24,2							
	Pre-cycle 5 (n=26)	84,02	24,323	80,50	31,1	143,3	21,2	23	3,83	12,447	3,67	-19,5	39,4	30,3
	Pre-cycle 9 (n=26)	84,51	21,121	83,75	43,8	140,8	21,2	24	3,80	15,166	0,75	-19,5	49,5	27,3
	Pre-cycle 13 (n=24)	78,64	26,457	79,25	16,8	143,5	27,3	21	-0,30	19,276	-0,50	-29,0	47,0	36,4
	Pre-cycle 25 (n=18)	82,53	29,536	92,17	7,6	128,3	45,5	16	0,15	22,404	-0,33	-52,8	44,2	51,5
6-minute walk test distance achieved (m) - Unilateral Upper	Baseline (n=8)	511,61	164,326	531,50	182,9	758,0	75,8							
	Pre-cycle 5 (n=8)	553,89	103,124	556,50	419,1	762,0	75,8	7	56,03	90,551	28,00	-38,0	236,2	78,8
	Pre-cycle 9 (n=8)	564,13	85,828	563,50	453,0	728,0	75,8	8	52,52	112,642	18,50	-60,0	297,2	75,8
	Pre-cycle 13 (n=7)	532,83	60,983	525,00	464,8	619,0	78,8	7	24,85	138,390	-19,00	-139,0	281,9	78,8
	Pre-cycle 25 (n=7)	549,29	105,861	597,00	363,0	644,0	78,8	7	39,74	130,853	19,00	-119,0	265,2	78,8
6-minute walk test distance achieved (m) - Unilateral Lower	Baseline (n=10)	486,46	107,170	450,25	366,0	684,0	69,7							
	Pre-cycle 5 (n=12)	467,76	118,530	435,00	311,0	660,0	63,6	10	8,35	77,961	1,00	-117,0	129,5	69,7
	Pre-cycle 9 (n=12)	477,37	97,047	493,00	311,0	603,0	63,6	10	19,58	72,193	-7,25	-81,0	129,0	69,7
	Pre-cycle 13 (n=10)	484,95	106,204	455,00	354,0	644,0	69,7	8	19,24	96,704	2,50	-119,0	152,4	75,8
	Pre-cycle 25 (n=6)	520,83	59,971	526,50	453,0	584,0	81,8	5	57,60	64,116	67,00	-11,0	131,0	84,8

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.1.2 Motor function secondary outcomes test score mean change from baseline
(Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=33) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - Bilateral Upper	Baseline (n=6)	557,79	261,181	586,00	135,0	836,0	81,8							
	Pre-cycle 5 (n=5)	517,12	257,987	434,00	186,6	860,0	84,8	5	0,12	37,325	-8,00	-37,0	51,6	84,8
	Pre-cycle 9 (n=5)	495,20	227,657	402,00	263,0	845,0	84,8	5	-21,80	96,564	-40,00	-117,0	128,0	84,8
	Pre-cycle 13 (n=6)	384,98	276,183	300,50	101,0	861,0	81,8	5	-75,22	113,532	-134,00	-174,0	68,9	84,8
	Pre-cycle 25 (n=5)	388,72	303,131	433,10	45,5	770,0	84,8	4	-137,98	126,584	-100,50	-317,0	-33,9	87,9
6-minute walk test distance achieved (m) - Bilateral Lower	Baseline (n=1)	NC	NC	NC	425,5	425,5	97,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	477,3	477,3	97,0	1	NC	NC	NC	51,8	51,8	97,0
	Pre-cycle 9 (n=1)	NC	NC	NC	466,3	466,3	97,0	1	NC	NC	NC	40,8	40,8	97,0
	Pre-cycle 13 (n=1)	NC	NC	NC	435,3	435,3	97,0	1	NC	NC	NC	9,8	9,8	97,0

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.1.2.1 Motor function secondary outcomes test score mean change from baseline
- Gender = Male (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=19) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - all	Baseline (n=13)	515,86	221,976	454,00	135,0	836,0	31,6							
	Pre-cycle 5 (n=13)	506,05	182,017	483,00	186,6	860,0	31,6	11	34,29	90,065	24,00	-117,0	236,2	42,1
	Pre-cycle 9 (n=13)	520,60	158,172	495,00	263,0	845,0	31,6	12	42,69	113,218	24,92	-117,0	297,2	36,8
	Pre-cycle 13 (n=13)	459,58	200,699	464,82	101,0	861,0	31,6	11	10,19	137,677	21,00	-174,0	281,9	42,1
	Pre-cycle 25 (n=9)	455,73	242,097	497,00	45,5	770,0	52,6	8	-28,10	184,439	-78,50	-317,0	265,2	57,9
6-minute walk test % normal distance achieved - all	Baseline (n=12)	72,12	26,717	72,75	20,5	114,4	36,8							
	Pre-cycle 5 (n=12)	71,60	18,166	76,32	28,2	95,6	36,8	11	5,14	13,545	1,70	-16,1	35,4	42,1
	Pre-cycle 9 (n=12)	72,39	16,058	73,30	36,6	92,1	36,8	11	6,03	17,204	0,70	-13,3	44,0	42,1
	Pre-cycle 13 (n=12)	67,37	18,155	68,98	30,8	93,6	36,8	11	-0,06	20,957	0,00	-32,6	40,7	42,1
	Pre-cycle 25 (n=7)	73,07	20,378	64,60	54,4	109,7	63,2	6	-2,07	23,254	-12,90	-19,6	36,6	68,4
6-minute walk test velocity achieved (m/min) - all	Baseline (n=13)	85,98	36,996	75,67	22,5	139,3	31,6							
	Pre-cycle 5 (n=13)	84,34	30,336	80,50	31,1	143,3	31,6	11	5,71	15,011	4,00	-19,5	39,4	42,1
	Pre-cycle 9 (n=13)	86,77	26,362	82,50	43,8	140,8	31,6	12	7,12	18,869	4,15	-19,5	49,5	36,8
	Pre-cycle 13 (n=13)	76,60	33,450	77,47	16,8	143,5	31,6	11	1,70	22,946	3,50	-29,0	47,0	42,1
	Pre-cycle 25 (n=9)	75,95	40,349	82,83	7,6	128,3	52,6	8	-4,68	30,741	-13,08	-52,8	44,2	57,9
6-minute walk test distance achieved (m) - Unilateral Upper	Baseline (n=4)	482,97	237,665	495,50	182,9	758,0	78,9							
	Pre-cycle 5 (n=4)	536,78	153,142	483,00	419,1	762,0	78,9	3	89,74	127,470	29,00	4,0	236,2	84,2
	Pre-cycle 9 (n=4)	565,27	125,900	540,03	453,0	728,0	78,9	4	82,30	148,432	31,00	-30,0	297,2	78,9
	Pre-cycle 13 (n=3)	519,61	86,228	475,00	464,8	619,0	84,2	3	54,65	212,478	21,00	-139,0	281,9	84,2
	Pre-cycle 25 (n=4)	523,52	140,608	543,53	363,0	644,0	78,9	4	40,55	180,403	8,00	-119,0	265,2	78,9
6-minute walk test distance achieved (m) - Unilateral Lower	Baseline (n=3)	489,70	170,350	419,10	366,0	684,0	84,2							
	Pre-cycle 5 (n=4)	449,66	127,571	460,32	311,0	567,0	78,9	3	6,18	123,270	6,00	-117,0	129,5	84,2
	Pre-cycle 9 (n=4)	485,60	124,688	514,20	311,0	603,0	78,9	3	54,10	117,231	114,30	-81,0	129,0	84,2
	Pre-cycle 13 (n=4)	500,88	131,043	502,75	354,0	644,0	78,9	3	60,13	96,441	68,00	-40,0	152,4	84,2
	Pre-cycle 25 (n=1)	NC	NC	NC	497,0	497,0	94,7	1	NC	NC	NC	131,0	131,0	94,7

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.
Mean, SD and Median not calculated for timepoints with <3 patients.

Table 2.11.1.2.1 Motor function secondary outcomes test score mean change from baseline
- Gender = Male (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=19) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - Bilateral Upper	Baseline (n=5)	575,95	287,743	705,00	135,0	836,0	73,7							
	Pre-cycle 5 (n=4)	538,90	292,541	554,50	186,6	860,0	78,9	4	9,40	35,823	8,00	-30,0	51,6	78,9
	Pre-cycle 9 (n=4)	524,50	251,755	495,00	263,0	845,0	78,9	4	-5,00	102,720	-15,50	-117,0	128,0	78,9
	Pre-cycle 13 (n=5)	395,38	307,467	268,00	101,0	861,0	73,7	4	-60,53	125,485	-68,50	-174,0	68,9	78,9
	Pre-cycle 25 (n=4)	377,63	348,852	347,50	45,5	770,0	78,9	3	-172,67	129,670	-135,00	-317,0	-66,0	84,2
6-minute walk test distance achieved (m) - Bilateral Lower	Baseline (n=1)	NC	NC	NC	425,5	425,5	94,7							
	Pre-cycle 5 (n=1)	NC	NC	NC	477,3	477,3	94,7	1	NC	NC	NC	51,8	51,8	94,7
	Pre-cycle 9 (n=1)	NC	NC	NC	466,3	466,3	94,7	1	NC	NC	NC	40,8	40,8	94,7
	Pre-cycle 13 (n=1)	NC	NC	NC	435,3	435,3	94,7	1	NC	NC	NC	9,8	9,8	94,7

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.
Mean, SD and Median not calculated for timepoints with <3 patients.

Table 2.11.1.2.2 Motor function secondary outcomes test score mean change from baseline
- Gender = Female (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - all	Baseline (n=12)	501,96	78,261	496,50	386,0	603,0	14,3							
	Pre-cycle 5 (n=13)	502,19	105,987	551,00	354,0	660,0	7,1	12	12,58	59,451	9,00	-86,0	123,0	14,3
	Pre-cycle 9 (n=13)	493,54	89,673	510,00	350,0	607,0	7,1	12	2,96	60,295	-7,75	-89,0	114,0	14,3
	Pre-cycle 13 (n=11)	486,36	95,884	485,00	333,0	596,0	21,4	10	-15,05	91,070	-30,00	-134,0	146,0	28,6
	Pre-cycle 25 (n=9)	534,68	67,967	556,00	433,1	604,0	35,7	8	29,89	52,715	10,00	-33,9	106,0	42,9
6-minute walk test % normal distance achieved - all	Baseline (n=12)	78,52	9,465	79,43	67,1	91,1	14,3							
	Pre-cycle 5 (n=13)	78,77	14,445	83,00	54,1	97,5	7,1	12	2,07	8,931	0,71	-13,0	17,5	14,3
	Pre-cycle 9 (n=13)	77,39	12,863	83,12	56,5	92,0	7,1	12	0,26	9,179	-1,18	-11,3	17,8	14,3
	Pre-cycle 13 (n=11)	75,76	16,662	73,15	45,7	107,2	21,4	10	-2,87	14,129	-5,06	-22,0	21,3	28,6
	Pre-cycle 25 (n=9)	83,92	10,137	86,00	65,2	95,2	35,7	8	4,31	6,242	2,30	-2,5	16,8	42,9
6-minute walk test velocity achieved (m/min) - all	Baseline (n=12)	83,66	13,043	82,75	64,3	100,5	14,3							
	Pre-cycle 5 (n=13)	83,70	17,664	91,83	59,0	110,0	7,1	12	2,10	9,908	1,50	-14,3	20,5	14,3
	Pre-cycle 9 (n=13)	82,26	14,945	85,00	58,3	101,2	7,1	12	0,49	10,049	-1,29	-14,8	19,0	14,3
	Pre-cycle 13 (n=11)	81,06	15,981	80,83	55,5	99,3	21,4	10	-2,51	15,178	-5,00	-22,3	24,3	28,6
	Pre-cycle 25 (n=9)	89,11	11,328	92,67	72,2	100,7	35,7	8	4,98	8,785	1,67	-5,6	17,7	42,9
6-minute walk test distance achieved (m) - Unilateral Upper	Baseline (n=4)	540,25	65,840	552,00	454,0	603,0	71,4							
	Pre-cycle 5 (n=4)	571,00	24,097	563,50	551,0	606,0	71,4	4	30,75	59,818	26,50	-38,0	108,0	71,4
	Pre-cycle 9 (n=4)	563,00	36,524	563,50	518,0	607,0	71,4	4	22,75	72,182	18,50	-60,0	114,0	71,4
	Pre-cycle 13 (n=4)	542,75	46,636	551,00	485,0	584,0	71,4	4	2,50	81,558	-30,00	-53,0	123,0	71,4
	Pre-cycle 25 (n=3)	583,67	29,366	597,00	550,0	604,0	78,6	3	38,67	50,461	19,00	1,0	96,0	78,6
6-minute walk test distance achieved (m) - Unilateral Lower	Baseline (n=7)	485,07	86,877	450,50	386,0	595,0	50,0							
	Pre-cycle 5 (n=8)	476,81	121,745	435,00	354,0	660,0	42,9	7	9,29	63,626	-4,00	-86,0	123,0	50,0
	Pre-cycle 9 (n=8)	473,25	89,882	487,00	350,0	600,0	42,9	7	4,79	48,841	-19,50	-43,0	97,0	50,0
	Pre-cycle 13 (n=6)	474,33	98,291	441,50	383,0	596,0	57,1	5	-5,30	98,529	-3,00	-119,0	146,0	64,3
	Pre-cycle 25 (n=5)	525,60	65,767	556,00	453,0	584,0	64,3	4	39,25	56,888	31,00	-11,0	106,0	71,4

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.
Mean, SD and Median not calculated for timepoints with <3 patients.
Bilateral Lower parameter omitted owing to insufficient data.

Table 2.11.1.2.2 Motor function secondary outcomes test score mean change from baseline
- Gender = Female (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - Bilateral Upper	Baseline (n=1)	NC	NC	NC	467,0	467,0	92,9							
	Pre-cycle 5 (n=1)	NC	NC	NC	430,0	430,0	92,9	1	NC	NC	NC	-37,0	-37,0	92,9
	Pre-cycle 9 (n=1)	NC	NC	NC	378,0	378,0	92,9	1	NC	NC	NC	-89,0	-89,0	92,9
	Pre-cycle 13 (n=1)	NC	NC	NC	333,0	333,0	92,9	1	NC	NC	NC	-134,0	-134,0	92,9
	Pre-cycle 25 (n=1)	NC	NC	NC	433,1	433,1	92,9	1	NC	NC	NC	-33,9	-33,9	92,9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.
Mean, SD and Median not calculated for timepoints with <3 patients.
Bilateral Lower parameter omitted owing to insufficient data.

Table 2.11.1.2.3 Motor function secondary outcomes test score mean change from baseline
- PN status at enrollment = Progressive (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - all	Baseline (n=9)	507,01	136,113	450,50	366,0	758,0	18,2							
	Pre-cycle 5 (n=10)	501,24	134,876	480,15	354,0	762,0	9,1	8	18,67	88,144	22,00	-117,0	129,5	27,3
	Pre-cycle 9 (n=10)	520,67	103,382	502,50	357,0	728,0	9,1	9	31,85	74,324	40,84	-81,0	129,0	18,2
	Pre-cycle 13 (n=8)	485,73	107,520	434,65	383,0	644,0	27,3	7	-1,47	93,348	-3,00	-139,0	152,4	36,4
	Pre-cycle 25 (n=5)	537,80	96,264	497,00	453,0	644,0	54,5	4	46,50	113,447	87,00	-119,0	131,0	63,6
6-minute walk test % normal distance achieved - all	Baseline (n=8)	75,59	9,173	71,40	67,1	96,0	27,3							
	Pre-cycle 5 (n=9)	76,12	14,244	78,00	54,1	97,5	18,2	8	2,93	13,038	3,98	-16,1	20,6	27,3
	Pre-cycle 9 (n=9)	78,01	10,744	77,10	60,8	92,1	18,2	8	4,57	11,663	1,60	-10,9	21,0	27,3
	Pre-cycle 13 (n=8)	72,99	14,009	68,93	56,0	93,6	27,3	7	-1,35	13,603	-2,90	-21,0	22,1	36,4
	Pre-cycle 25 (n=5)	80,80	19,157	76,50	57,9	109,7	54,5	3	0,72	17,827	5,80	-19,1	15,5	72,7
6-minute walk test velocity achieved (m/min) - all	Baseline (n=9)	84,50	22,685	75,08	61,0	126,3	18,2							
	Pre-cycle 5 (n=10)	83,54	22,479	80,03	59,0	127,0	9,1	8	3,11	14,691	3,67	-19,5	21,6	27,3
	Pre-cycle 9 (n=10)	86,78	17,230	83,75	59,5	121,3	9,1	9	5,31	12,387	6,81	-13,5	21,5	18,2
	Pre-cycle 13 (n=8)	80,95	17,920	72,44	63,8	107,3	27,3	7	-0,25	15,558	-0,50	-23,2	25,4	36,4
	Pre-cycle 25 (n=5)	89,63	16,044	82,83	75,5	107,3	54,5	4	7,75	18,908	14,50	-19,8	21,8	63,6
6-minute walk test distance achieved (m) - Unilateral Upper	Baseline (n=2)	NC	NC	NC	537,0	758,0	81,8							
	Pre-cycle 5 (n=2)	NC	NC	NC	483,0	762,0	81,8	1	NC	NC	NC	4,0	4,0	90,9
	Pre-cycle 9 (n=2)	NC	NC	NC	600,0	728,0	81,8	2	NC	NC	NC	-30,0	63,0	81,8
	Pre-cycle 13 (n=1)	NC	NC	NC	619,0	619,0	90,9	1	NC	NC	NC	-139,0	-139,0	90,9
	Pre-cycle 25 (n=2)	NC	NC	NC	639,0	644,0	81,8	2	NC	NC	NC	-119,0	107,0	81,8
6-minute walk test distance achieved (m) - Unilateral Lower	Baseline (n=6)	473,77	119,200	434,80	366,0	684,0	45,5							
	Pre-cycle 5 (n=7)	470,02	121,106	424,00	354,0	660,0	36,4	6	15,59	102,972	22,00	-117,0	129,5	45,5
	Pre-cycle 9 (n=7)	487,49	77,731	495,00	357,0	603,0	36,4	6	35,47	88,586	38,75	-81,0	129,0	45,5
	Pre-cycle 13 (n=6)	471,92	109,063	420,50	383,0	644,0	45,5	5	23,78	86,680	-3,00	-58,5	152,4	54,5
	Pre-cycle 25 (n=3)	468,67	24,583	456,00	453,0	497,0	72,7	2	NC	NC	NC	67,0	131,0	81,8

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.
Mean, SD and Median not calculated for timepoints with <3 patients.
Bilateral Upper parameter omitted owing to insufficient data.

Table 2.11.1.2.3 Motor function secondary outcomes test score mean change from baseline
- PN status at enrollment = Progressive (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - Bilateral Lower	Baseline (n=1)	NC	NC	NC	425,5	425,5	90,9							
	Pre-cycle 5 (n=1)	NC	NC	NC	477,3	477,3	90,9	1	NC	NC	NC	51,8	51,8	90,9
	Pre-cycle 9 (n=1)	NC	NC	NC	466,3	466,3	90,9	1	NC	NC	NC	40,8	40,8	90,9
	Pre-cycle 13 (n=1)	NC	NC	NC	435,3	435,3	90,9	1	NC	NC	NC	9,8	9,8	90,9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.
Mean, SD and Median not calculated for timepoints with <3 patients.
Bilateral Upper parameter omitted owing to insufficient data.

Table 2.11.1.2.4 Motor function secondary outcomes test score mean change from baseline
- PN status at enrollment = Non-progressive (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - all	Baseline (n=8)	495,86	162,660	519,00	182,9	705,0	27,3							
	Pre-cycle 5 (n=8)	519,26	104,004	524,00	375,0	675,0	27,3	8	23,40	89,065	-7,00	-38,0	236,2	27,3
	Pre-cycle 9 (n=8)	516,63	89,653	527,50	350,0	607,0	27,3	8	20,77	121,022	1,50	-117,0	297,2	27,3
	Pre-cycle 13 (n=8)	478,98	162,432	509,50	101,0	596,0	27,3	7	22,42	151,964	8,00	-162,0	281,9	36,4
	Pre-cycle 25 (n=8)	468,70	189,867	563,00	45,5	604,0	27,3	7	18,60	132,783	-5,00	-135,0	265,2	36,4
6-minute walk test % normal distance achieved - all	Baseline (n=8)	77,89	22,391	86,31	28,0	99,8	27,3							
	Pre-cycle 5 (n=8)	81,91	12,362	83,35	63,4	95,6	27,3	8	4,02	13,723	-2,35	-5,2	35,4	27,3
	Pre-cycle 9 (n=8)	80,64	11,550	84,81	59,5	92,0	27,3	8	2,75	17,617	-0,45	-13,3	44,0	27,3
	Pre-cycle 13 (n=7)	82,25	13,023	76,70	68,7	107,2	36,4	7	3,05	22,017	0,68	-23,1	40,7	36,4
	Pre-cycle 25 (n=7)	80,84	15,601	86,00	54,4	95,2	36,4	7	1,64	18,949	2,20	-19,6	36,6	36,4
6-minute walk test velocity achieved (m/min) - all	Baseline (n=8)	82,64	27,110	86,50	30,5	117,5	27,3							
	Pre-cycle 5 (n=8)	86,54	17,334	87,33	62,5	112,5	27,3	8	3,90	14,844	-1,17	-6,3	39,4	27,3
	Pre-cycle 9 (n=8)	86,11	14,942	87,92	58,3	101,2	27,3	8	3,46	20,170	0,25	-19,5	49,5	27,3
	Pre-cycle 13 (n=8)	79,83	27,072	84,92	16,8	99,3	27,3	7	3,74	25,327	1,33	-27,0	47,0	36,4
	Pre-cycle 25 (n=8)	78,12	31,644	93,83	7,6	100,7	27,3	7	3,10	22,132	-0,83	-22,5	44,2	36,4
6-minute walk test distance achieved (m) - Unilateral Upper	Baseline (n=3)	413,29	212,998	454,00	182,9	603,0	72,7							
	Pre-cycle 5 (n=3)	489,03	73,137	483,00	419,1	565,0	72,7	3	75,74	142,960	29,00	-38,0	236,2	72,7
	Pre-cycle 9 (n=3)	513,35	82,221	480,06	453,0	607,0	72,7	3	100,06	170,729	4,00	-1,0	297,2	72,7
	Pre-cycle 13 (n=3)	507,94	66,066	475,00	464,8	584,0	72,7	3	94,65	163,429	21,00	-19,0	281,9	72,7
	Pre-cycle 25 (n=3)	471,69	122,225	448,06	363,0	604,0	72,7	3	58,39	184,896	1,00	-91,0	265,2	72,7
6-minute walk test distance achieved (m) - Unilateral Lower	Baseline (n=4)	505,50	99,848	517,00	393,0	595,0	63,6							
	Pre-cycle 5 (n=4)	503,00	111,005	515,50	375,0	606,0	63,6	4	-2,50	17,311	-7,00	-18,0	22,0	63,6
	Pre-cycle 9 (n=4)	501,25	110,560	527,50	350,0	600,0	63,6	4	-4,25	35,976	-7,50	-43,0	41,0	63,6
	Pre-cycle 13 (n=3)	554,67	68,157	592,00	476,0	596,0	72,7	3	11,67	132,538	8,00	-119,0	146,0	72,7
	Pre-cycle 25 (n=3)	573,00	14,933	579,00	556,0	584,0	72,7	3	30,00	65,886	-5,00	-11,0	106,0	72,7

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.
Mean, SD and Median not calculated for timepoints with <3 patients.
Bilateral Lower parameter omitted owing to insufficient data.

Table 2.11.1.2.4 Motor function secondary outcomes test score mean change from baseline
- PN status at enrollment = Non-progressive (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - Bilateral Upper	Baseline (n=1)	NC	NC	NC	705,0	705,0	90,9							
	Pre-cycle 5 (n=1)	NC	NC	NC	675,0	675,0	90,9	1	NC	NC	NC	-30,0	-30,0	90,9
	Pre-cycle 9 (n=1)	NC	NC	NC	588,0	588,0	90,9	1	NC	NC	NC	-117,0	-117,0	90,9
	Pre-cycle 13 (n=2)	NC	NC	NC	101,0	543,0	81,8	1	NC	NC	NC	-162,0	-162,0	90,9
	Pre-cycle 25 (n=2)	NC	NC	NC	45,5	570,0	81,8	1	NC	NC	NC	-135,0	-135,0	90,9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.
Mean, SD and Median not calculated for timepoints with <3 patients.
Bilateral Lower parameter omitted owing to insufficient data.

Table 2.11.1.2.5 Motor function secondary outcomes test score mean change from baseline
- PN status at enrollment = Unknown (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - all	Baseline (n=8)	524,97	214,802	496,50	135,0	836,0	27,3							
	Pre-cycle 5 (n=8)	492,58	203,551	492,50	186,6	860,0	27,3	7	27,37	45,645	25,00	-37,0	108,0	36,4
	Pre-cycle 9 (n=8)	480,50	185,469	460,00	263,0	845,0	27,3	7	13,57	84,045	9,00	-89,0	128,0	36,4
	Pre-cycle 13 (n=8)	450,86	209,928	419,50	203,9	861,0	27,3	7	-26,44	106,715	-41,00	-174,0	123,0	36,4
	Pre-cycle 25 (n=5)	495,02	239,680	550,00	125,0	770,0	54,5	5	-60,38	155,999	-33,90	-317,0	96,0	54,5
6-minute walk test % normal distance achieved - all	Baseline (n=8)	72,48	26,365	73,01	20,5	114,4	27,3							
	Pre-cycle 5 (n=8)	67,86	20,575	70,32	28,2	92,5	27,3	7	3,69	6,491	3,21	-3,7	15,3	36,4
	Pre-cycle 9 (n=8)	65,95	17,445	66,43	36,6	86,3	27,3	7	1,56	12,370	0,70	-11,3	17,8	36,4
	Pre-cycle 13 (n=8)	60,28	19,199	61,15	30,8	88,1	27,3	7	-5,89	17,941	-7,21	-32,6	19,6	36,4
	Pre-cycle 25 (n=4)	74,23	15,473	75,25	57,2	89,2	63,6	4	2,10	10,373	-0,66	-7,1	16,8	63,6
6-minute walk test velocity achieved (m/min) - all	Baseline (n=8)	87,49	35,800	82,75	22,5	139,3	27,3							
	Pre-cycle 5 (n=8)	82,10	33,925	82,08	31,1	143,3	27,3	7	4,56	7,607	4,17	-6,2	18,0	36,4
	Pre-cycle 9 (n=8)	80,08	30,911	76,67	43,8	140,8	27,3	7	2,26	14,006	1,50	-14,8	21,3	36,4
	Pre-cycle 13 (n=8)	75,14	34,989	69,92	34,0	143,5	27,3	7	-4,41	17,785	-6,83	-29,0	20,5	36,4
	Pre-cycle 25 (n=5)	82,50	39,946	91,67	20,8	128,3	54,5	5	-10,06	26,000	-5,65	-52,8	16,0	54,5
6-minute walk test distance achieved (m) - Unilateral Upper	Baseline (n=3)	519,33	62,268	526,00	454,0	578,0	72,7							
	Pre-cycle 5 (n=3)	573,00	29,103	562,00	551,0	606,0	72,7	3	53,67	47,078	28,00	25,0	108,0	72,7
	Pre-cycle 9 (n=3)	548,33	26,652	559,00	518,0	568,0	72,7	3	29,00	87,069	33,00	-60,0	114,0	72,7
	Pre-cycle 13 (n=3)	529,00	46,130	525,00	485,0	577,0	72,7	3	9,67	98,333	-41,00	-53,0	123,0	72,7
	Pre-cycle 25 (n=2)	NC	NC	NC	550,0	597,0	81,8	2	NC	NC	NC	19,0	96,0	81,8
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 5 (n=1)	NC	NC	NC	311,0	311,0	90,9	0	NC	NC	NC	NC	NC	NC
	Pre-cycle 9 (n=1)	NC	NC	NC	311,0	311,0	90,9	0	NC	NC	NC	NC	NC	NC
	Pre-cycle 13 (n=1)	NC	NC	NC	354,0	354,0	90,9	0	NC	NC	NC	NC	NC	NC

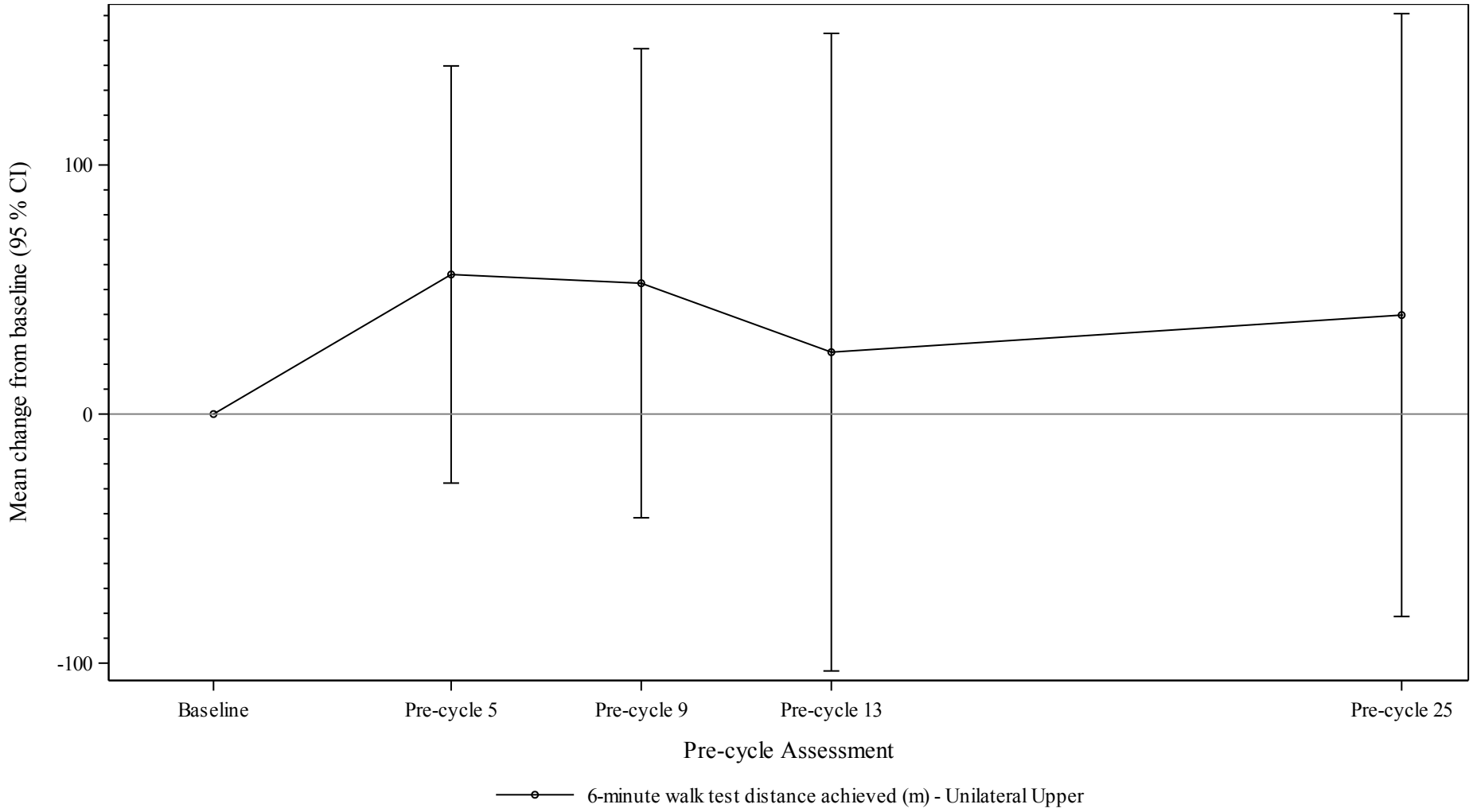
[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.
Mean, SD and Median not calculated for timepoints with <3 patients.
Bilateral Lower parameter omitted owing to insufficient data.

Table 2.11.1.2.5 Motor function secondary outcomes test score mean change from baseline
- PN status at enrollment = Unknown (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
Motor function test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m) - Bilateral Upper	Baseline (n=5)	528,35	280,657	467,00	135,0	836,0	54,5							
	Pre-cycle 5 (n=4)	477,65	279,924	432,00	186,6	860,0	63,6	4	7,65	38,464	8,00	-37,0	51,6	63,6
	Pre-cycle 9 (n=4)	472,00	255,960	390,00	263,0	845,0	63,6	4	2,00	93,041	-15,50	-89,0	128,0	63,6
	Pre-cycle 13 (n=4)	416,48	301,000	300,50	203,9	861,0	63,6	4	-53,53	118,525	-54,50	-174,0	68,9	63,6
	Pre-cycle 25 (n=3)	442,70	322,607	433,10	125,0	770,0	72,7	3	-138,97	155,015	-66,00	-317,0	-33,9	72,7

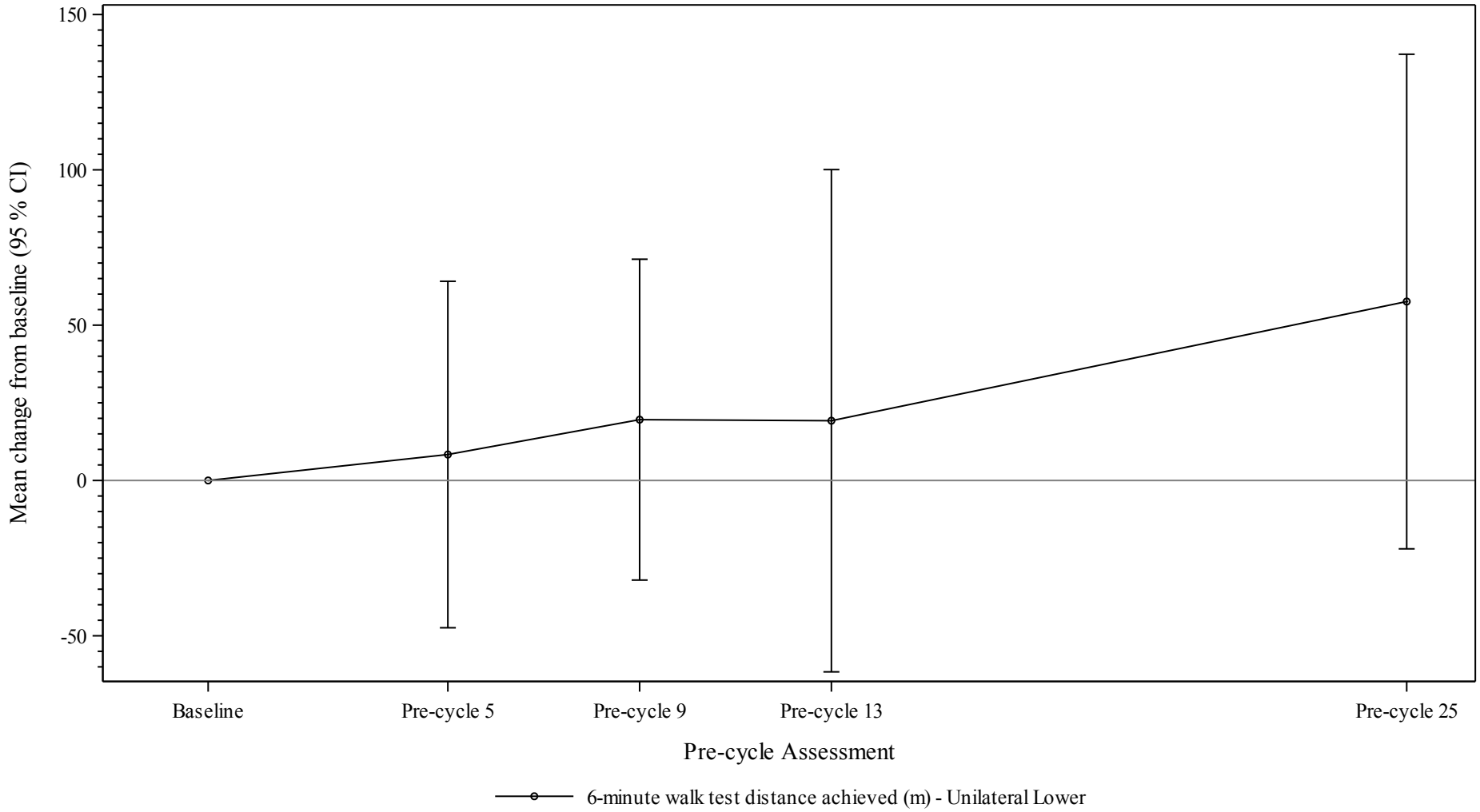
[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.
Mean, SD and Median not calculated for timepoints with <3 patients.
Bilateral Lower parameter omitted owing to insufficient data.

Figure 2.11.1.3 Motor function secondary outcomes test score categories of change over time
(Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 33



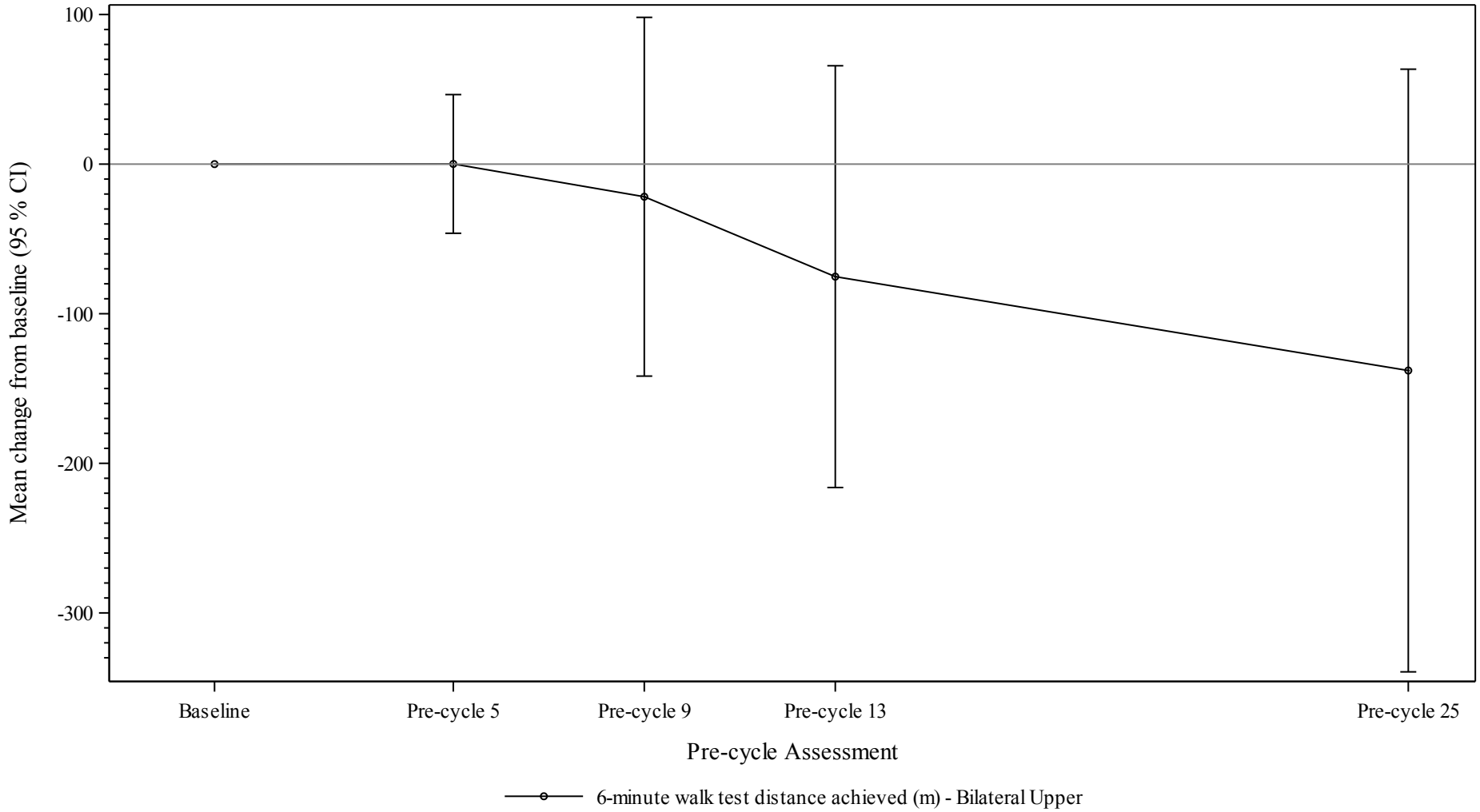
CI = Confidence interval.
Bilateral lower patients omitted owing to insufficient data.

Figure 2.11.1.3 Motor function secondary outcomes test score categories of change over time
(Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 33



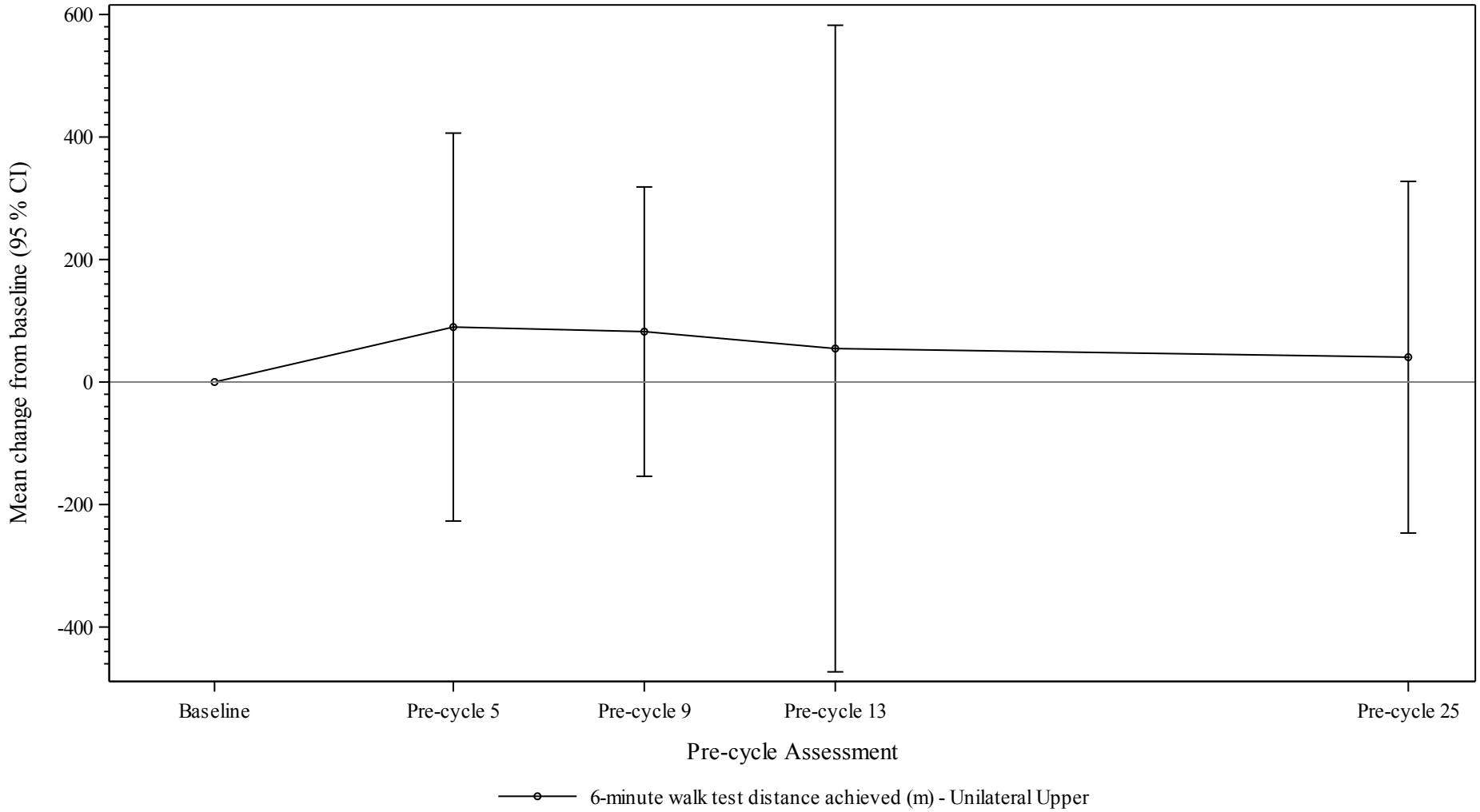
CI = Confidence interval.
Bilateral lower patients omitted owing to insufficient data.

Figure 2.11.1.3 Motor function secondary outcomes test score categories of change over time
(Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 33



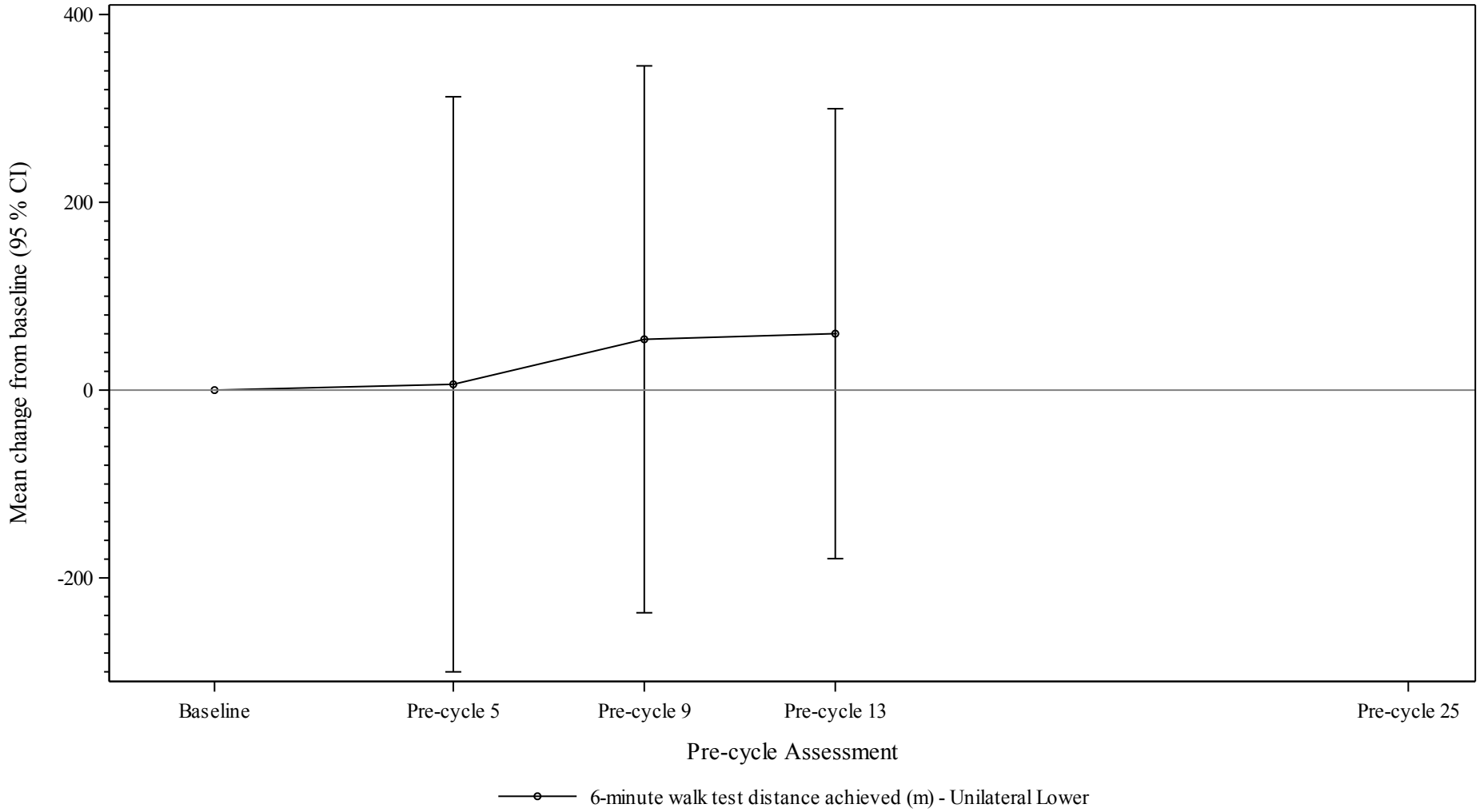
CI = Confidence interval.
Bilateral lower patients omitted owing to insufficient data.

Figure 2.11.1.4.1 Motor function secondary outcomes test score categories of change over time
Gender = Male (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 19



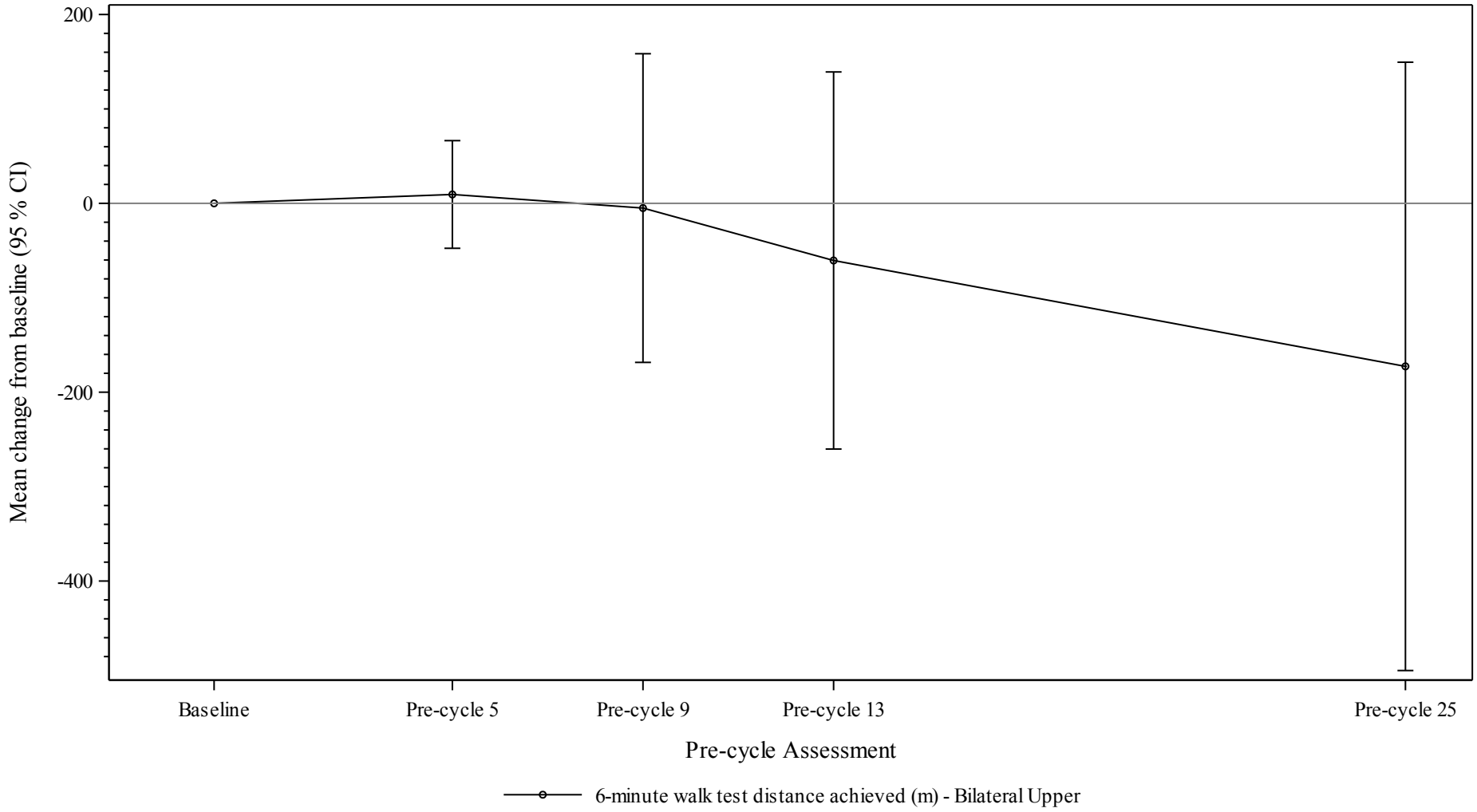
CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral lower patients omitted owing to insufficient data.

Figure 2.11.1.4.1 Motor function secondary outcomes test score categories of change over time
Gender = Male (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 19



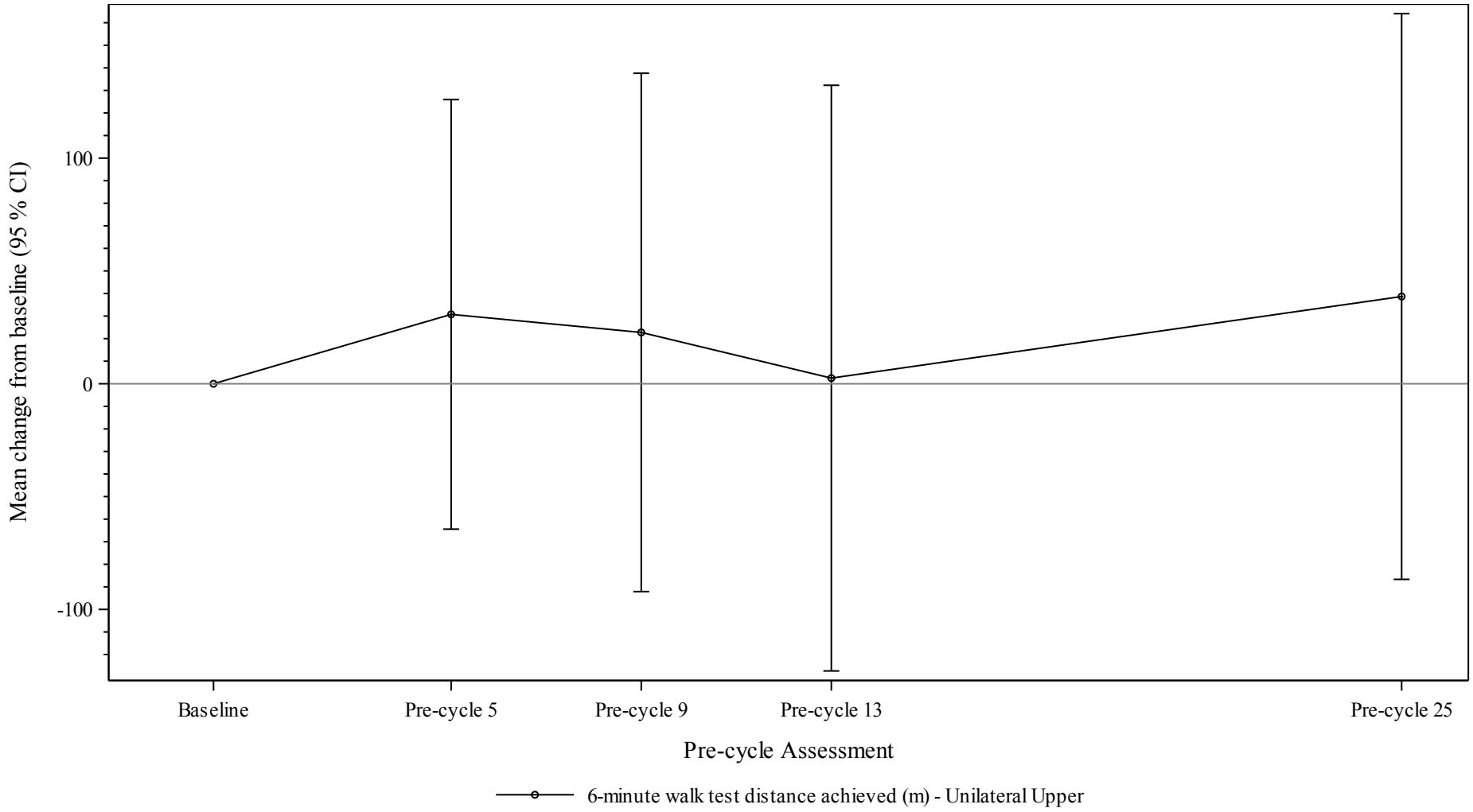
CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral lower patients omitted owing to insufficient data.

Figure 2.11.1.4.1 Motor function secondary outcomes test score categories of change over time
Gender = Male (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 19



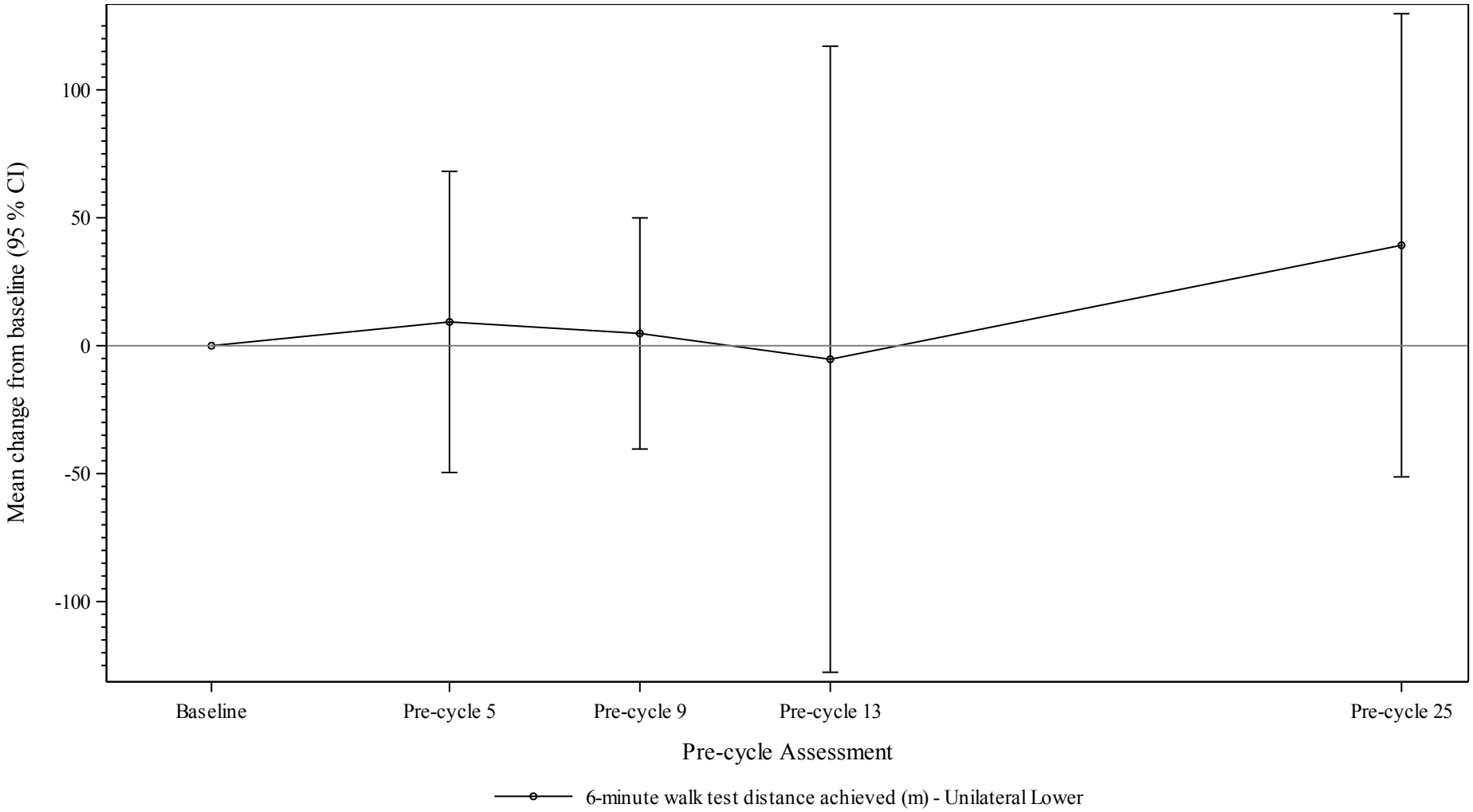
CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral lower patients omitted owing to insufficient data.

Figure 2.11.1.4.2 Motor function secondary outcomes test score categories of change over time
Gender = Female (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 14



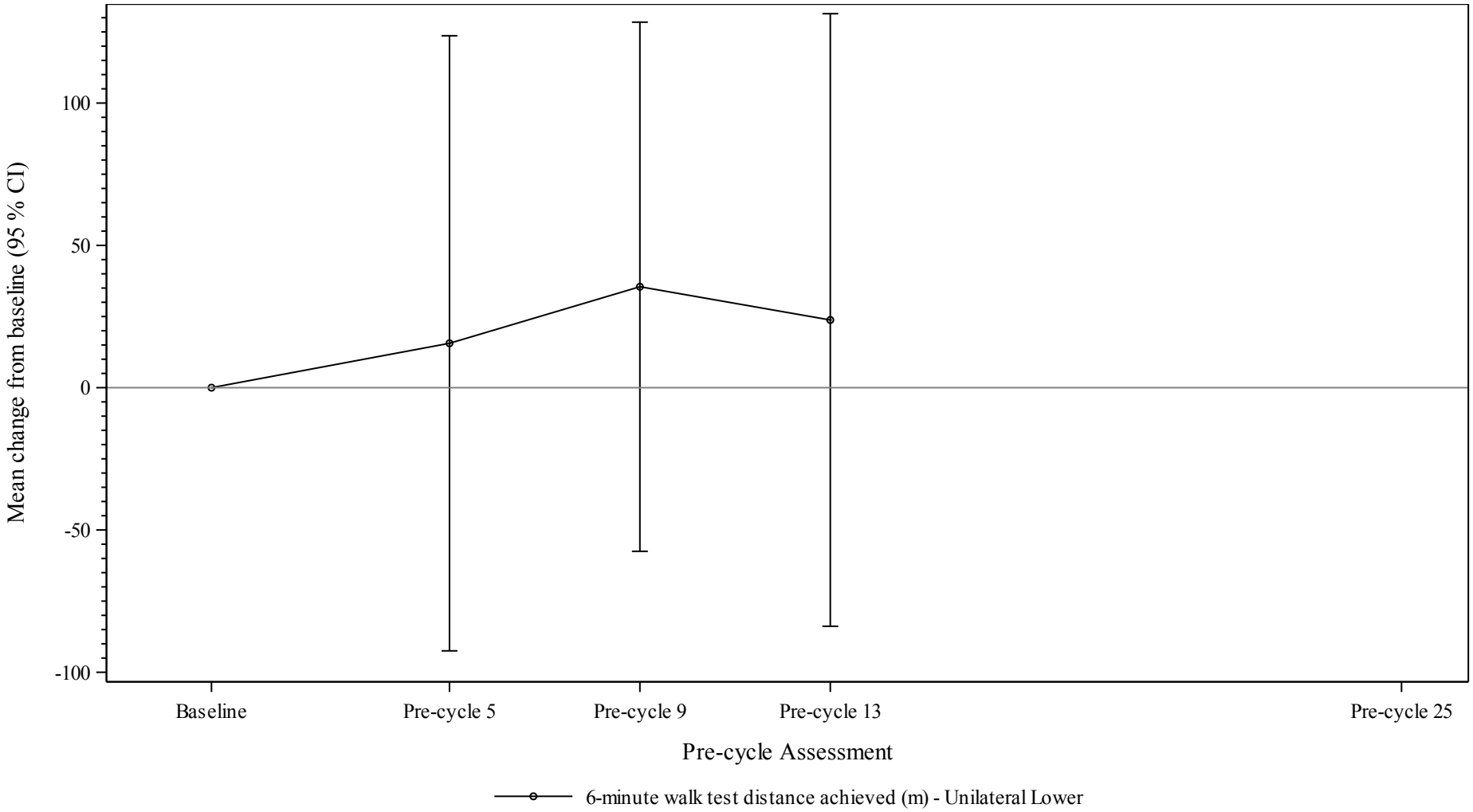
CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral upper patients and bilateral lower patients omitted owing to insufficient data.

Figure 2.11.1.4.2 Motor function secondary outcomes test score categories of change over time
Gender = Female (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 14



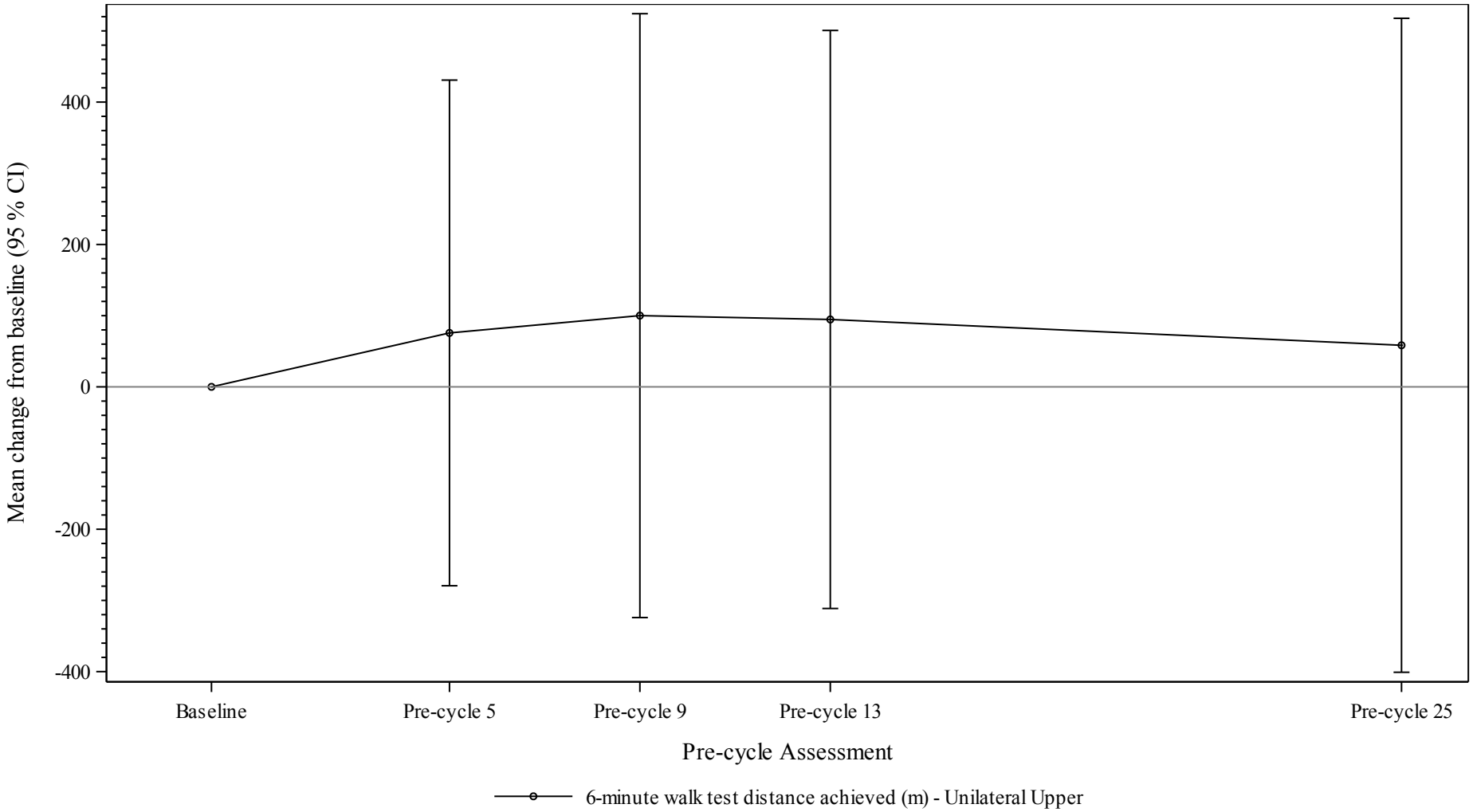
CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral upper patients and bilateral lower patients omitted owing to insufficient data.

Figure 2.11.1.4.3 Motor function secondary outcomes test score categories of change over time
PN status at enrollment = Progressive (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 11



CI = Confidence interval.
Timepoints with <3 patients are omitted.
Unilateral upper patients, bilateral upper patients and bilateral lower patients omitted owing to insufficient data.

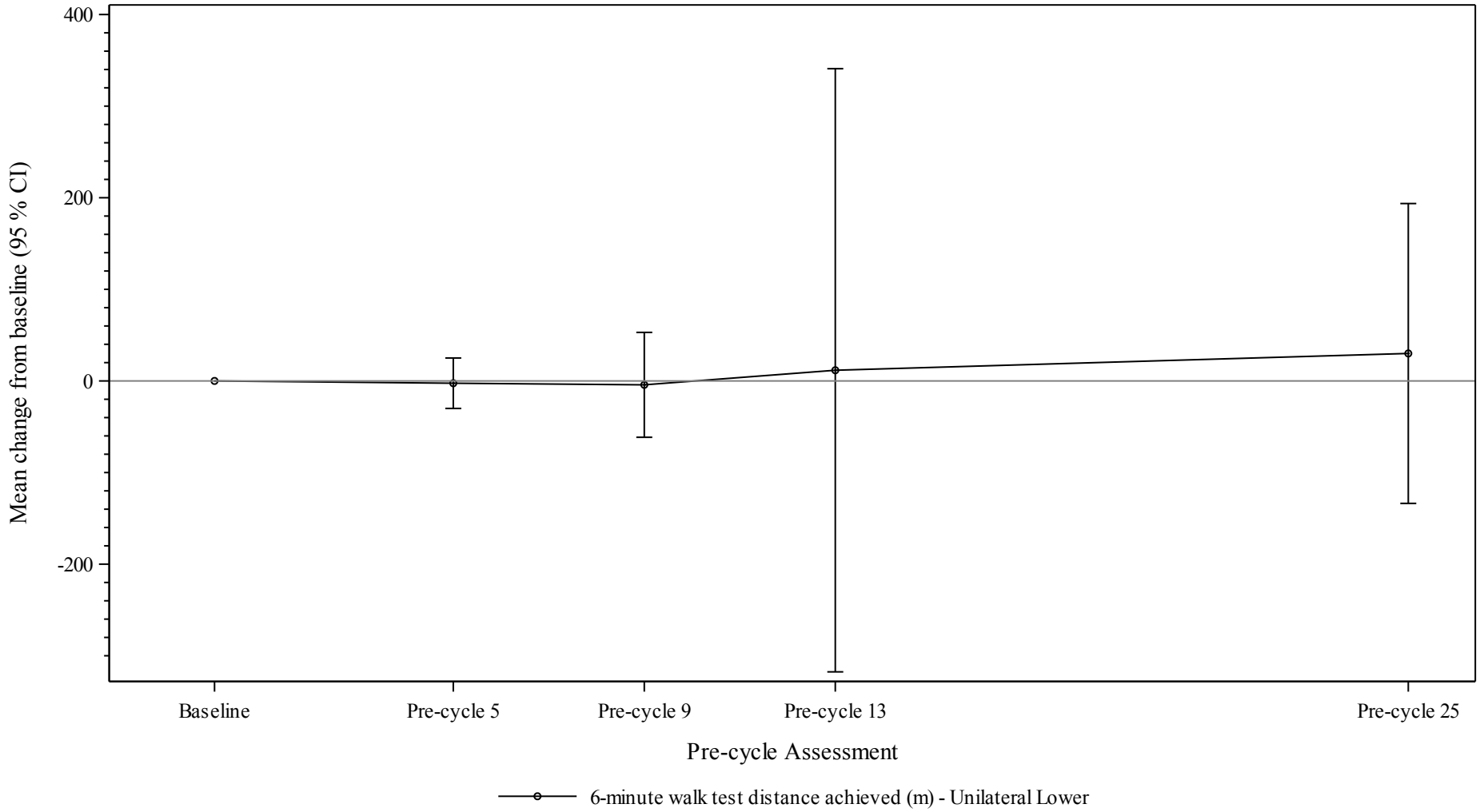
Figure 2.11.1.4.4 Motor function secondary outcomes test score categories of change over time
PN status at enrollment = Non-progressive (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 11



CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral upper patients and bilateral lower patients omitted owing to insufficient data.

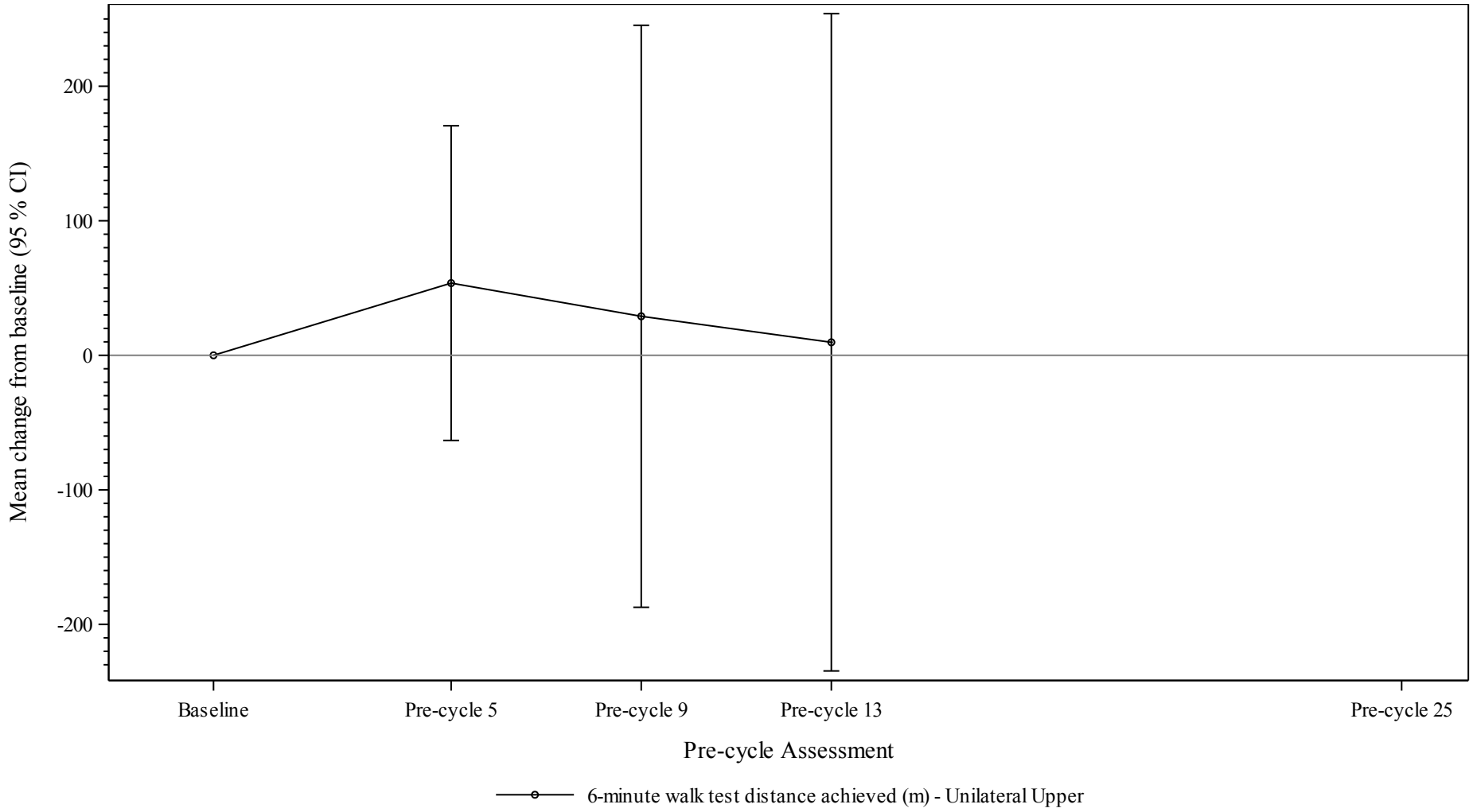
root/cdar/d153/_iemt/ar/payer/tlf_gp/prod/program/smpt6mplchgsub.sas smpt6mplchgsubad.rtf 10MAY2021:08:21 icesas404PD

Figure 2.11.1.4.4 Motor function secondary outcomes test score categories of change over time
PN status at enrollment = Non-progressive (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 11



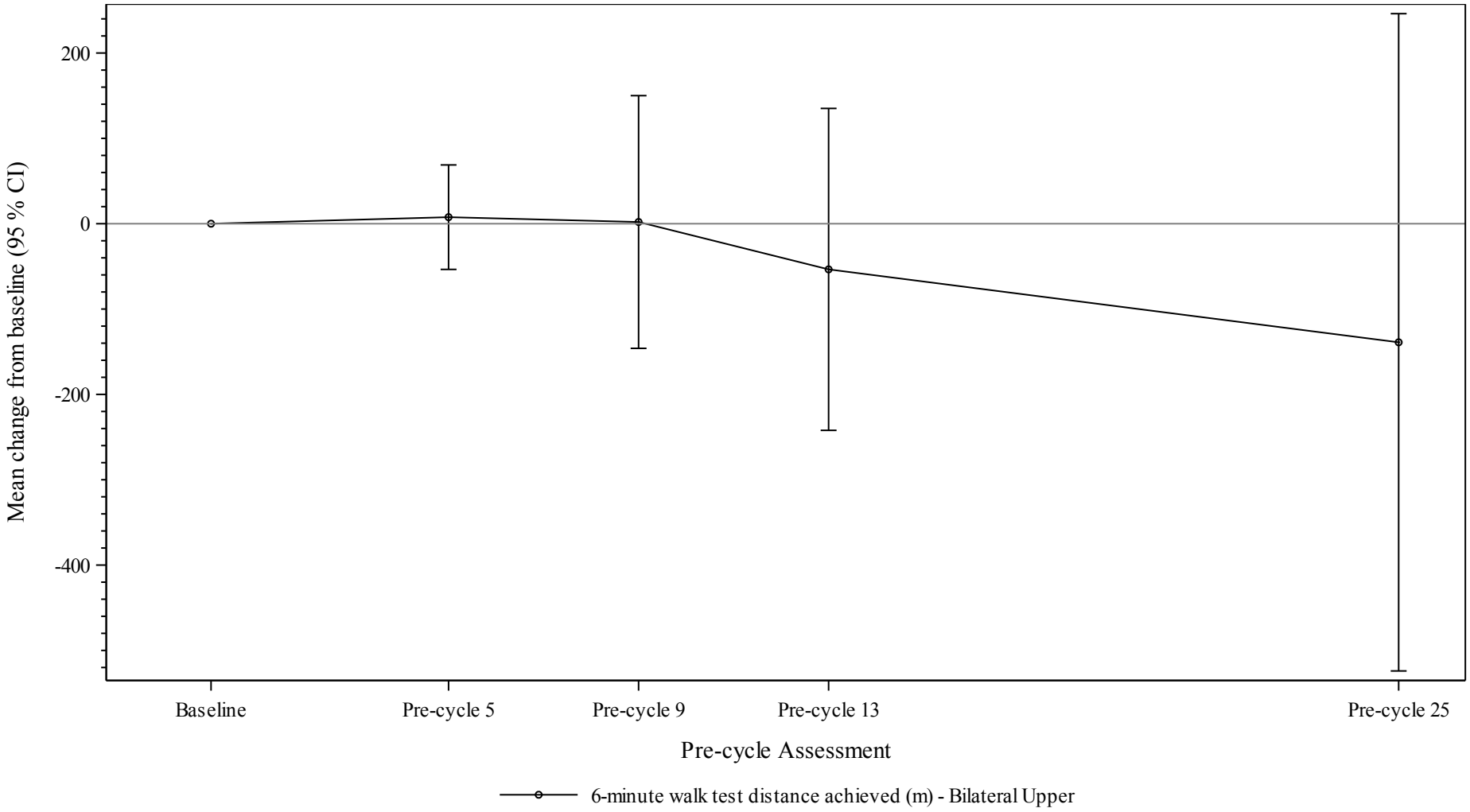
CI = Confidence interval.
Timepoints with <3 patients are omitted.
Bilateral upper patients and bilateral lower patients omitted owing to insufficient data.

Figure 2.11.1.4.5 Motor function secondary outcomes test score categories of change over time
PN status at enrollment = Unknown (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 11



CI = Confidence interval.
Timepoints with <3 patients are omitted.
Unilateral lower patients and bilateral lower patients omitted owing to insufficient data.

Figure 2.11.1.4.5 Motor function secondary outcomes test score categories of change over time
PN status at enrollment = Unknown (Full analysis set, with a motor PN-related morbidity)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 11



CI = Confidence interval.
Timepoints with <3 patients are omitted.
Unilateral lower patients and bilateral lower patients omitted owing to insufficient data.

Table 2.11.2.1 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=34) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=28)	Categories of change [d]			
		Improvement	15	53,6	33,9, 72,5
		No improvement	13	46,4	27,5, 66,1

[a] Patients aged 5-18 years at enrolment, with lower extremity PN, cord compression or airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.1.1.1 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - Gender = Male
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=18) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=14)	Categories of change [d]			
		Improvement	8	57,1	28,9, 82,3
		No improvement	6	42,9	17,7, 71,1

[a] Patients aged 5-18 years at enrolment, with lower extremity PN, cord compression or airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.1.1.2 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - Gender = Female
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=16) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=14)	Categories of change [d]			
		Improvement	7	50,0	23,0, 77,0
		No improvement	7	50,0	23,0, 77,0

[a] Patients aged 5-18 years at enrolment, with lower extremity PN, cord compression or airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.1.1.3 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - PN status at enrollment = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=12)	Categories of change [d]			
		Improvement	9	75,0	42,8, 94,5
		No improvement	3	25,0	5,5, 57,2

[a] Patients aged 5-18 years at enrolment, with lower extremity PN, cord compression or airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.1.1.4 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - PN status at enrollment = Non-progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=9) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8

[a] Patients aged 5-18 years at enrolment, with lower extremity PN, cord compression or airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.1.1.5 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - PN status at enrollment = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=8)	Categories of change [d]			
		Improvement	4	50,0	15,7, 84,3
		No improvement	4	50,0	15,7, 84,3

[a] Patients aged 5-18 years at enrolment, with lower extremity PN, cord compression or airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.1.2.1 Endurance evaluation secondary outcome scores change from baseline over time - Gender = Male
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=18) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=15)	517,55	218,420	454,00	135,0	850,0	16,7							
	Pre-cycle 5 (n=15)	481,71	157,223	477,30	186,6	860,0	16,7	13	-2,53	143,033	6,00	-389,0	236,2	27,8
	Pre-cycle 9 (n=15)	518,12	151,826	495,00	263,0	845,0	16,7	14	32,81	114,630	24,92	-145,0	297,2	22,2
	Pre-cycle 13 (n=15)	462,30	185,195	464,82	101,0	861,0	16,7	13	1,16	148,360	21,00	-296,0	281,9	27,8
	Pre-cycle 25 (n=10)	476,76	248,290	498,50	45,5	805,0	44,4	9	-26,31	170,833	-66,00	-317,0	265,2	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	761,0	761,0	94,4	1	NC	NC	NC	-89,0	-89,0	94,4
6-minute walk test % normal distance achieved	Baseline (n=14)	73,71	25,467	72,75	20,5	114,4	22,2							
	Pre-cycle 5 (n=13)	72,11	18,335	74,64	28,2	95,6	27,8	12	3,86	13,446	0,53	-16,1	35,4	33,3
	Pre-cycle 9 (n=14)	73,49	17,107	72,10	36,6	102,4	22,2	13	4,62	16,601	0,70	-14,0	44,0	27,8
	Pre-cycle 13 (n=14)	69,85	18,102	72,33	30,8	93,6	22,2	13	0,18	19,530	0,00	-32,6	40,7	27,8
	Pre-cycle 25 (n=8)	75,53	17,908	75,30	54,4	109,7	55,6	7	-2,46	21,130	-7,10	-19,6	36,6	61,1
	Pre-cycle 37 (n=1)	NC	NC	NC	68,3	68,3	94,4	1	NC	NC	NC	-9,7	-9,7	94,4
6-minute walk test velocity achieved (m/min)	Baseline (n=15)	86,26	36,403	75,67	22,5	141,7	16,7							
	Pre-cycle 5 (n=15)	80,28	26,203	79,55	31,1	143,3	16,7	13	-0,42	23,839	1,00	-64,8	39,4	27,8
	Pre-cycle 9 (n=15)	86,35	25,304	82,50	43,8	140,8	16,7	14	5,47	19,105	4,15	-24,2	49,5	22,2
	Pre-cycle 13 (n=15)	77,05	30,866	77,47	16,8	143,5	16,7	13	0,19	24,727	3,50	-49,3	47,0	27,8
	Pre-cycle 25 (n=10)	79,46	41,381	83,08	7,6	134,2	44,4	9	-4,39	28,473	-11,00	-52,8	44,2	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	126,8	126,8	94,4	1	NC	NC	NC	-14,8	-14,8	94,4

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.1.2.2 Endurance evaluation secondary outcome scores change from baseline over time - Gender = Female
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=16) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=15)	482,55	86,126	456,00	308,8	603,0	6,3							
	Pre-cycle 5 (n=16)	490,30	98,634	453,50	354,0	660,0	0,0	14	10,86	54,863	0,50	-86,0	123,0	12,5
	Pre-cycle 9 (n=16)	486,82	82,564	487,00	350,0	607,0	0,0	14	6,18	56,064	4,50	-89,0	114,0	12,5
	Pre-cycle 13 (n=14)	486,29	88,847	480,50	333,0	596,0	12,5	12	-2,96	90,353	-11,00	-134,0	146,0	25,0
	Pre-cycle 25 (n=12)	537,13	65,023	553,00	433,1	611,0	25,0	10	49,21	63,255	43,00	-33,9	155,0	37,5
	Pre-cycle 37 (n=1)	NC	NC	NC	642,0	642,0	93,8	1	NC	NC	NC	186,0	186,0	93,8
6-minute walk test % normal distance achieved	Baseline (n=14)	76,81	10,694	78,40	55,2	91,1	12,5							
	Pre-cycle 5 (n=15)	78,46	13,399	82,07	54,1	97,5	6,3	13	1,79	8,613	-1,65	-13,0	17,5	18,8
	Pre-cycle 9 (n=15)	77,44	11,915	78,74	56,5	92,0	6,3	13	0,30	8,790	0,80	-11,3	17,8	18,8
	Pre-cycle 13 (n=13)	75,90	15,246	74,20	45,7	107,2	18,8	11	-2,95	13,406	-3,74	-22,0	21,3	31,3
	Pre-cycle 25 (n=12)	83,02	9,396	85,65	65,2	95,2	25,0	9	4,87	6,076	2,40	-2,5	16,8	43,8
	Pre-cycle 37 (n=1)	NC	NC	NC	75,8	75,8	93,8	0	NC	NC	NC	NC	NC	NC
6-minute walk test velocity achieved (m/min)	Baseline (n=15)	80,43	14,354	76,00	51,5	100,5	6,3							
	Pre-cycle 5 (n=16)	81,72	16,439	75,58	59,0	110,0	0,0	14	1,81	9,144	0,08	-14,3	20,5	12,5
	Pre-cycle 9 (n=16)	81,14	13,761	81,17	58,3	101,2	0,0	14	1,03	9,344	0,75	-14,8	19,0	12,5
	Pre-cycle 13 (n=14)	81,05	14,808	80,08	55,5	99,3	12,5	12	-0,49	15,058	-1,83	-22,3	24,3	25,0
	Pre-cycle 25 (n=12)	89,52	10,837	92,17	72,2	101,8	25,0	10	8,20	10,542	7,17	-5,6	25,8	37,5
	Pre-cycle 37 (n=1)	NC	NC	NC	107,0	107,0	93,8	1	NC	NC	NC	31,0	31,0	93,8

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.1.2.3 Endurance evaluation secondary outcome scores change from baseline over time - PN status at enrol. = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=12)	506,34	143,995	453,25	366,0	850,0	7,7							
	Pre-cycle 5 (n=13)	470,50	94,569	461,00	354,0	660,0	0,0	11	-23,61	142,330	1,00	-389,0	129,5	15,4
	Pre-cycle 9 (n=13)	514,83	99,932	495,00	357,0	705,0	0,0	12	21,64	80,563	33,42	-145,0	129,0	7,7
	Pre-cycle 13 (n=11)	492,35	91,482	450,00	383,0	644,0	15,4	10	0,67	124,162	3,40	-296,0	152,4	23,1
	Pre-cycle 25 (n=7)	566,57	128,591	500,00	453,0	805,0	46,2	6	54,83	98,493	87,00	-86,0	155,0	53,8
	Pre-cycle 37 (n=2)	NC	NC	NC	642,0	761,0	84,6	2	NC	NC	NC	-89,0	186,0	84,6
6-minute walk test % normal distance achieved	Baseline (n=10)	77,12	10,804	71,40	67,1	96,5	23,1							
	Pre-cycle 5 (n=10)	76,33	14,874	78,03	54,1	97,5	23,1	9	1,46	12,655	-0,65	-16,1	20,6	30,8
	Pre-cycle 9 (n=11)	78,39	13,405	77,10	60,8	102,4	15,4	10	3,02	11,796	2,50	-14,0	21,0	23,1
	Pre-cycle 13 (n=10)	75,33	13,795	73,88	55,4	93,6	23,1	9	-0,72	12,766	-2,90	-22,6	22,1	30,8
	Pre-cycle 25 (n=7)	81,24	13,552	76,50	72,0	109,7	46,2	4	-0,66	14,457	-0,10	-17,9	15,5	69,2
	Pre-cycle 37 (n=2)	NC	NC	NC	68,3	75,8	84,6	1	NC	NC	NC	-9,7	-9,7	92,3
6-minute walk test velocity achieved (m/min)	Baseline (n=12)	84,39	23,999	75,54	61,0	141,7	7,7							
	Pre-cycle 5 (n=13)	78,42	15,761	76,83	59,0	110,0	0,0	11	-3,93	23,722	0,17	-64,8	21,6	15,4
	Pre-cycle 9 (n=13)	85,80	16,655	82,50	59,5	117,5	0,0	12	3,61	13,427	5,57	-24,2	21,5	7,7
	Pre-cycle 13 (n=11)	82,06	15,247	75,00	63,8	107,3	15,4	10	0,11	20,694	0,57	-49,3	25,4	23,1
	Pre-cycle 25 (n=7)	94,43	21,432	83,33	75,5	134,2	46,2	6	9,14	16,416	14,50	-14,3	25,8	53,8
	Pre-cycle 37 (n=2)	NC	NC	NC	107,0	126,8	84,6	2	NC	NC	NC	-14,8	31,0	84,6

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.1.2.4 Endurance evaluation secondary outcome scores change from baseline - PN status at enrol. = Non-progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=9) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=8)	495,86	162,660	519,00	182,9	705,0	11,1							
	Pre-cycle 5 (n=8)	519,26	104,004	524,00	375,0	675,0	11,1	8	23,40	89,065	-7,00	-38,0	236,2	11,1
	Pre-cycle 9 (n=8)	516,63	89,653	527,50	350,0	607,0	11,1	8	20,77	121,022	1,50	-117,0	297,2	11,1
	Pre-cycle 13 (n=8)	478,98	162,432	509,50	101,0	596,0	11,1	7	22,42	151,964	8,00	-162,0	281,9	22,2
	Pre-cycle 25 (n=8)	468,70	189,867	563,00	45,5	604,0	11,1	7	18,60	132,783	-5,00	-135,0	265,2	22,2
6-minute walk test % normal distance achieved	Baseline (n=8)	77,89	22,391	86,31	28,0	99,8	11,1							
	Pre-cycle 5 (n=8)	81,91	12,362	83,35	63,4	95,6	11,1	8	4,02	13,723	-2,35	-5,2	35,4	11,1
	Pre-cycle 9 (n=8)	80,64	11,550	84,81	59,5	92,0	11,1	8	2,75	17,617	-0,45	-13,3	44,0	11,1
	Pre-cycle 13 (n=7)	82,25	13,023	76,70	68,7	107,2	22,2	7	3,05	22,017	0,68	-23,1	40,7	22,2
	Pre-cycle 25 (n=7)	80,84	15,601	86,00	54,4	95,2	22,2	7	1,64	18,949	2,20	-19,6	36,6	22,2
6-minute walk test velocity achieved (m/min)	Baseline (n=8)	82,64	27,110	86,50	30,5	117,5	11,1							
	Pre-cycle 5 (n=8)	86,54	17,334	87,33	62,5	112,5	11,1	8	3,90	14,844	-1,17	-6,3	39,4	11,1
	Pre-cycle 9 (n=8)	86,11	14,942	87,92	58,3	101,2	11,1	8	3,46	20,170	0,25	-19,5	49,5	11,1
	Pre-cycle 13 (n=8)	79,83	27,072	84,92	16,8	99,3	11,1	7	3,74	25,327	1,33	-27,0	47,0	22,2
	Pre-cycle 25 (n=8)	78,12	31,644	93,83	7,6	100,7	11,1	7	3,10	22,132	-0,83	-22,5	44,2	22,2

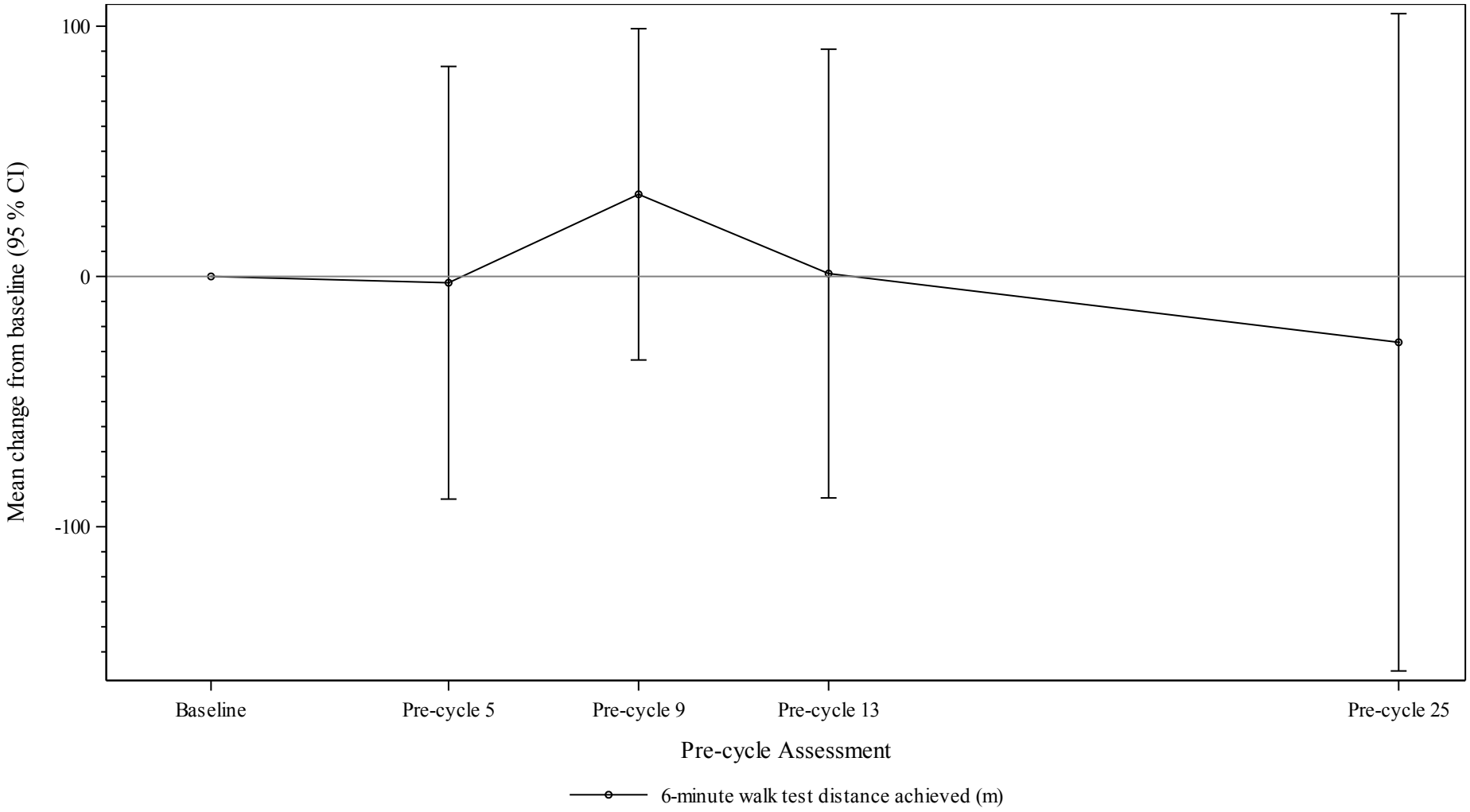
[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.1.2.5 Endurance evaluation secondary outcome scores change from baseline over time - PN status at enrol. = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=10)	495,86	201,895	460,50	135,0	836,0	16,7							
	Pre-cycle 5 (n=10)	479,99	181,718	442,00	186,6	860,0	16,7	8	23,95	43,353	24,50	-37,0	108,0	33,3
	Pre-cycle 9 (n=10)	473,51	164,818	445,53	263,0	845,0	16,7	8	15,00	77,916	17,00	-89,0	128,0	33,3
	Pre-cycle 13 (n=10)	449,49	185,191	444,00	203,9	861,0	16,7	8	-23,01	99,274	-20,00	-174,0	123,0	33,3
	Pre-cycle 25 (n=7)	499,66	197,004	548,00	125,0	770,0	41,7	6	-33,98	153,783	-7,45	-317,0	98,0	50,0
6-minute walk test % normal distance achieved	Baseline (n=10)	71,30	23,988	73,01	20,5	114,4	16,7							
	Pre-cycle 5 (n=10)	69,58	18,505	75,47	28,2	92,5	16,7	8	3,02	6,299	2,46	-3,7	15,3	33,3
	Pre-cycle 9 (n=10)	68,32	16,177	72,32	36,6	86,3	16,7	8	1,46	11,456	0,75	-11,3	17,8	33,3
	Pre-cycle 13 (n=10)	63,55	18,321	67,98	30,8	88,1	16,7	8	-5,62	16,628	-5,48	-32,6	19,6	33,3
	Pre-cycle 25 (n=6)	77,63	13,220	83,45	57,2	89,2	50,0	5	3,55	9,552	1,20	-7,1	16,8	58,3
6-minute walk test velocity achieved (m/min)	Baseline (n=10)	82,64	33,648	76,75	22,5	139,3	16,7							
	Pre-cycle 5 (n=10)	80,00	30,286	73,67	31,1	143,3	16,7	8	3,99	7,225	4,08	-6,2	18,0	33,3
	Pre-cycle 9 (n=10)	78,92	27,469	74,25	43,8	140,8	16,7	8	2,50	12,985	2,83	-14,8	21,3	33,3
	Pre-cycle 13 (n=10)	74,91	30,866	74,00	34,0	143,5	16,7	8	-3,83	16,545	-3,33	-29,0	20,5	33,3
	Pre-cycle 25 (n=7)	83,28	32,833	91,33	20,8	128,3	41,7	6	-5,66	25,631	-1,24	-52,8	16,3	50,0

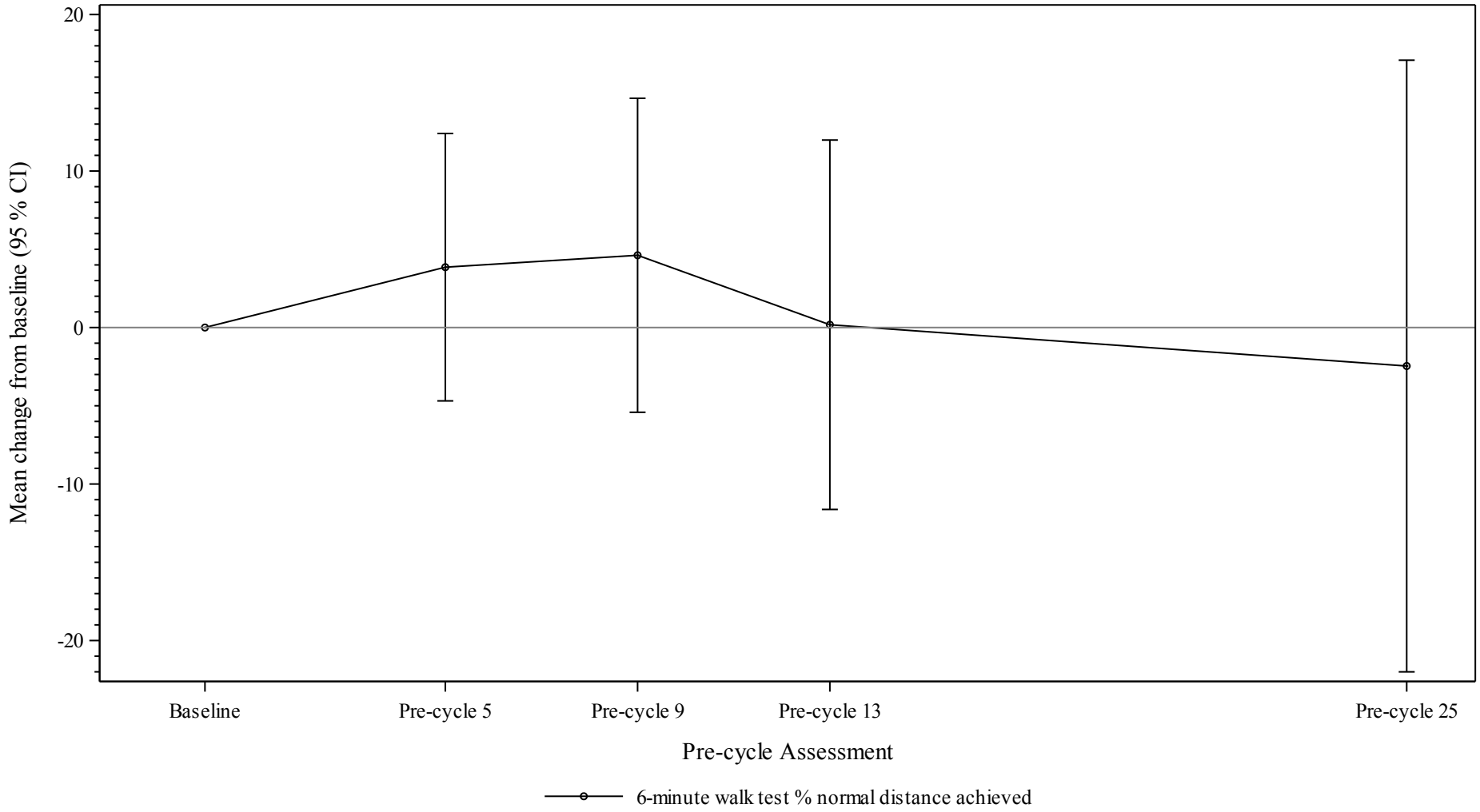
[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Figure 2.11.2.1.3.1 Mean change from baseline of 6-minute walk test scores over time - Gender = Male
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 18



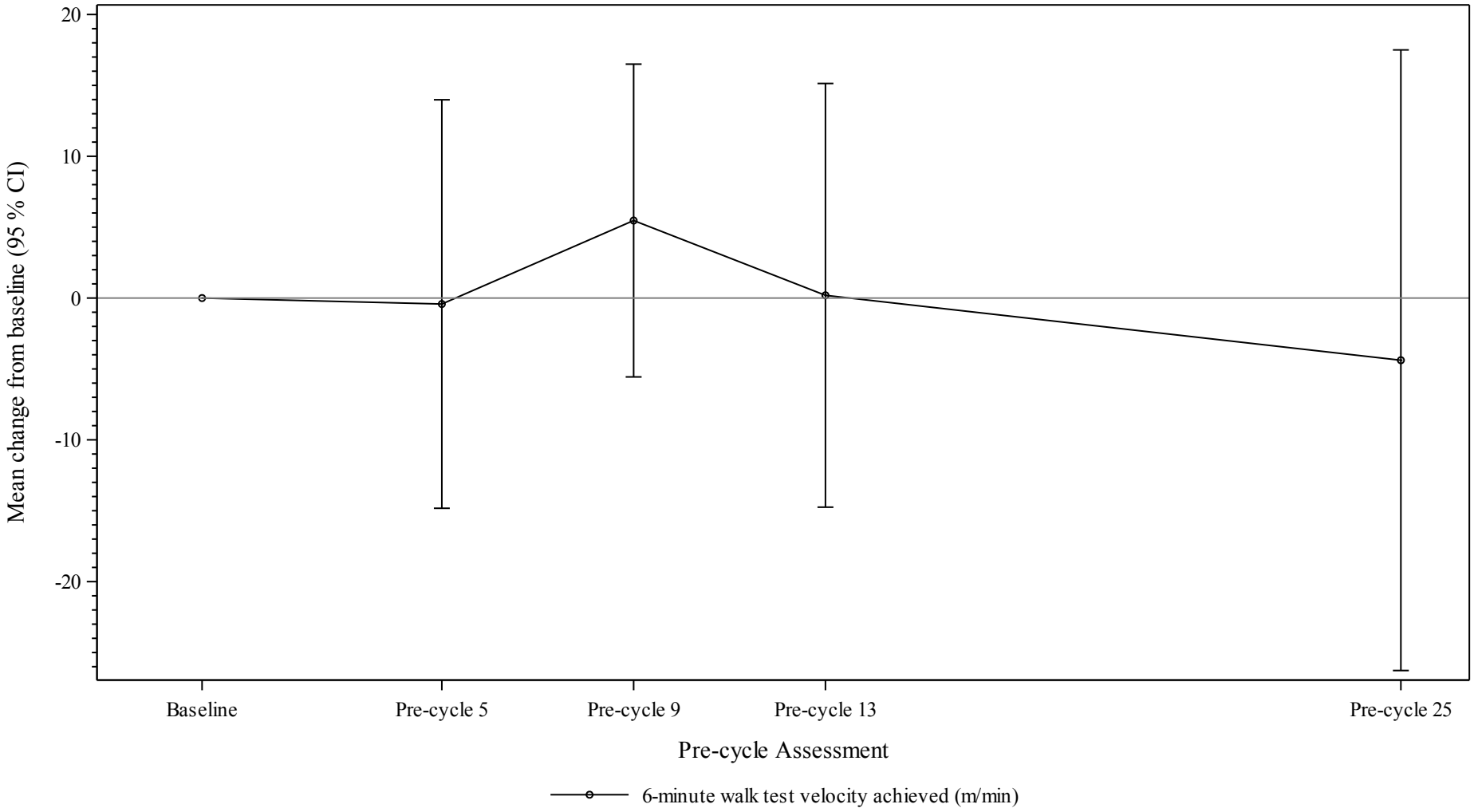
CI = Confidence interval.

Figure 2.11.2.1.3.1 Mean change from baseline of 6-minute walk test scores over time - Gender = Male
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 18



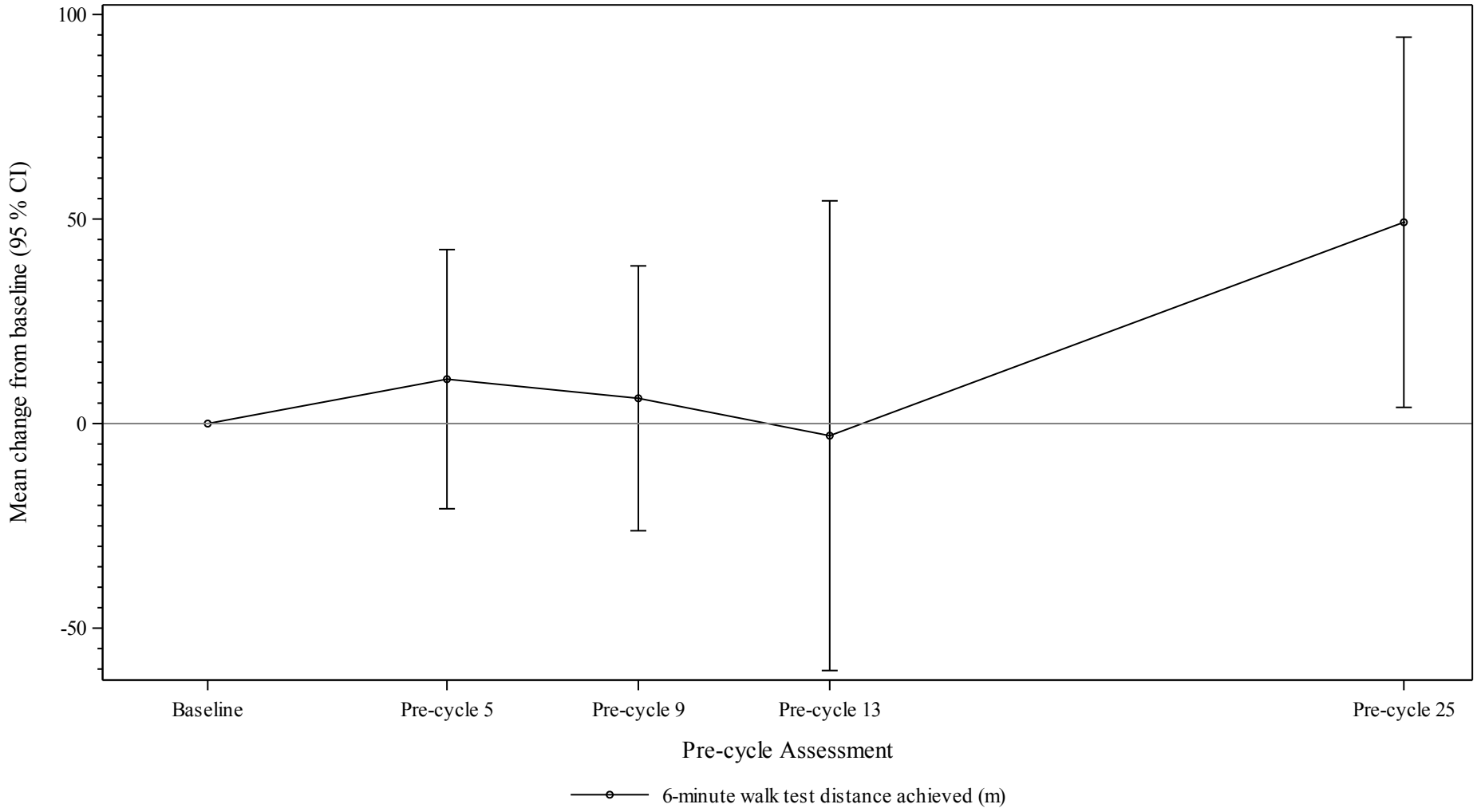
CI = Confidence interval.

Figure 2.11.2.1.3.1 Mean change from baseline of 6-minute walk test scores over time - Gender = Male
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 18



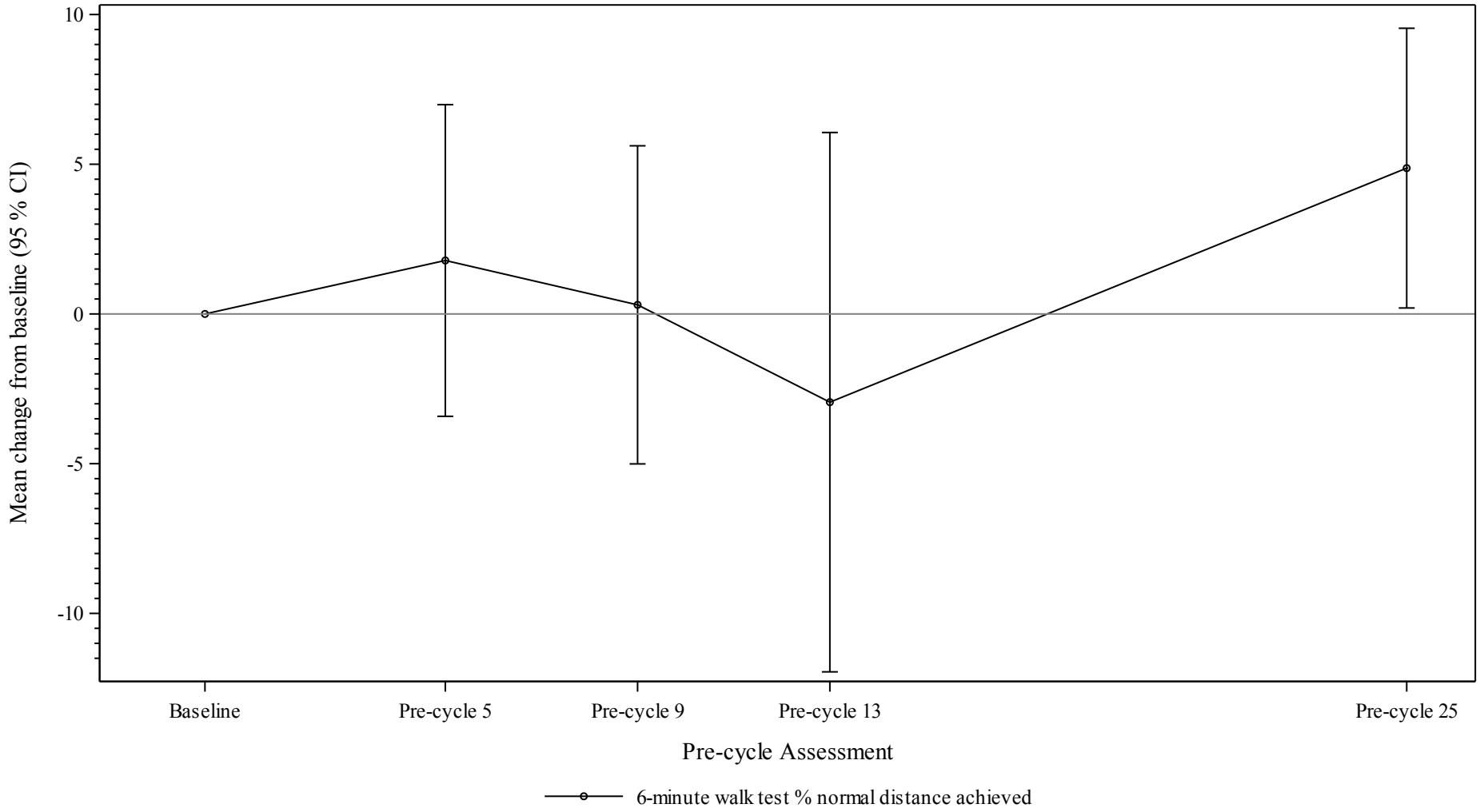
CI = Confidence interval.

Figure 2.11.2.1.3.2 Mean change from baseline of 6-minute walk test scores over time - Gender = Female
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 16



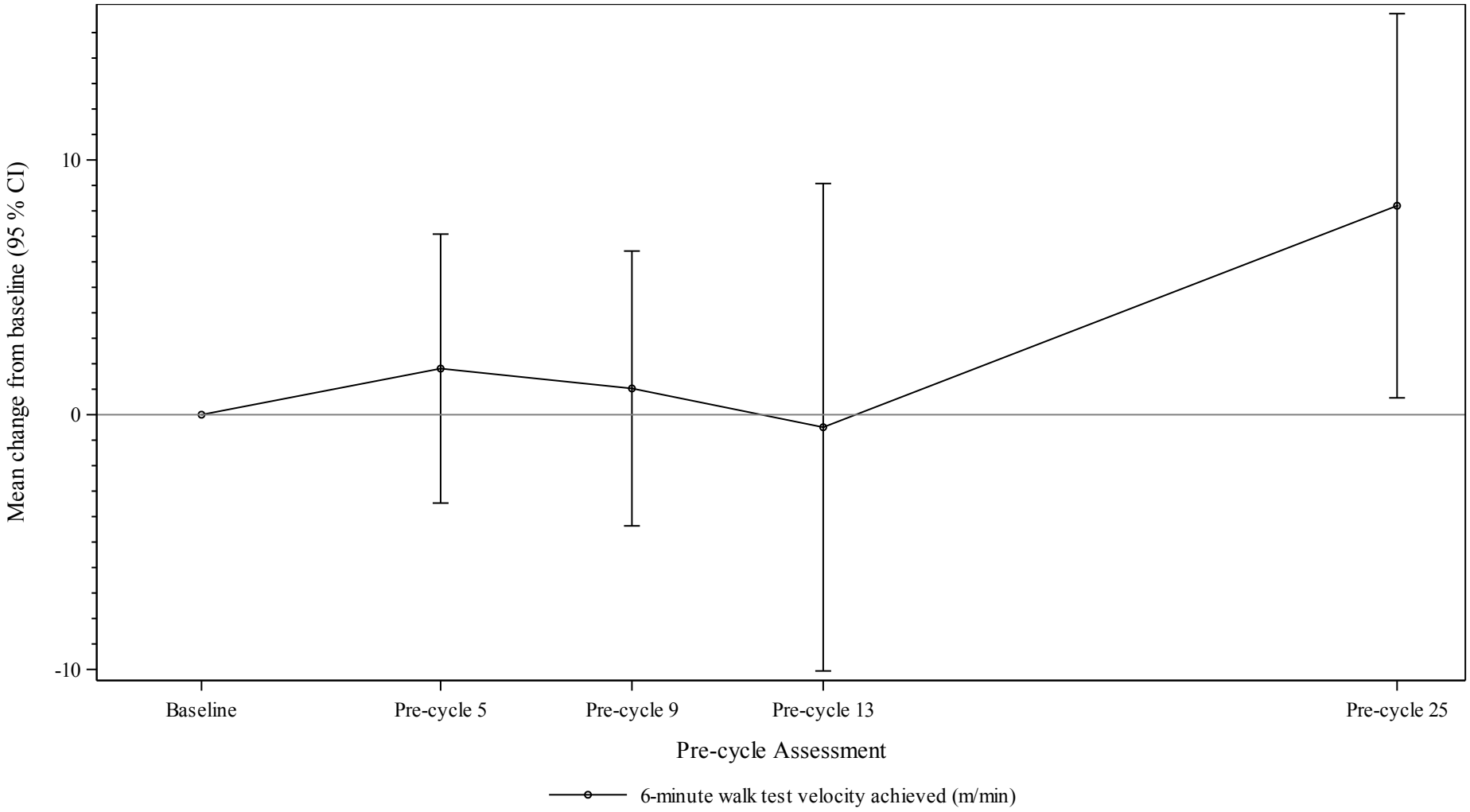
CI = Confidence interval.

Figure 2.11.2.1.3.2 Mean change from baseline of 6-minute walk test scores over time - Gender = Female
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 16



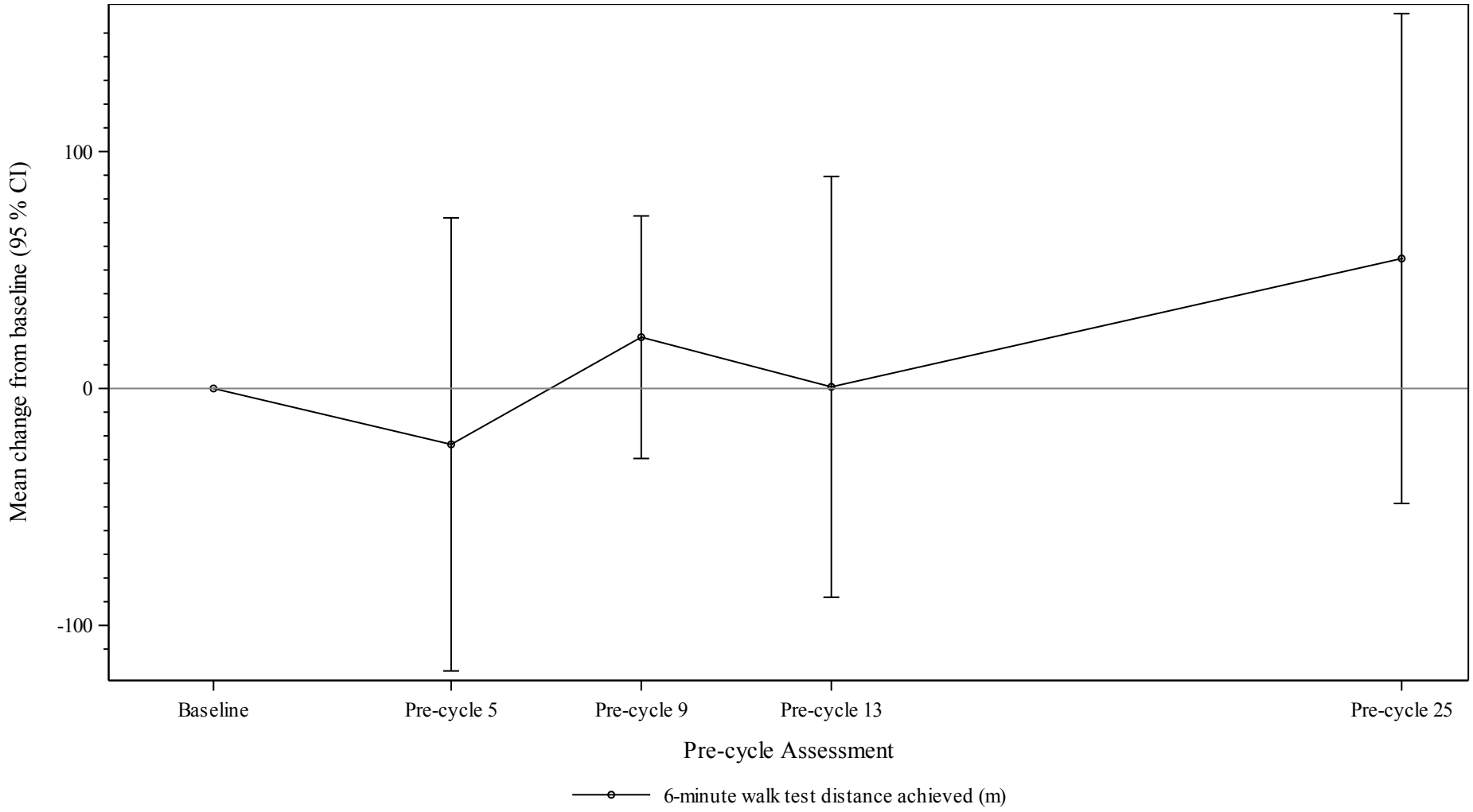
CI = Confidence interval.

Figure 2.11.2.1.3.2 Mean change from baseline of 6-minute walk test scores over time - Gender = Female
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 16



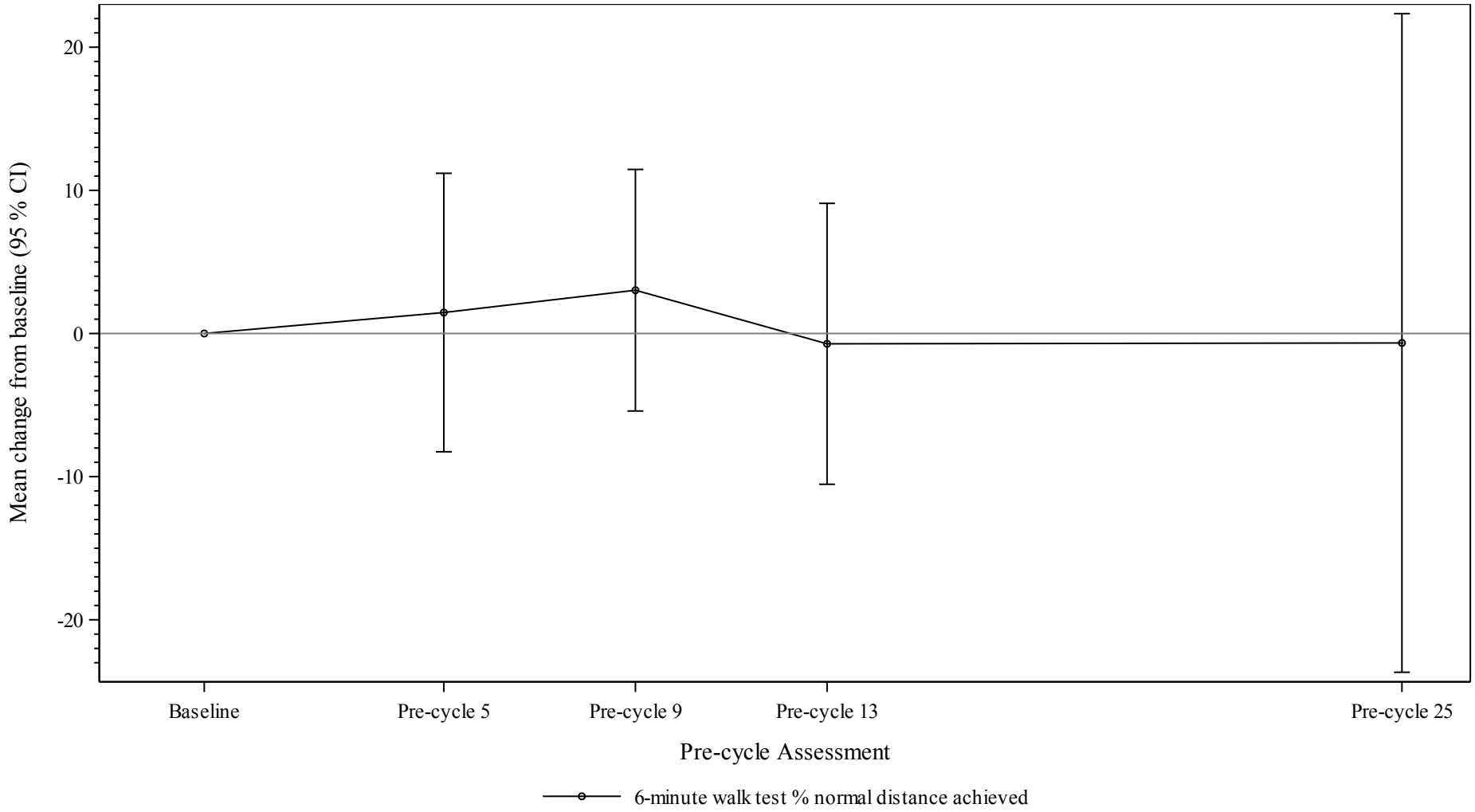
CI = Confidence interval.

Figure 2.11.2.1.3.3 Mean change from baseline of 6-minute walk test scores over time - PN status at enrollment = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 13



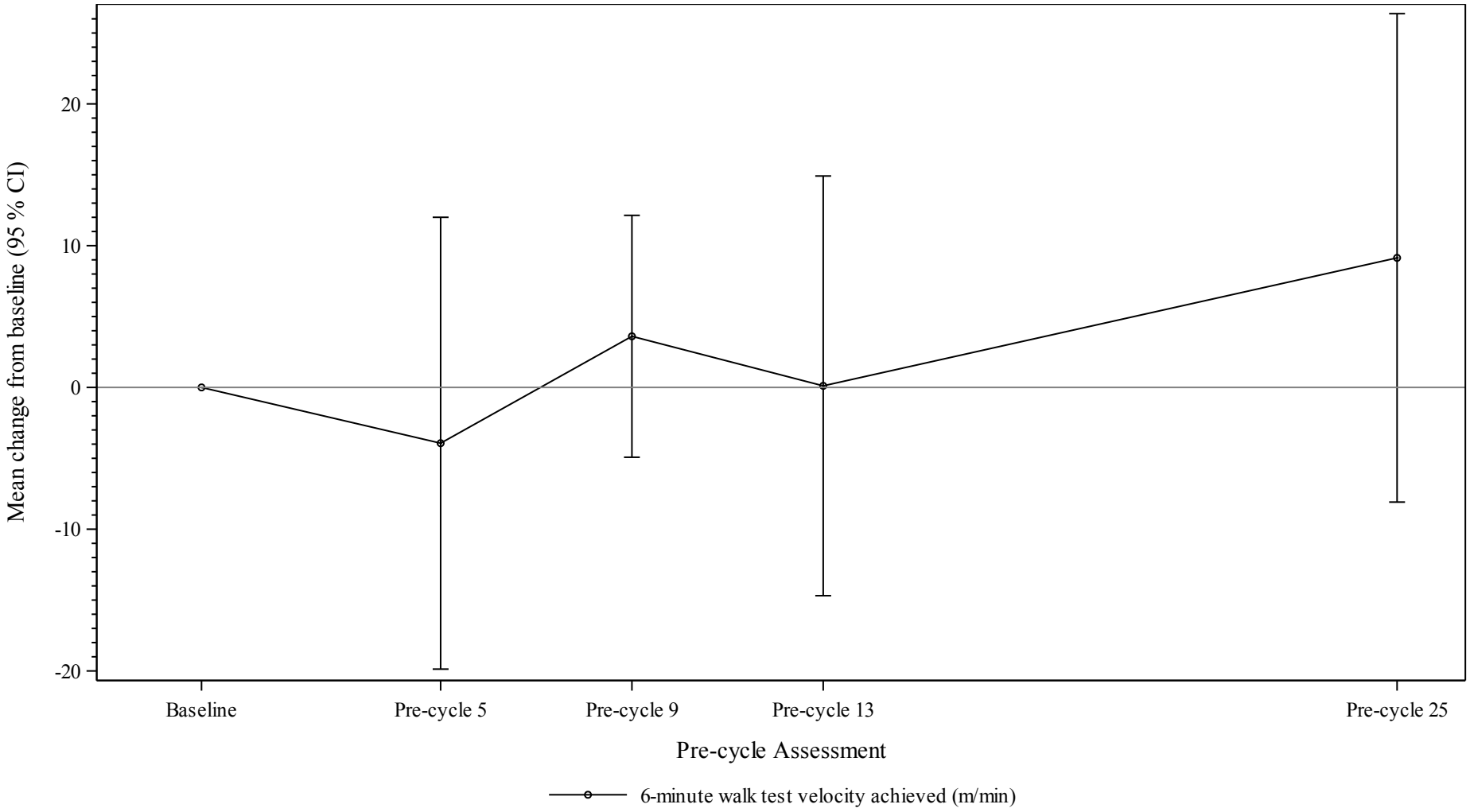
CI = Confidence interval.

Figure 2.11.2.1.3.3 Mean change from baseline of 6-minute walk test scores over time - PN status at enrollment = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 13



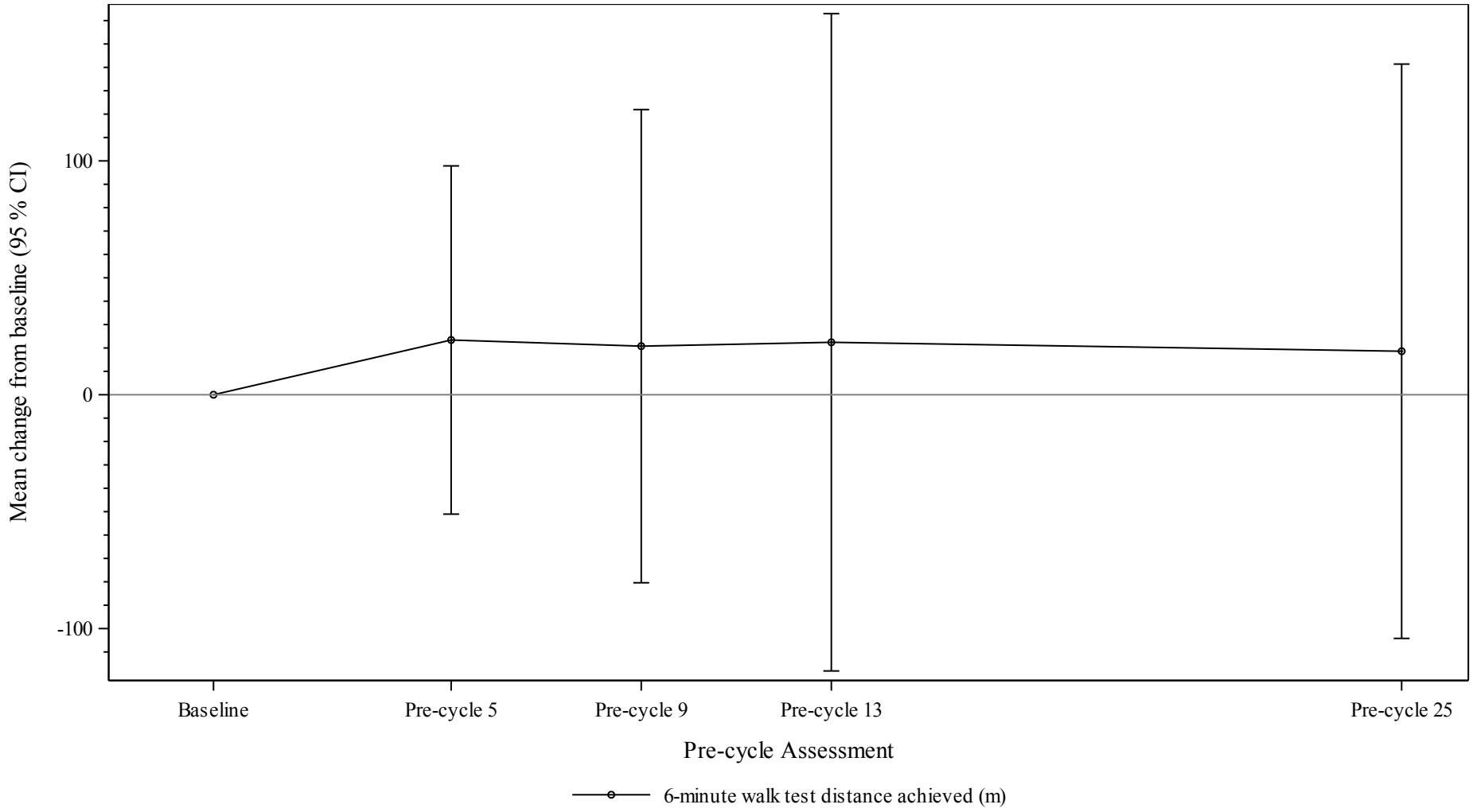
CI = Confidence interval.

Figure 2.11.2.1.3.3 Mean change from baseline of 6-minute walk test scores over time - PN status at enrollment = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 13



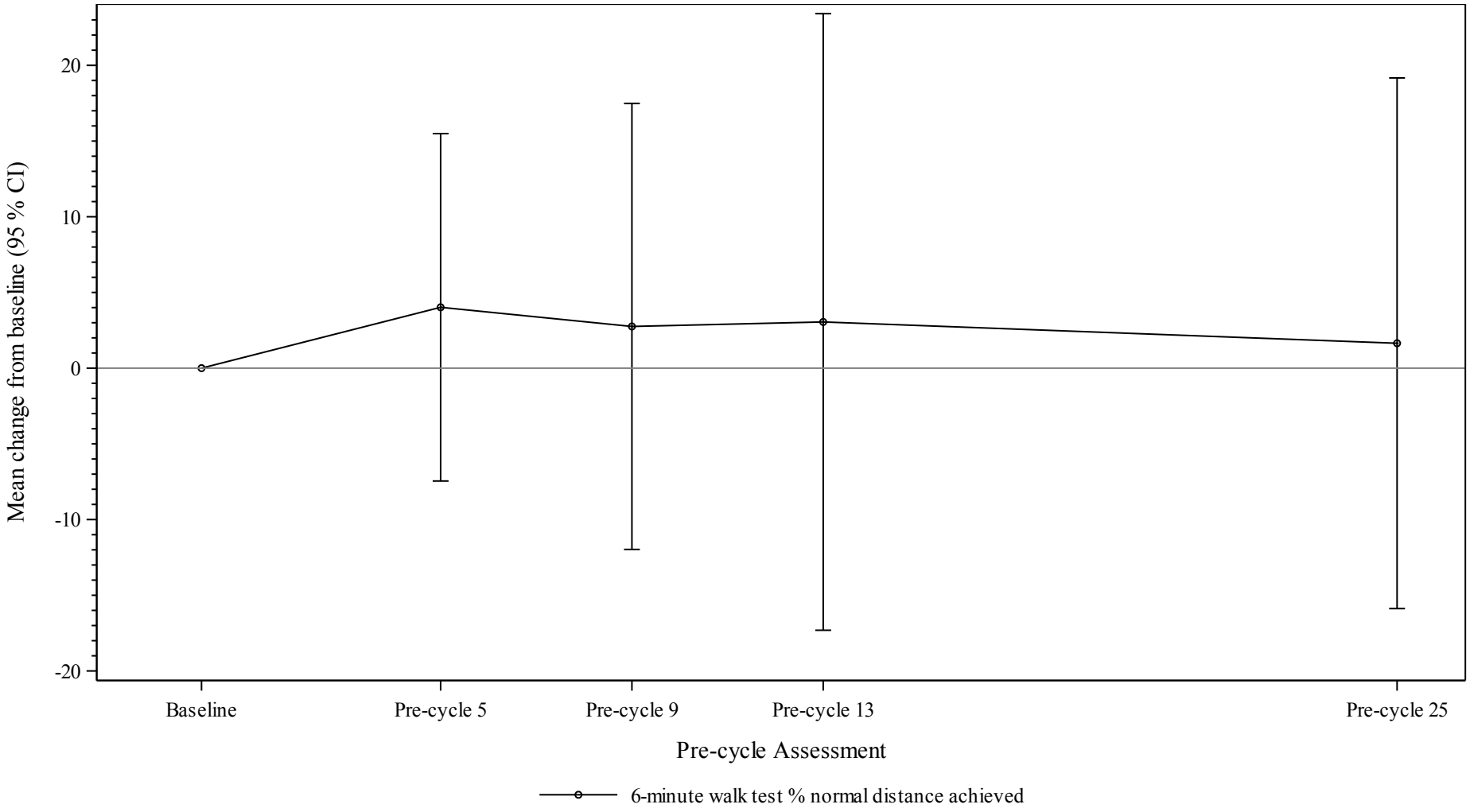
CI = Confidence interval.

Figure 2.11.2.1.3.4 Mean change from baseline of 6-minute walk test scores over time - PN status at enrollment = Non-progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 9



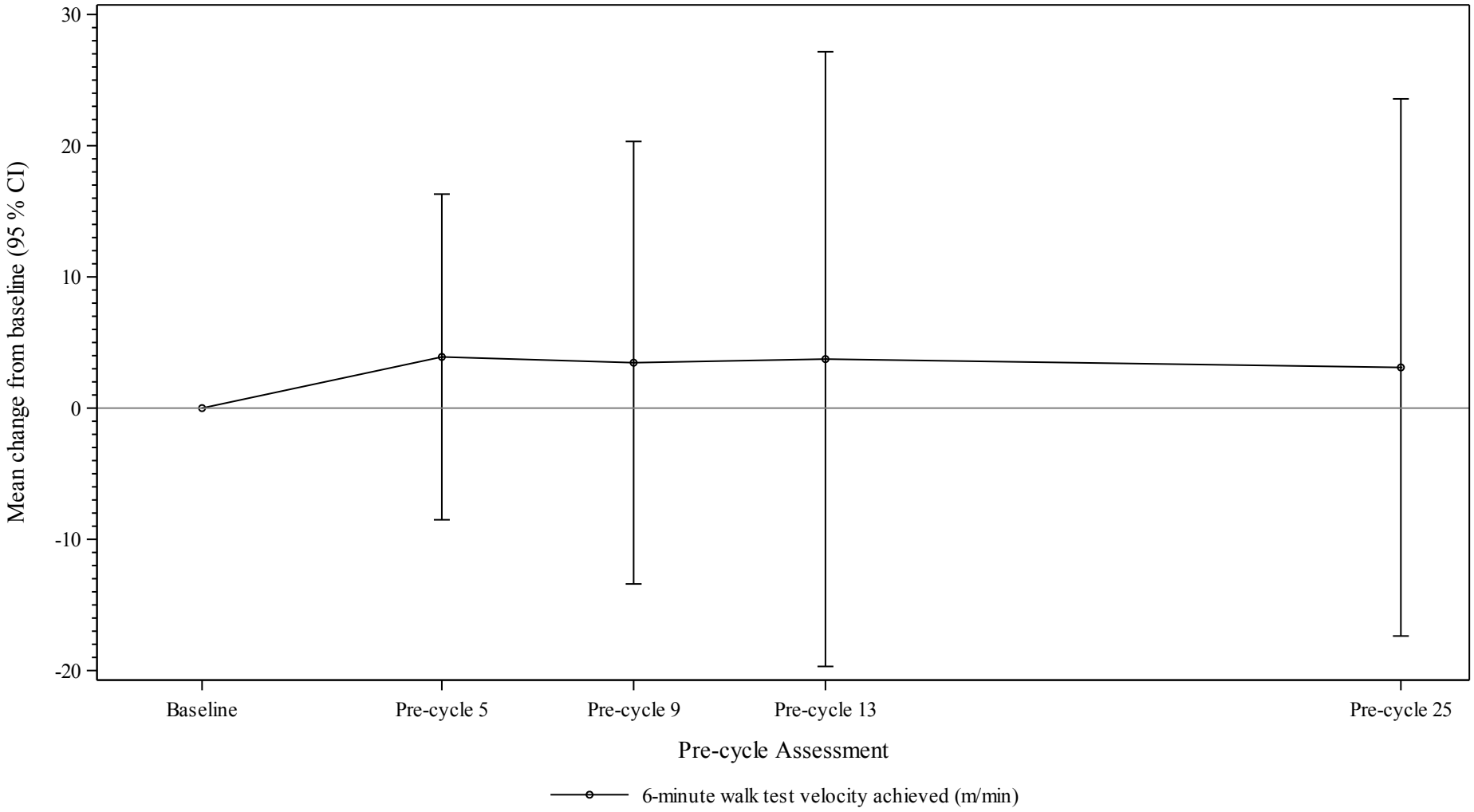
CI = Confidence interval.

Figure 2.11.2.1.3.4 Mean change from baseline of 6-minute walk test scores over time - PN status at enrollment = Non-progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 9



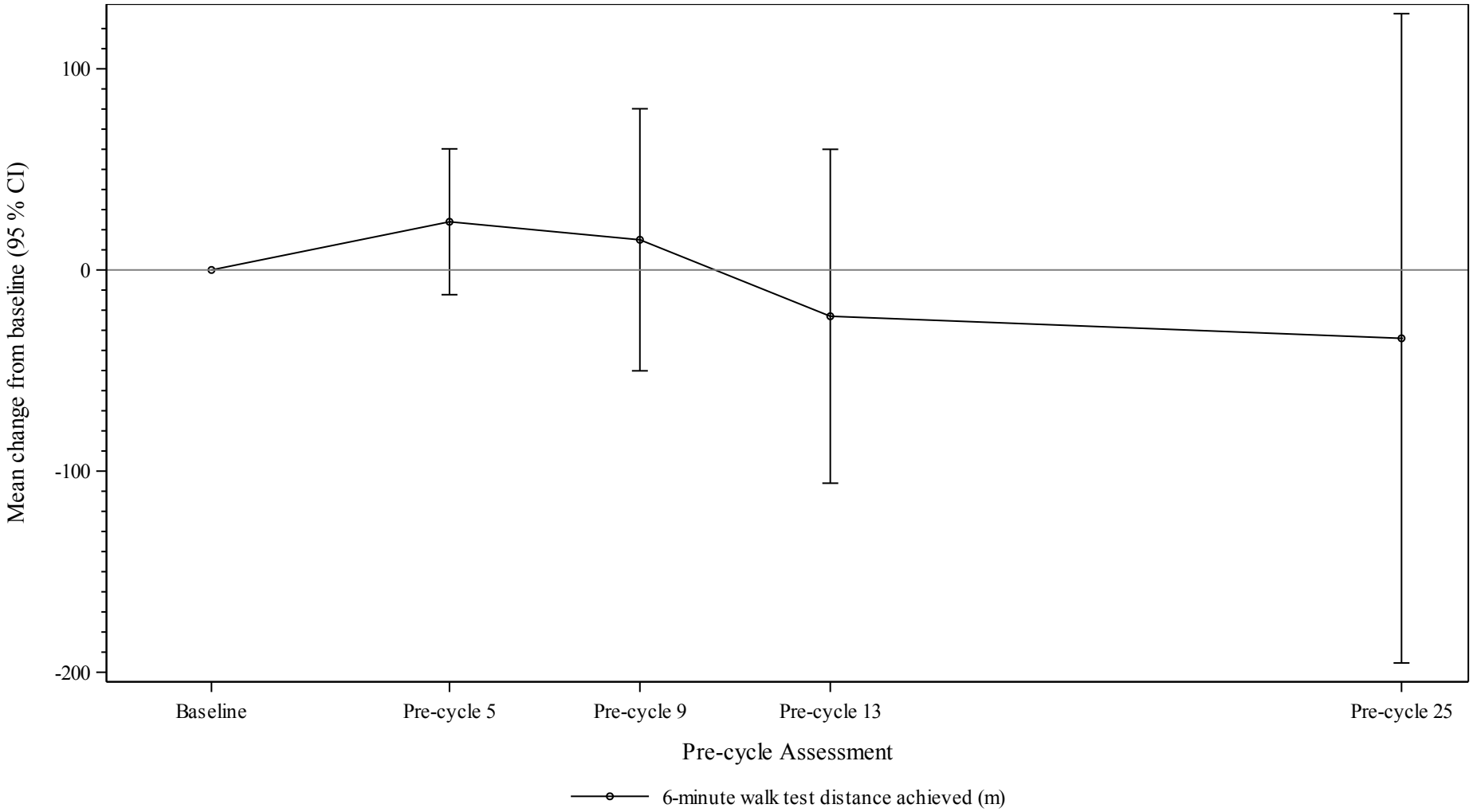
CI = Confidence interval.

Figure 2.11.2.1.3.4 Mean change from baseline of 6-minute walk test scores over time - PN status at enrollment = Non-progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 9



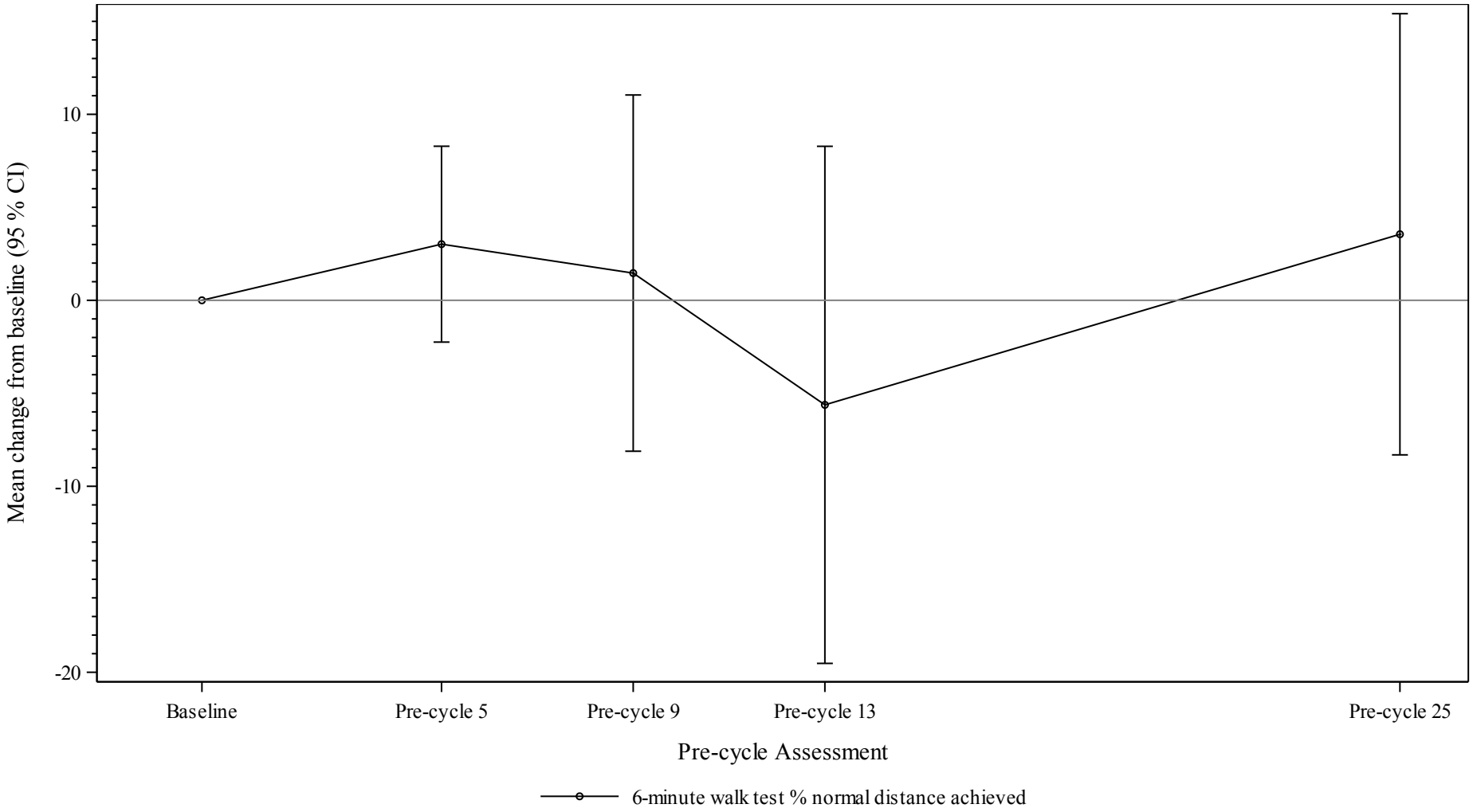
CI = Confidence interval.

Figure 2.11.2.1.3.5 Mean change from baseline of 6-minute walk test scores over time - PN status at enrollment = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 12



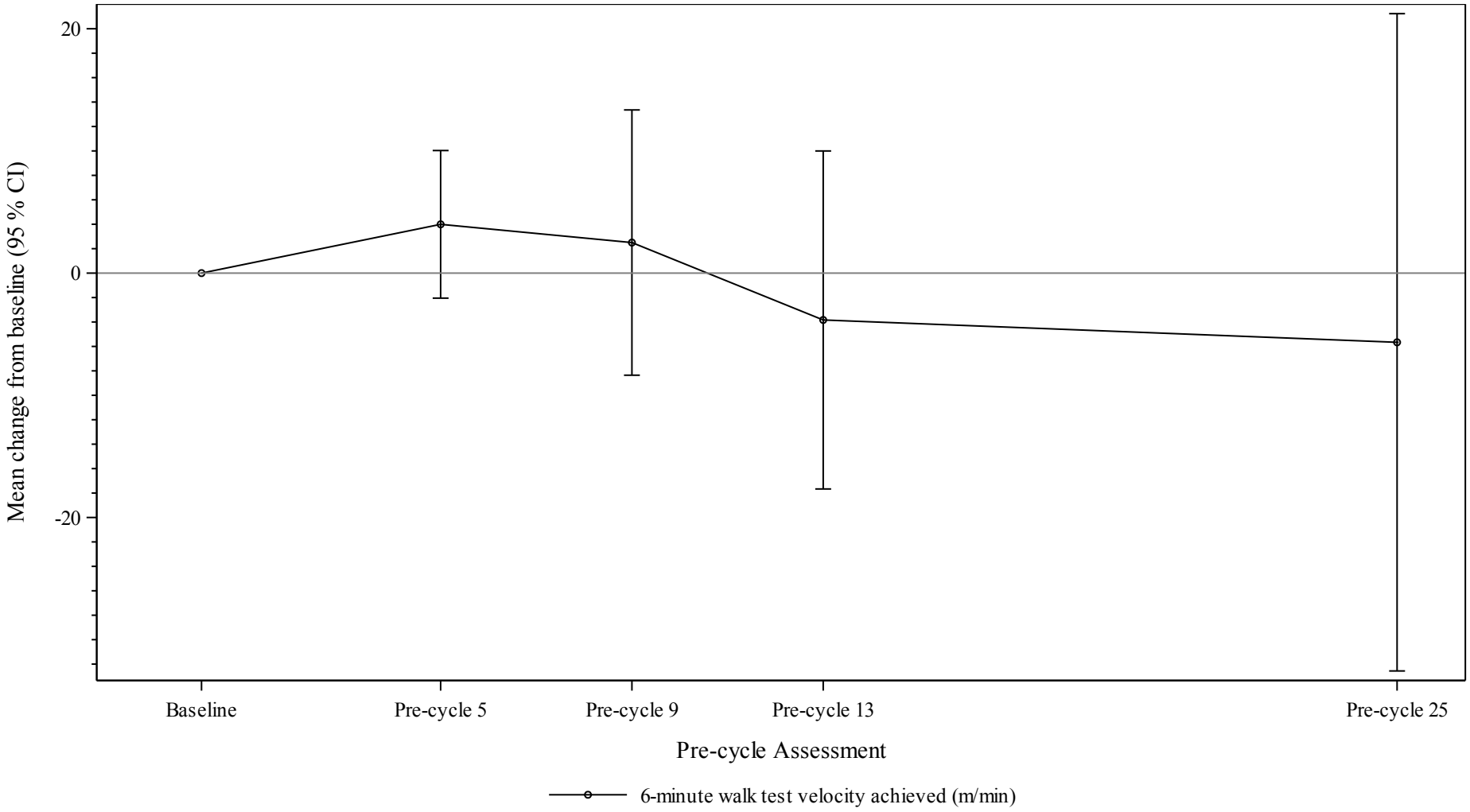
CI = Confidence interval.

Figure 2.11.2.1.3.5 Mean change from baseline of 6-minute walk test scores over time - PN status at enrollment = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 12



CI = Confidence interval.

Figure 2.11.2.1.3.5 Mean change from baseline of 6-minute walk test scores over time - PN status at enrollment = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 12



CI = Confidence interval.

Table 2.11.2.2 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=28) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=23)	Categories of change [d]			
		Improvement	12	52,2	30,6, 73,2
		No improvement	11	47,8	26,8, 69,4

[a] Patients aged 5-18 years at enrolment, with lower extremity PN or cord compression.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.2.1.1 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - Gender = Male
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=14) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=11)	Categories of change [d]			
		Improvement	7	63,6	30,8, 89,1
		No improvement	4	36,4	10,9, 69,2

[a] Patients aged 5-18 years at enrolment, with lower extremity PN or cord compression.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.2.1.2 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - Gender = Female
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=14) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8

[a] Patients aged 5-18 years at enrolment, with lower extremity PN or cord compression.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.2.1.3 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - PN status at enrollment = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=9)	Categories of change [d]			
		Improvement	7	77,8	40,0, 97,2
		No improvement	2	22,2	2,8, 60,0

[a] Patients aged 5-18 years at enrolment, with lower extremity PN or cord compression.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.2.1.4 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - PN status at enrollment = Non-progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8

[a] Patients aged 5-18 years at enrolment, with lower extremity PN or cord compression.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.2.1.5 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - PN status at enrollment = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=6)	Categories of change [d]			
		Improvement	3	50,0	11,8, 88,2
		No improvement	3	50,0	11,8, 88,2

[a] Patients aged 5-18 years at enrolment, with lower extremity PN or cord compression.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.2.2.1 Endurance evaluation secondary outcome scores change from baseline over time - Gender = Male
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=12)	490,44	221,188	439,75	135,0	836,0	14,3							
	Pre-cycle 5 (n=12)	479,97	174,604	480,15	186,6	860,0	14,3	10	37,92	94,043	26,50	-117,0	236,2	28,6
	Pre-cycle 9 (n=12)	502,15	152,744	487,53	263,0	845,0	14,3	11	53,76	113,432	40,84	-117,0	297,2	21,4
	Pre-cycle 13 (n=11)	494,23	167,197	464,82	203,9	861,0	21,4	10	49,60	116,203	46,50	-162,0	281,9	28,6
	Pre-cycle 25 (n=6)	548,68	145,462	533,50	363,0	770,0	57,1	6	35,20	156,435	20,50	-135,0	265,2	57,1
6-minute walk test % normal distance achieved	Baseline (n=11)	70,90	27,915	71,30	20,5	114,4	21,4							
	Pre-cycle 5 (n=11)	70,11	18,984	70,50	28,2	95,6	21,4	10	5,40	14,309	4,33	-16,1	35,4	28,6
	Pre-cycle 9 (n=11)	72,24	16,821	72,20	36,6	92,1	21,4	10	7,78	17,175	3,25	-13,3	44,0	28,6
	Pre-cycle 13 (n=11)	71,46	17,126	75,40	30,8	93,6	21,4	10	6,25	16,961	4,96	-23,1	40,7	28,6
	Pre-cycle 25 (n=6)	75,60	21,086	72,85	54,4	109,7	57,1	5	1,34	24,268	-7,10	-19,6	36,6	64,3
6-minute walk test velocity achieved (m/min)	Baseline (n=12)	81,74	36,864	73,29	22,5	139,3	14,3							
	Pre-cycle 5 (n=12)	79,99	29,100	80,03	31,1	143,3	14,3	10	6,32	15,674	4,42	-19,5	39,4	28,6
	Pre-cycle 9 (n=12)	83,69	25,457	81,26	43,8	140,8	14,3	11	8,96	18,905	6,81	-19,5	49,5	21,4
	Pre-cycle 13 (n=11)	82,37	27,867	77,47	34,0	143,5	21,4	10	8,27	19,367	7,75	-27,0	47,0	28,6
	Pre-cycle 25 (n=6)	91,45	24,242	88,92	60,5	128,3	57,1	6	5,87	26,073	3,42	-22,5	44,2	57,1

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.2.2.2 Endurance evaluation secondary outcome scores change from baseline over time - Gender = Female
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=13)	487,10	92,111	467,00	308,8	603,0	7,1							
	Pre-cycle 5 (n=14)	495,56	104,811	498,50	354,0	660,0	0,0	12	12,58	59,451	9,00	-86,0	123,0	14,3
	Pre-cycle 9 (n=14)	488,00	88,609	500,50	350,0	607,0	0,0	12	2,96	60,295	-7,75	-89,0	114,0	14,3
	Pre-cycle 13 (n=12)	482,25	92,525	480,50	333,0	596,0	14,3	10	-15,05	91,070	-30,00	-134,0	146,0	28,6
	Pre-cycle 25 (n=10)	528,66	66,846	553,00	433,1	604,0	28,6	8	29,89	52,715	10,00	-33,9	106,0	42,9
6-minute walk test % normal distance achieved	Baseline (n=13)	76,72	11,126	78,86	55,2	91,1	7,1							
	Pre-cycle 5 (n=14)	78,61	13,890	82,54	54,1	97,5	0,0	12	2,07	8,931	0,71	-13,0	17,5	14,3
	Pre-cycle 9 (n=14)	77,35	12,359	80,76	56,5	92,0	0,0	12	0,26	9,179	-1,18	-11,3	17,8	14,3
	Pre-cycle 13 (n=12)	76,04	15,915	75,93	45,7	107,2	14,3	10	-2,87	14,129	-5,06	-22,0	21,3	28,6
	Pre-cycle 25 (n=10)	83,69	9,585	85,65	65,2	95,2	28,6	8	4,31	6,242	2,30	-2,5	16,8	42,9
6-minute walk test velocity achieved (m/min)	Baseline (n=13)	81,18	15,351	77,83	51,5	100,5	7,1							
	Pre-cycle 5 (n=14)	82,59	17,468	83,08	59,0	110,0	0,0	12	2,10	9,908	1,50	-14,3	20,5	14,3
	Pre-cycle 9 (n=14)	81,33	14,768	83,42	58,3	101,2	0,0	12	0,49	10,049	-1,29	-14,8	19,0	14,3
	Pre-cycle 13 (n=12)	80,37	15,421	80,08	55,5	99,3	14,3	10	-2,51	15,178	-5,00	-22,3	24,3	28,6
	Pre-cycle 25 (n=10)	88,11	11,141	92,17	72,2	100,7	28,6	8	4,98	8,785	1,67	-5,6	17,7	42,9

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.2.2.3 Endurance evaluation secondary outcome scores change from baseline over time - PN status at enrol. = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=10) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=9)	464,90	103,468	425,50	366,0	684,0	10,0							
	Pre-cycle 5 (n=10)	462,74	103,465	450,65	354,0	660,0	0,0	8	17,92	88,312	22,00	-117,0	129,5	20,0
	Pre-cycle 9 (n=10)	486,67	81,138	489,00	357,0	603,0	0,0	9	36,18	71,344	40,84	-81,0	129,0	10,0
	Pre-cycle 13 (n=8)	464,60	93,249	434,65	383,0	644,0	20,0	7	28,53	73,395	9,80	-58,5	152,4	30,0
	Pre-cycle 25 (n=4)	512,50	89,935	476,50	453,0	644,0	60,0	3	101,67	32,332	107,00	67,0	131,0	70,0
6-minute walk test % normal distance achieved	Baseline (n=8)	74,59	9,433	71,23	67,1	96,0	20,0							
	Pre-cycle 5 (n=9)	74,63	14,714	77,80	54,1	97,5	10,0	8	2,26	13,286	3,16	-16,1	20,6	20,0
	Pre-cycle 9 (n=9)	77,32	11,196	77,10	60,8	92,1	10,0	8	4,79	11,521	2,50	-10,9	21,0	20,0
	Pre-cycle 13 (n=8)	75,80	12,260	73,88	57,9	93,6	20,0	7	3,02	10,871	-2,04	-9,2	22,1	30,0
	Pre-cycle 25 (n=4)	86,53	16,457	81,55	73,3	109,7	60,0	2	NC	NC	NC	5,8	15,5	80,0
6-minute walk test velocity achieved (m/min)	Baseline (n=9)	77,48	17,245	70,92	61,0	114,0	10,0							
	Pre-cycle 5 (n=10)	77,12	17,244	75,11	59,0	110,0	0,0	8	2,99	14,719	3,67	-19,5	21,6	20,0
	Pre-cycle 9 (n=10)	81,11	13,523	81,50	59,5	100,5	0,0	9	6,03	11,891	6,81	-13,5	21,5	10,0
	Pre-cycle 13 (n=8)	77,43	15,541	72,44	63,8	107,3	20,0	7	4,75	12,232	1,63	-9,8	25,4	30,0
	Pre-cycle 25 (n=4)	85,42	14,989	79,42	75,5	107,3	60,0	3	16,94	5,389	17,83	11,2	21,8	70,0

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.2.2.4 Endurance evaluation secondary outcome scores change from baseline - PN status at enrol. = Non-progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=8) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=8)	495,86	162,660	519,00	182,9	705,0	0,0							
	Pre-cycle 5 (n=8)	519,26	104,004	524,00	375,0	675,0	0,0	8	23,40	89,065	-7,00	-38,0	236,2	0,0
	Pre-cycle 9 (n=8)	516,63	89,653	527,50	350,0	607,0	0,0	8	20,77	121,022	1,50	-117,0	297,2	0,0
	Pre-cycle 13 (n=7)	532,97	59,739	543,00	464,8	596,0	12,5	7	22,42	151,964	8,00	-162,0	281,9	12,5
	Pre-cycle 25 (n=7)	529,15	89,132	570,00	363,0	604,0	12,5	7	18,60	132,783	-5,00	-135,0	265,2	12,5
6-minute walk test % normal distance achieved	Baseline (n=8)	77,89	22,391	86,31	28,0	99,8	0,0							
	Pre-cycle 5 (n=8)	81,91	12,362	83,35	63,4	95,6	0,0	8	4,02	13,723	-2,35	-5,2	35,4	0,0
	Pre-cycle 9 (n=8)	80,64	11,550	84,81	59,5	92,0	0,0	8	2,75	17,617	-0,45	-13,3	44,0	0,0
	Pre-cycle 13 (n=7)	82,25	13,023	76,70	68,7	107,2	12,5	7	3,05	22,017	0,68	-23,1	40,7	12,5
	Pre-cycle 25 (n=7)	80,84	15,601	86,00	54,4	95,2	12,5	7	1,64	18,949	2,20	-19,6	36,6	12,5
6-minute walk test velocity achieved (m/min)	Baseline (n=8)	82,64	27,110	86,50	30,5	117,5	0,0							
	Pre-cycle 5 (n=8)	86,54	17,334	87,33	62,5	112,5	0,0	8	3,90	14,844	-1,17	-6,3	39,4	0,0
	Pre-cycle 9 (n=8)	86,11	14,942	87,92	58,3	101,2	0,0	8	3,46	20,170	0,25	-19,5	49,5	0,0
	Pre-cycle 13 (n=7)	88,83	9,957	90,50	77,5	99,3	12,5	7	3,74	25,327	1,33	-27,0	47,0	12,5
	Pre-cycle 25 (n=7)	88,19	14,855	95,00	60,5	100,7	12,5	7	3,10	22,132	-0,83	-22,5	44,2	12,5

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.2.2.5 Endurance evaluation secondary outcome scores change from baseline over time - PN status at enrol. = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=10) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=8)	508,32	226,970	496,50	135,0	836,0	20,0							
	Pre-cycle 5 (n=8)	489,49	204,750	490,50	186,6	860,0	20,0	6	33,27	46,991	26,50	-37,0	108,0	40,0
	Pre-cycle 9 (n=8)	482,26	184,684	467,03	263,0	845,0	20,0	6	22,50	88,356	21,00	-89,0	128,0	40,0
	Pre-cycle 13 (n=8)	471,99	197,003	461,00	203,9	861,0	20,0	6	-1,85	92,657	-8,00	-134,0	123,0	40,0
	Pre-cycle 25 (n=5)	564,92	131,208	550,00	433,1	770,0	50,0	4	3,78	70,770	-7,45	-66,0	96,0	60,0
6-minute walk test % normal distance achieved	Baseline (n=8)	69,69	26,927	68,11	20,5	114,4	20,0							
	Pre-cycle 5 (n=8)	68,11	20,681	71,32	28,2	92,5	20,0	6	4,78	6,364	3,86	-3,7	15,3	40,0
	Pre-cycle 9 (n=8)	67,07	17,864	70,89	36,6	86,3	20,0	6	3,43	12,418	3,78	-11,3	17,8	40,0
	Pre-cycle 13 (n=8)	64,55	19,097	67,98	30,8	88,1	20,0	6	-1,44	14,830	-3,61	-22,0	19,6	40,0
	Pre-cycle 25 (n=5)	75,70	13,800	81,60	57,2	89,2	50,0	4	2,10	10,373	-0,66	-7,1	16,8	60,0
6-minute walk test velocity achieved (m/min)	Baseline (n=8)	84,72	37,827	82,75	22,5	139,3	20,0							
	Pre-cycle 5 (n=8)	81,58	34,124	81,75	31,1	143,3	20,0	6	5,55	7,831	4,42	-6,2	18,0	40,0
	Pre-cycle 9 (n=8)	80,37	30,780	77,84	43,8	140,8	20,0	6	3,75	14,724	3,50	-14,8	21,3	40,0
	Pre-cycle 13 (n=8)	78,66	32,835	76,83	34,0	143,5	20,0	6	-0,31	15,441	-1,33	-22,3	20,5	40,0
	Pre-cycle 25 (n=5)	94,15	21,867	91,67	72,2	128,3	50,0	4	0,63	11,795	-1,24	-11,0	16,0	60,0

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.3 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=16) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=14)	Categories of change [d]			
		Improvement	7	50,0	23,0, 77,0
		No improvement	7	50,0	23,0, 77,0

[a] Patients aged 5-18 years at enrolment, with airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.3.1.1 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - Gender = Male
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=8)	Categories of change [d]			
		Improvement	4	50,0	15,7, 84,3
		No improvement	4	50,0	15,7, 84,3

[a] Patients aged 5-18 years at enrolment, with airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.3.1.2 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - Gender = Female
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=6)	Categories of change [d]			
		Improvement	3	50,0	11,8, 88,2
		No improvement	3	50,0	11,8, 88,2

[a] Patients aged 5-18 years at enrolment, with airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.3.1.3 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - PN status at enrollment = Progressive
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6

[a] Patients aged 5-18 years at enrolment, with airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.3.1.4 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - PN status at enrollment = Non-progressive
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=5) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4

[a] Patients aged 5-18 years at enrolment, with airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.3.1.5 Endurance evaluation secondary outcome test score categories of change over time - percentage of patients with Improvement - PN status at enrollment = Unknown
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

Parameter	Time point	Selumetinib 25 mg/m² BID (N=7) [a] Response category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Overall (N=6)	Categories of change [d]			
		Improvement	3	50,0	11,8, 88,2
		No improvement	3	50,0	11,8, 88,2

[a] Patients aged 5-18 years at enrolment, with airway PN.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement/No improvement are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Table 2.11.2.3.2.1 Endurance evaluation secondary outcome scores change from baseline over time - Gender = Male
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=10) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=8)	486,49	242,339	495,50	135,0	850,0	20,0							
	Pre-cycle 5 (n=8)	464,09	139,674	472,00	186,6	675,0	20,0	7	-17,88	186,894	-8,00	-389,0	236,2	30,0
	Pre-cycle 9 (n=8)	516,26	144,101	534,03	263,0	705,0	20,0	8	29,77	141,775	26,00	-145,0	297,2	20,0
	Pre-cycle 13 (n=8)	398,09	181,213	469,91	101,0	575,0	20,0	7	-38,74	190,802	-11,00	-296,0	281,9	30,0
	Pre-cycle 25 (n=8)	437,57	255,271	474,03	45,5	805,0	20,0	7	-43,12	184,920	-86,00	-317,0	265,2	30,0
	Pre-cycle 37 (n=1)	NC	NC	NC	761,0	761,0	90,0	1	NC	NC	NC	-89,0	-89,0	90,0
6-minute walk test % normal distance achieved	Baseline (n=7)	67,76	31,370	77,52	20,5	99,8	30,0							
	Pre-cycle 5 (n=6)	72,41	24,582	77,82	28,2	95,6	40,0	6	6,35	15,302	2,06	-4,9	35,4	40,0
	Pre-cycle 9 (n=7)	71,65	20,278	72,00	36,6	102,4	30,0	7	3,89	20,798	-1,80	-14,0	44,0	30,0
	Pre-cycle 13 (n=7)	63,35	20,840	68,70	30,8	91,5	30,0	7	-4,41	25,038	-5,00	-32,6	40,7	30,0
	Pre-cycle 25 (n=6)	76,73	18,856	75,30	54,4	109,7	40,0	5	-5,11	23,986	-17,90	-19,6	36,6	50,0
	Pre-cycle 37 (n=1)	NC	NC	NC	68,3	68,3	90,0	1	NC	NC	NC	-9,7	-9,7	90,0
6-minute walk test velocity achieved (m/min)	Baseline (n=8)	81,08	40,390	82,58	22,5	141,7	20,0							
	Pre-cycle 5 (n=8)	77,35	23,280	78,67	31,1	112,5	20,0	7	-2,98	31,149	-1,33	-64,8	39,4	30,0
	Pre-cycle 9 (n=8)	86,04	24,018	89,01	43,8	117,5	20,0	8	4,96	23,629	4,33	-24,2	49,5	20,0
	Pre-cycle 13 (n=8)	66,35	30,203	78,32	16,8	95,8	20,0	7	-6,46	31,800	-1,83	-49,3	47,0	30,0
	Pre-cycle 25 (n=8)	72,93	42,545	79,01	7,6	134,2	20,0	7	-7,19	30,821	-14,33	-52,8	44,2	30,0
	Pre-cycle 37 (n=1)	NC	NC	NC	126,8	126,8	90,0	1	NC	NC	NC	-14,8	-14,8	90,0

[a] Patients with airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.3.2.2 Endurance evaluation secondary outcome scores change from baseline over time - Gender = Female
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=6) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=6)	501,33	69,747	461,50	450,0	603,0	0,0							
	Pre-cycle 5 (n=6)	511,67	74,481	509,50	430,0	606,0	0,0	6	10,33	54,076	0,50	-38,0	108,0	0,0
	Pre-cycle 9 (n=6)	504,67	80,124	500,00	378,0	607,0	0,0	6	3,33	71,788	14,50	-89,0	114,0	0,0
	Pre-cycle 13 (n=6)	506,67	98,522	547,50	333,0	584,0	0,0	6	5,33	99,077	-9,00	-134,0	123,0	0,0
	Pre-cycle 25 (n=6)	557,18	66,642	573,50	433,1	611,0	0,0	6	55,85	71,611	57,50	-33,9	155,0	0,0
	Pre-cycle 37 (n=1)	NC	NC	NC	642,0	642,0	83,3	1	NC	NC	NC	186,0	186,0	83,3
6-minute walk test % normal distance achieved	Baseline (n=5)	78,21	10,182	77,94	67,7	88,9	16,7							
	Pre-cycle 5 (n=5)	80,06	10,644	83,70	64,0	92,5	16,7	5	1,85	8,373	-1,65	-5,2	15,3	16,7
	Pre-cycle 9 (n=5)	78,00	13,042	78,74	56,5	90,1	16,7	5	-0,21	11,594	0,80	-11,3	17,8	16,7
	Pre-cycle 13 (n=5)	74,78	17,266	78,70	45,7	88,1	16,7	5	-3,43	15,106	-3,74	-22,0	19,6	16,7
	Pre-cycle 25 (n=6)	81,72	10,574	86,30	65,2	91,3	0,0	5	5,45	7,662	2,40	-2,5	16,8	16,7
	Pre-cycle 37 (n=1)	NC	NC	NC	75,8	75,8	83,3	0	NC	NC	NC	NC	NC	NC
6-minute walk test velocity achieved (m/min)	Baseline (n=6)	83,55	11,624	76,92	75,0	100,5	0,0							
	Pre-cycle 5 (n=6)	85,28	12,414	84,92	71,7	101,0	0,0	6	1,72	9,012	0,08	-6,3	18,0	0,0
	Pre-cycle 9 (n=6)	84,11	13,354	83,33	63,0	101,2	0,0	6	0,56	11,964	2,42	-14,8	19,0	0,0
	Pre-cycle 13 (n=6)	84,44	16,420	91,25	55,5	97,3	0,0	6	0,89	16,512	-1,50	-22,3	20,5	0,0
	Pre-cycle 25 (n=6)	92,86	11,107	95,58	72,2	101,8	0,0	6	9,31	11,934	9,59	-5,6	25,8	0,0
	Pre-cycle 37 (n=1)	NC	NC	NC	107,0	107,0	83,3	1	NC	NC	NC	31,0	31,0	83,3

[a] Patients with airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.3.2.3 Endurance evaluation secondary outcome scores change from baseline over time - PN status at enrol. = Progressive
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=4) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=4)	607,25	170,480	561,50	456,0	850,0	0,0							
	Pre-cycle 5 (n=4)	493,00	53,242	472,00	457,0	571,0	0,0	3	-134,33	220,693	-15,00	-389,0	1,0	25,0
	Pre-cycle 9 (n=4)	606,50	93,632	619,50	482,0	705,0	0,0	4	-0,75	97,428	39,50	-145,0	63,0	0,0
	Pre-cycle 13 (n=3)	566,33	10,970	570,00	554,0	575,0	25,0	3	-64,33	210,139	-11,00	-296,0	114,0	25,0
	Pre-cycle 25 (n=4)	640,00	126,071	627,50	500,0	805,0	0,0	4	32,75	116,340	31,00	-86,0	155,0	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	642,0	761,0	50,0	2	NC	NC	NC	-89,0	186,0	50,0
6-minute walk test % normal distance achieved	Baseline (n=2)	NC	NC	NC	78,0	96,5	50,0							
	Pre-cycle 5 (n=1)	NC	NC	NC	91,6	91,6	75,0	1	NC	NC	NC	-4,9	-4,9	75,0
	Pre-cycle 9 (n=2)	NC	NC	NC	64,0	102,4	50,0	2	NC	NC	NC	-14,0	5,9	50,0
	Pre-cycle 13 (n=2)	NC	NC	NC	55,4	91,5	50,0	2	NC	NC	NC	-22,6	-5,0	50,0
	Pre-cycle 25 (n=4)	83,08	18,021	75,30	72,0	109,7	0,0	2	NC	NC	NC	-17,9	-6,0	50,0
	Pre-cycle 37 (n=2)	NC	NC	NC	68,3	75,8	50,0	1	NC	NC	NC	-9,7	-9,7	75,0
6-minute walk test velocity achieved (m/min)	Baseline (n=4)	101,21	28,413	93,58	76,0	141,7	0,0							
	Pre-cycle 5 (n=4)	82,17	8,874	78,67	76,2	95,2	0,0	3	-22,39	36,782	-2,50	-64,8	0,2	25,0
	Pre-cycle 9 (n=4)	101,08	15,605	103,25	80,3	117,5	0,0	4	-0,13	16,238	6,58	-24,2	10,5	0,0
	Pre-cycle 13 (n=3)	94,39	1,828	95,00	92,3	95,8	25,0	3	-10,72	35,023	-1,83	-49,3	19,0	25,0
	Pre-cycle 25 (n=4)	106,67	21,012	104,58	83,3	134,2	0,0	4	5,46	19,390	5,17	-14,3	25,8	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	107,0	126,8	50,0	2	NC	NC	NC	-14,8	31,0	50,0

[a] Patients with airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.3.2.4 Endurance evaluation secondary outcome scores change from baseline - PN status at enrol. = Non-progressive
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=5) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=4)	486,22	226,977	528,50	182,9	705,0	20,0							
	Pre-cycle 5 (n=4)	535,53	110,507	524,00	419,1	675,0	20,0	4	49,31	128,142	-0,50	-38,0	236,2	20,0
	Pre-cycle 9 (n=4)	532,02	76,811	534,03	453,0	607,0	20,0	4	45,80	176,667	1,50	-117,0	297,2	20,0
	Pre-cycle 13 (n=5)	433,56	192,289	475,00	101,0	584,0	0,0	4	30,49	185,130	1,00	-162,0	281,9	20,0
	Pre-cycle 25 (n=5)	406,11	223,427	448,06	45,5	604,0	0,0	4	10,05	179,280	-45,00	-135,0	265,2	20,0
6-minute walk test % normal distance achieved	Baseline (n=4)	72,67	31,619	81,45	28,0	99,8	20,0							
	Pre-cycle 5 (n=4)	80,93	13,294	82,35	63,4	95,6	20,0	4	8,26	18,940	1,40	-5,2	35,4	20,0
	Pre-cycle 9 (n=4)	80,20	9,468	79,35	72,0	90,1	20,0	4	7,53	25,121	-0,30	-13,3	44,0	20,0
	Pre-cycle 13 (n=4)	77,00	7,650	76,05	68,7	87,2	20,0	4	4,33	26,598	-0,15	-23,1	40,7	20,0
	Pre-cycle 25 (n=4)	72,85	16,502	72,85	54,4	91,3	20,0	4	0,18	26,339	-8,15	-19,6	36,6	20,0
6-minute walk test velocity achieved (m/min)	Baseline (n=4)	81,04	37,829	88,08	30,5	117,5	20,0							
	Pre-cycle 5 (n=4)	89,25	18,418	87,33	69,9	112,5	20,0	4	8,22	21,357	-0,08	-6,3	39,4	20,0
	Pre-cycle 9 (n=4)	88,67	12,802	89,01	75,5	101,2	20,0	4	7,63	29,444	0,25	-19,5	49,5	20,0
	Pre-cycle 13 (n=5)	72,26	32,048	79,17	16,8	97,3	0,0	4	5,08	30,855	0,17	-27,0	47,0	20,0
	Pre-cycle 25 (n=5)	67,69	37,238	74,68	7,6	100,7	0,0	4	1,68	29,882	-7,50	-22,5	44,2	20,0

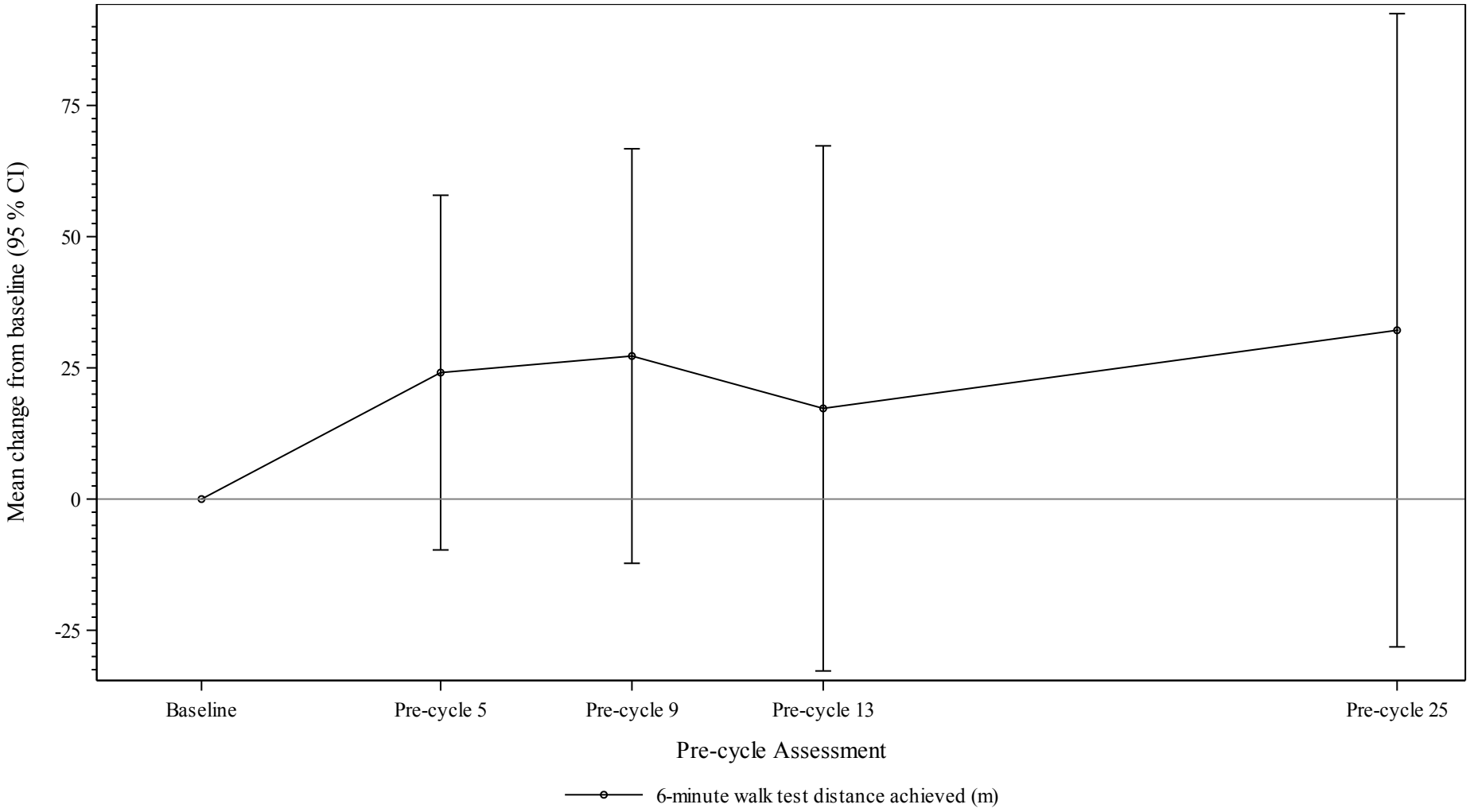
[a] Patients with airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Table 2.11.2.3.2.5 Endurance evaluation secondary outcome scores change from baseline over time - PN status at enrol. = Unknown
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=7) [a]												
		Absolute values						Change from baseline						
Endurance evaluation test score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
6-minute walk test distance achieved (m)	Baseline (n=6)	421,00	148,951	452,00	135,0	578,0	14,3							
	Pre-cycle 5 (n=6)	444,77	146,114	442,00	186,6	606,0	14,3	6	23,77	51,293	14,00	-37,0	108,0	14,3
	Pre-cycle 9 (n=6)	434,00	109,630	438,50	263,0	568,0	14,3	6	13,00	91,774	-7,50	-89,0	128,0	14,3
	Pre-cycle 13 (n=6)	392,98	148,073	392,00	203,9	577,0	14,3	6	-28,02	115,073	-26,00	-174,0	123,0	14,3
	Pre-cycle 25 (n=5)	450,62	191,782	548,00	125,0	597,0	28,6	5	-27,58	171,038	19,00	-317,0	98,0	28,6
6-minute walk test % normal distance achieved	Baseline (n=6)	66,70	23,800	73,01	20,5	88,0	14,3							
	Pre-cycle 5 (n=6)	69,91	22,545	75,47	28,2	92,5	14,3	6	3,21	7,426	1,43	-3,7	15,3	14,3
	Pre-cycle 9 (n=6)	67,39	18,303	73,13	36,6	86,3	14,3	6	0,69	13,307	-4,40	-11,3	17,8	14,3
	Pre-cycle 13 (n=6)	60,41	22,905	59,96	30,8	88,1	14,3	6	-6,29	19,486	-6,52	-32,6	19,6	14,3
	Pre-cycle 25 (n=4)	81,75	11,148	86,30	65,2	89,2	42,9	4	6,21	8,626	5,28	-2,5	16,8	42,9
6-minute walk test velocity achieved (m/min)	Baseline (n=6)	70,17	24,824	75,33	22,5	96,3	14,3							
	Pre-cycle 5 (n=6)	74,13	24,353	73,67	31,1	101,0	14,3	6	3,96	8,548	2,34	-6,2	18,0	14,3
	Pre-cycle 9 (n=6)	72,33	18,272	73,08	43,8	94,7	14,3	6	2,17	15,294	-1,25	-14,8	21,3	14,3
	Pre-cycle 13 (n=6)	65,50	24,680	65,33	34,0	96,2	14,3	6	-4,67	19,177	-4,33	-29,0	20,5	14,3
	Pre-cycle 25 (n=5)	75,10	31,964	91,33	20,8	99,5	28,6	5	-4,60	28,507	3,17	-52,8	16,3	28,6

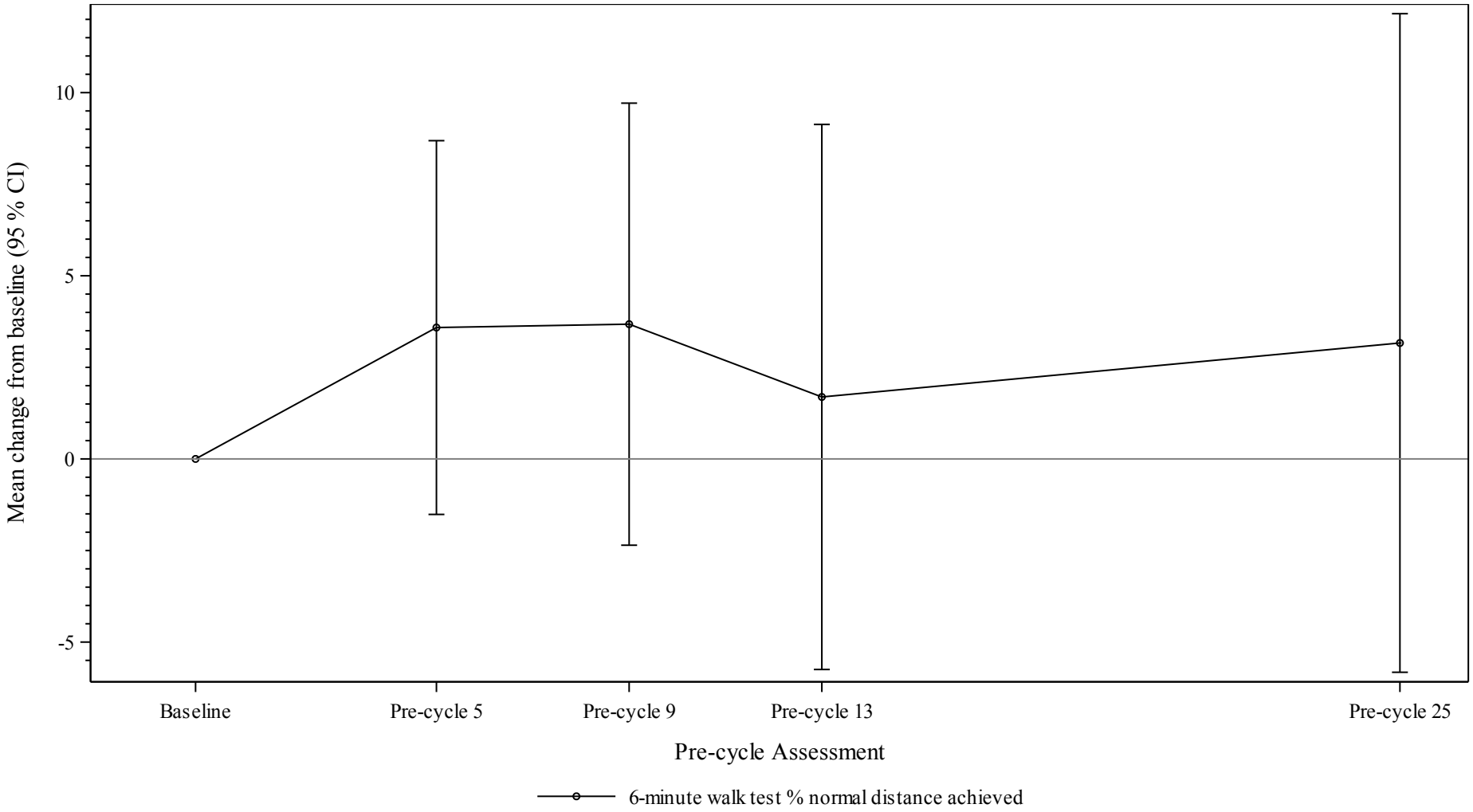
[a] Patients with airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

Figure 2.11.2.4 Endurance evaluation secondary outcome test score categories of change over time
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 28



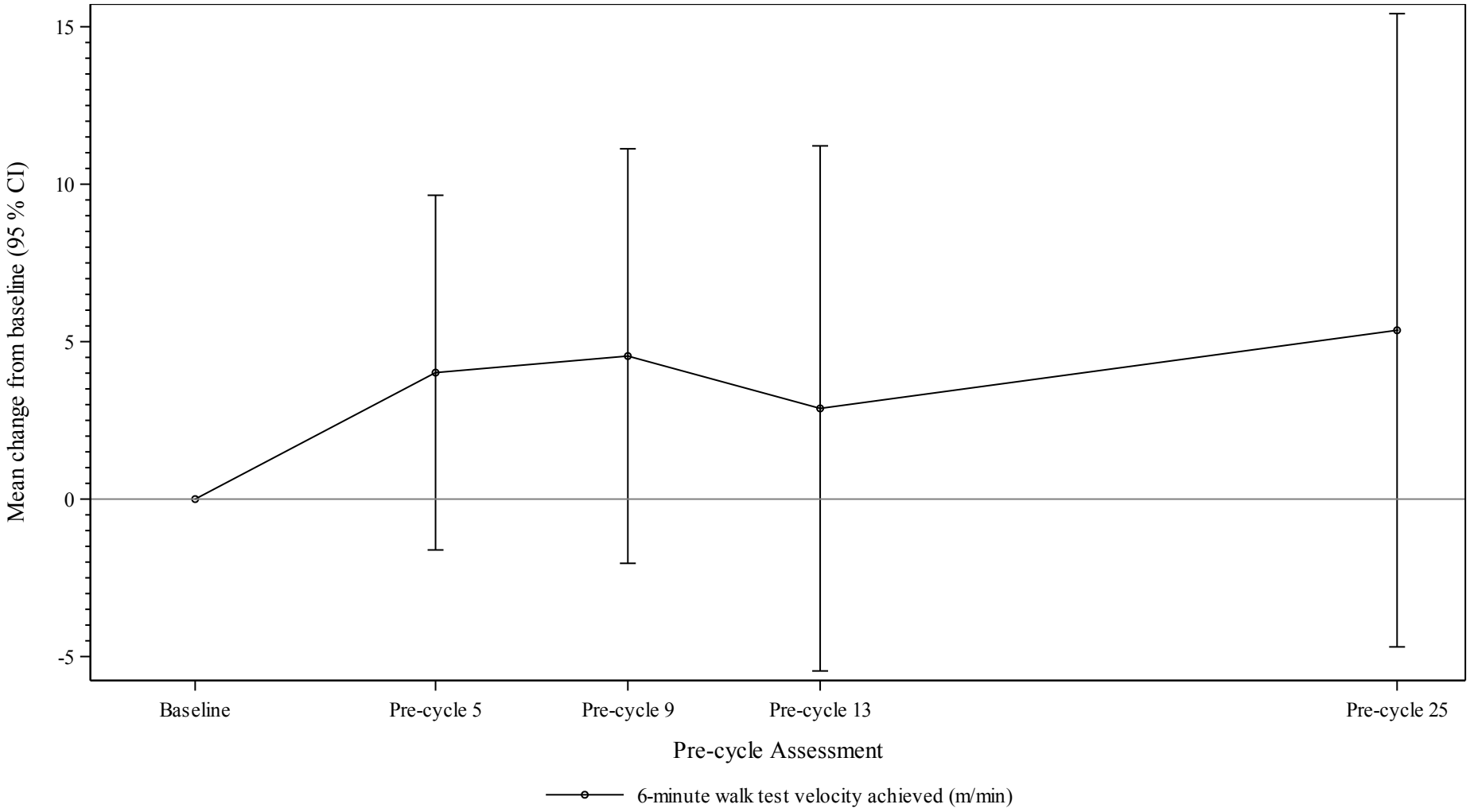
CI = Confidence interval.

Figure 2.11.2.4 Endurance evaluation secondary outcome test score categories of change over time
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 28



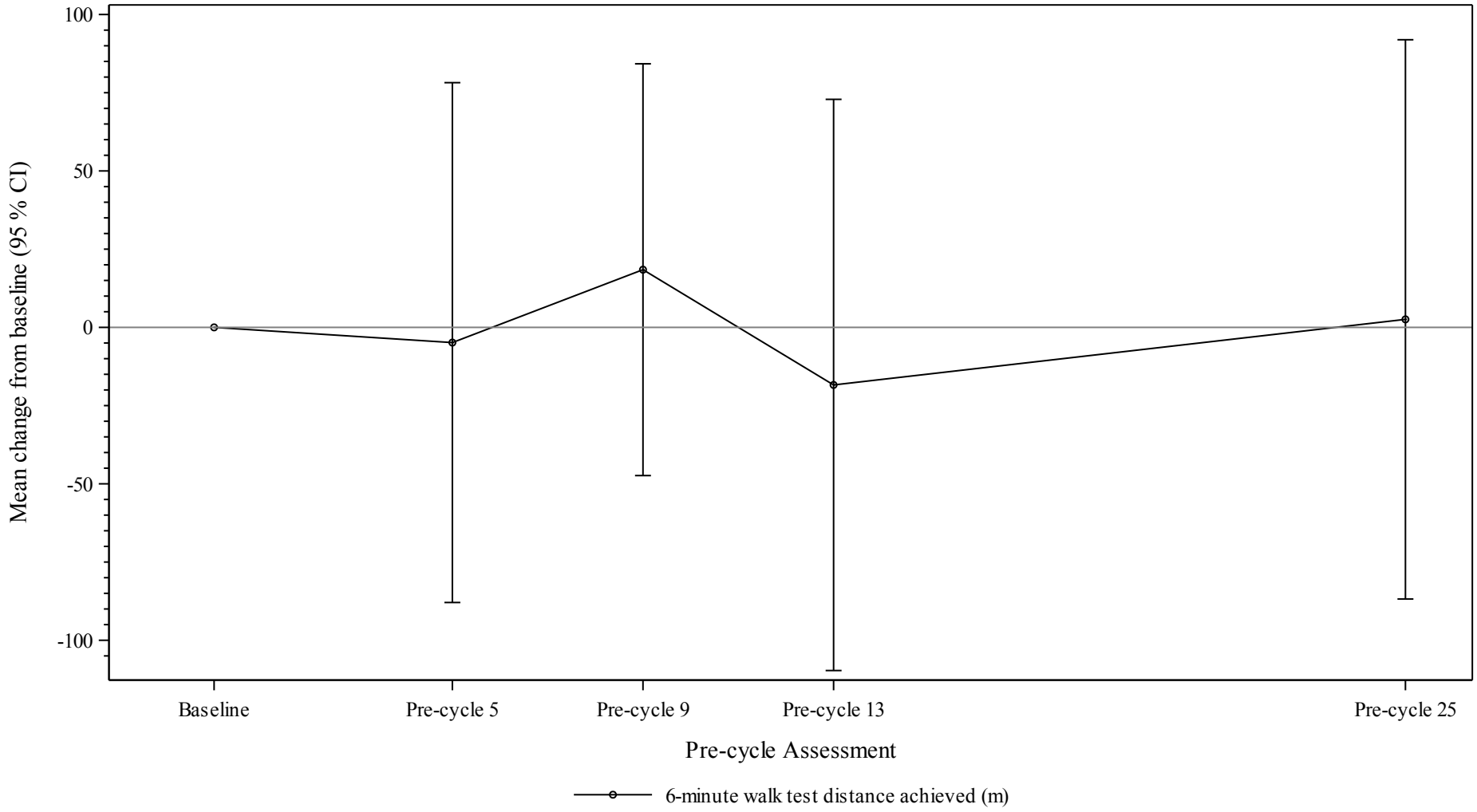
CI = Confidence interval.

Figure 2.11.2.4 Endurance evaluation secondary outcome test score categories of change over time
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 28



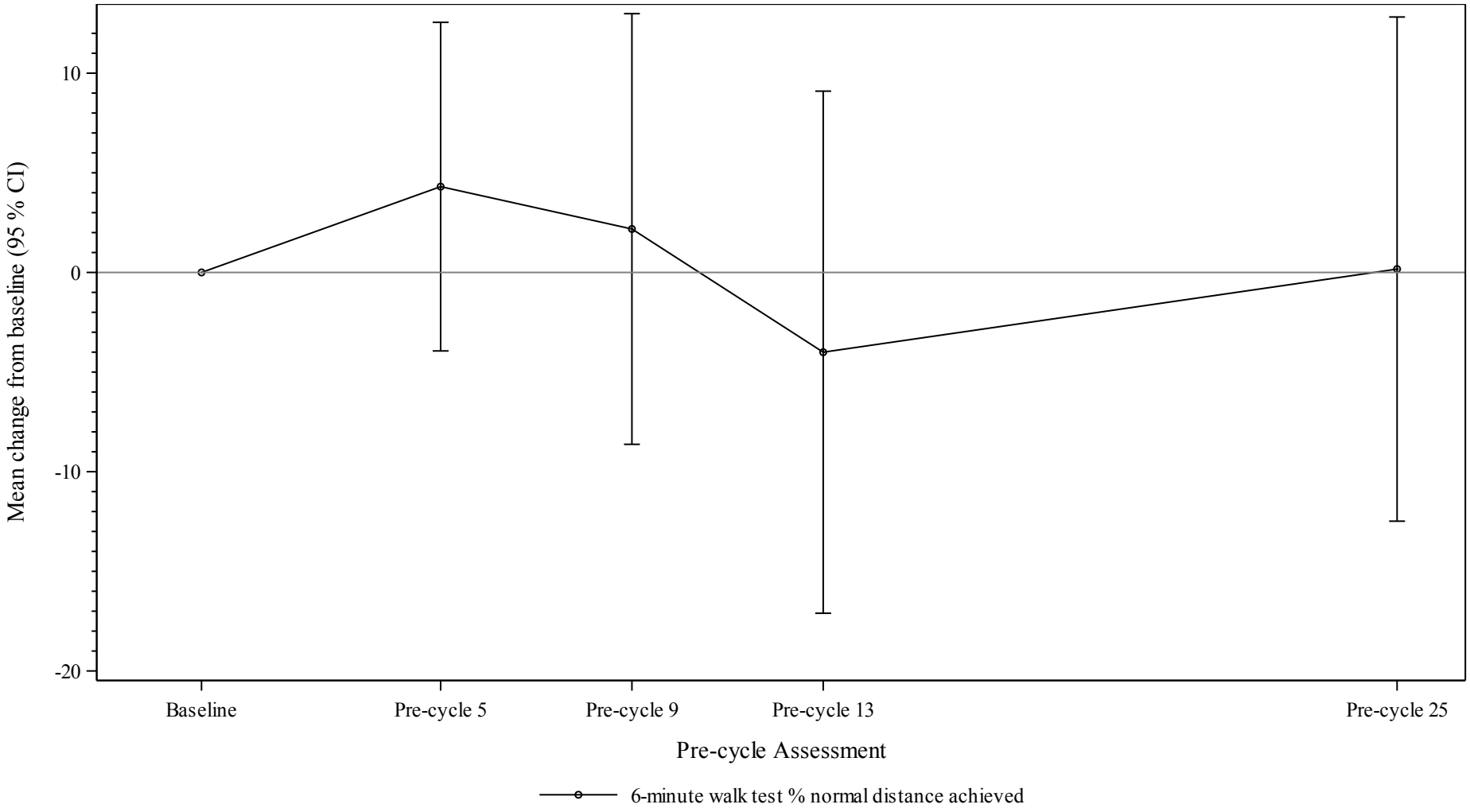
CI = Confidence interval.

Figure 2.11.2.5 Endurance evaluation secondary outcome test score categories of change over time
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 16



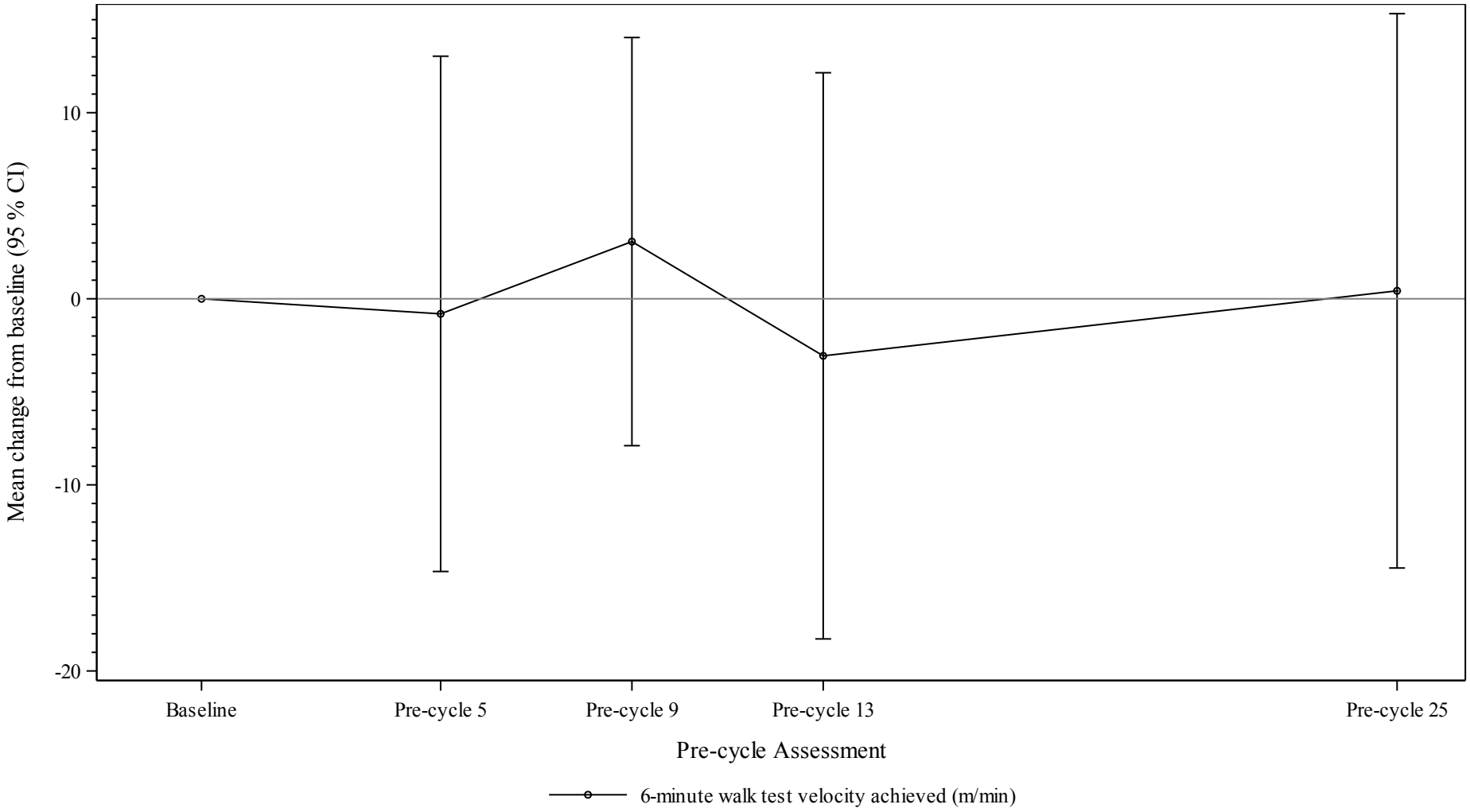
CI = Confidence interval.

Figure 2.11.2.5 Endurance evaluation secondary outcome test score categories of change over time
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 16



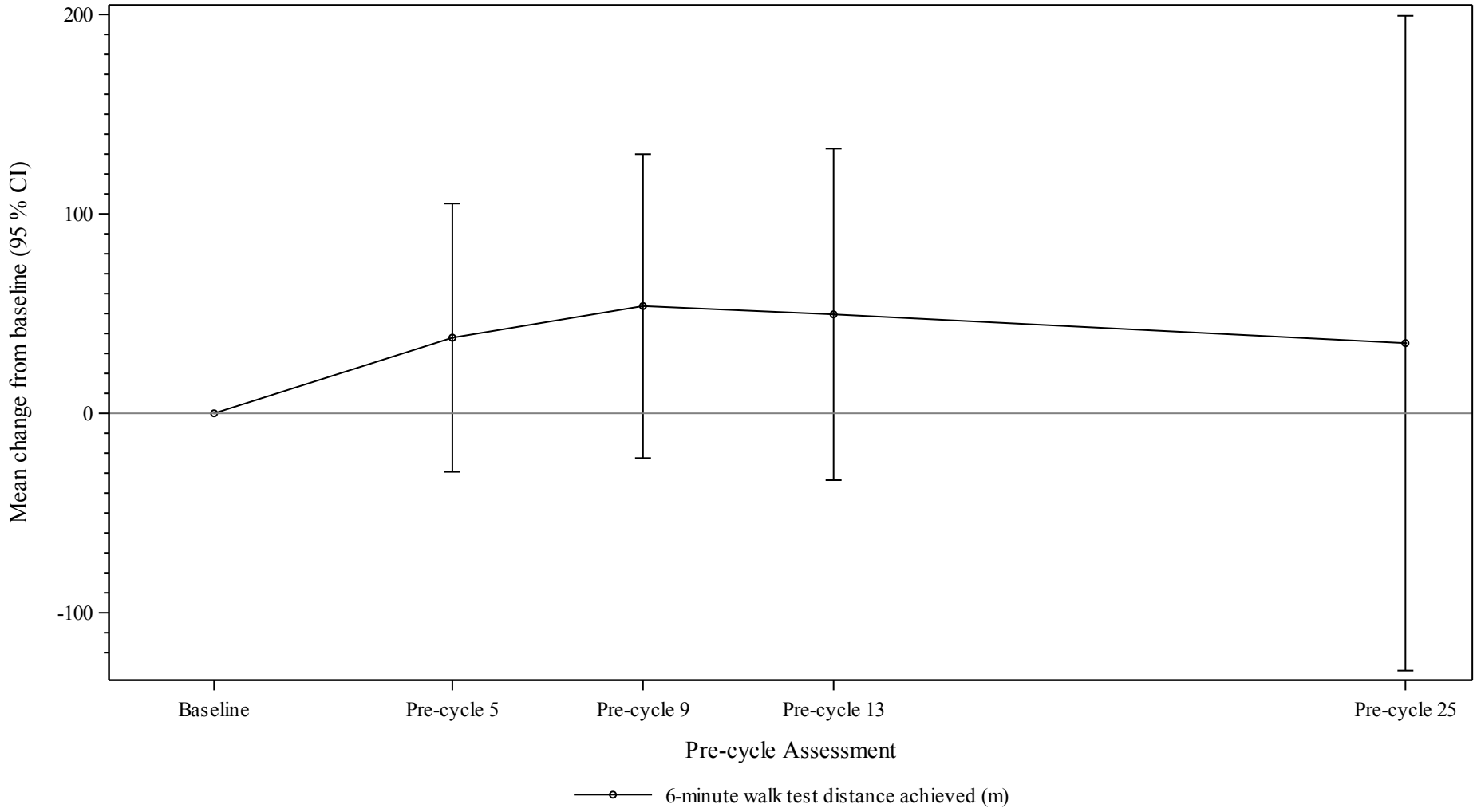
CI = Confidence interval.

Figure 2.11.2.5 Endurance evaluation secondary outcome test score categories of change over time
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 16



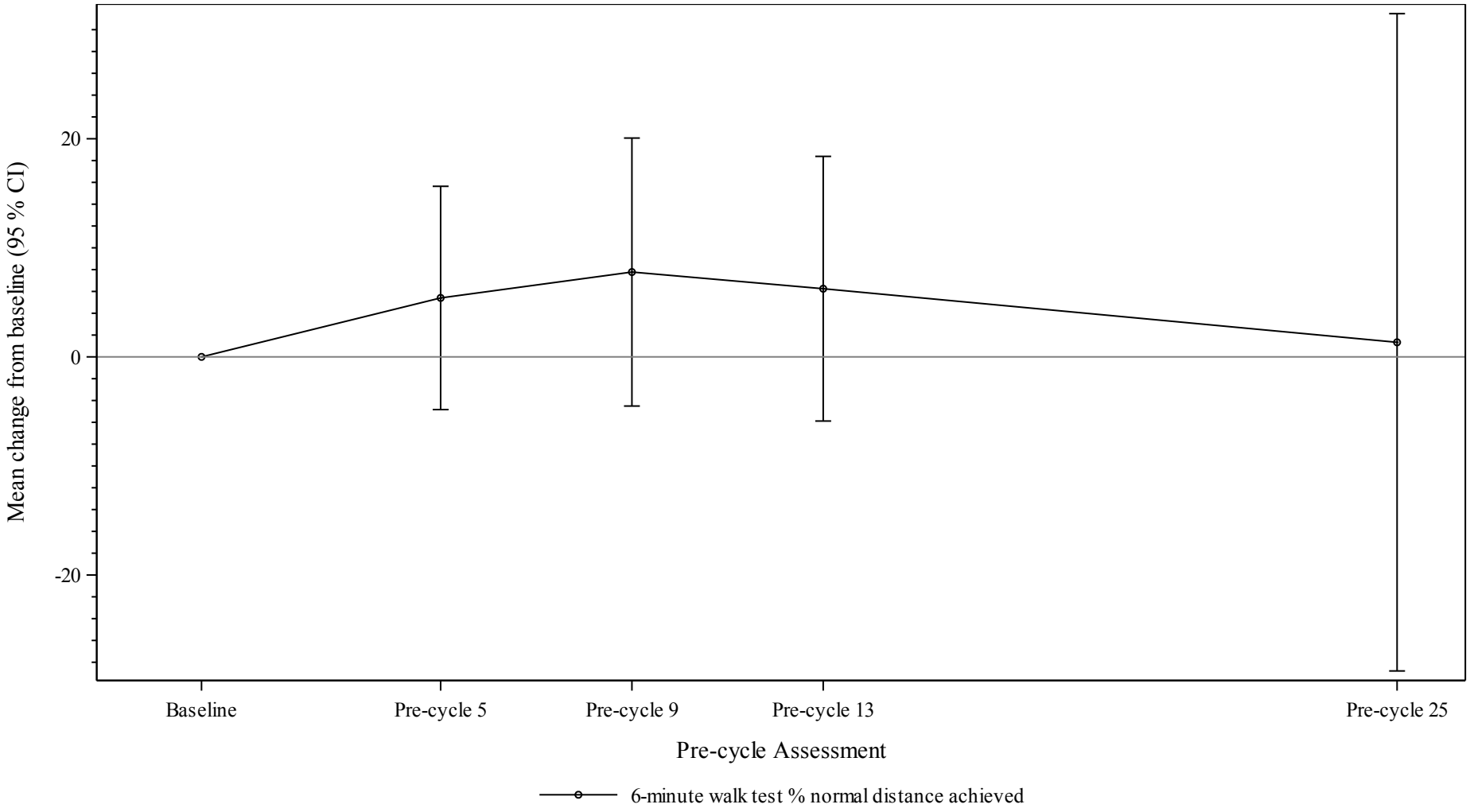
CI = Confidence interval.

Figure 2.11.2.6.1 Endurance evaluation secondary outcome test score categories of change over time
Gender = Male (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 14



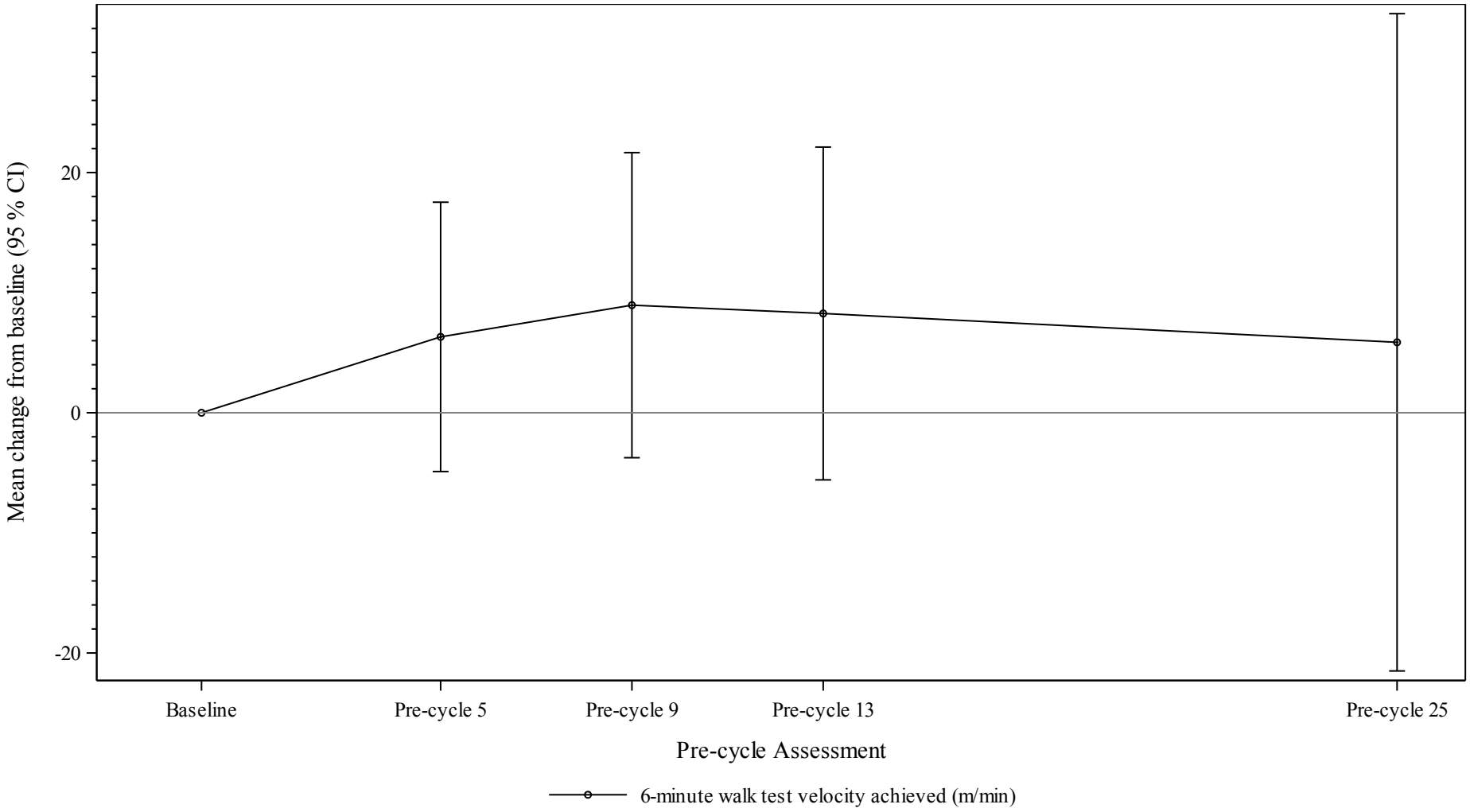
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.1 Endurance evaluation secondary outcome test score categories of change over time
Gender = Male (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 14



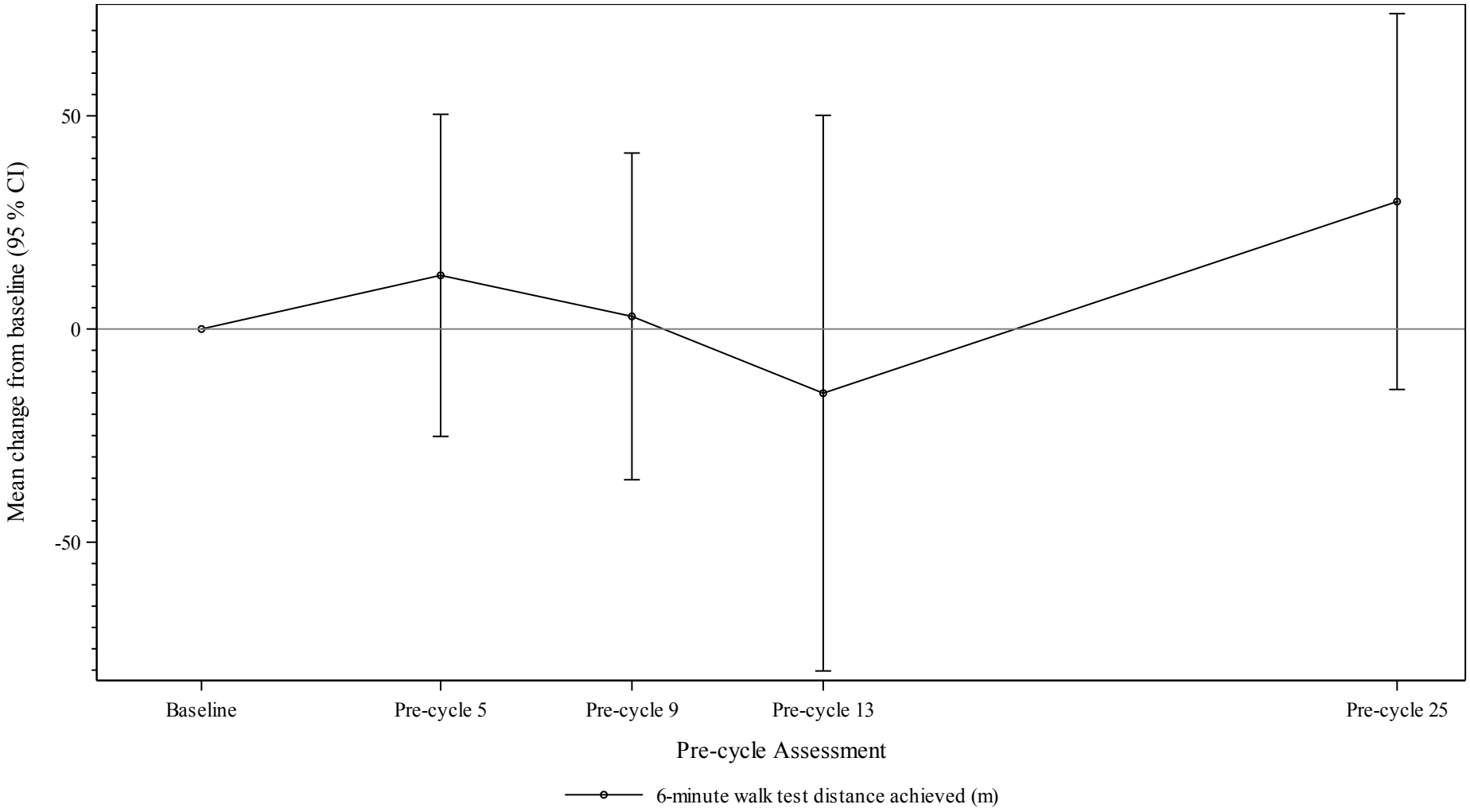
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.1 Endurance evaluation secondary outcome test score categories of change over time
Gender = Male (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 14



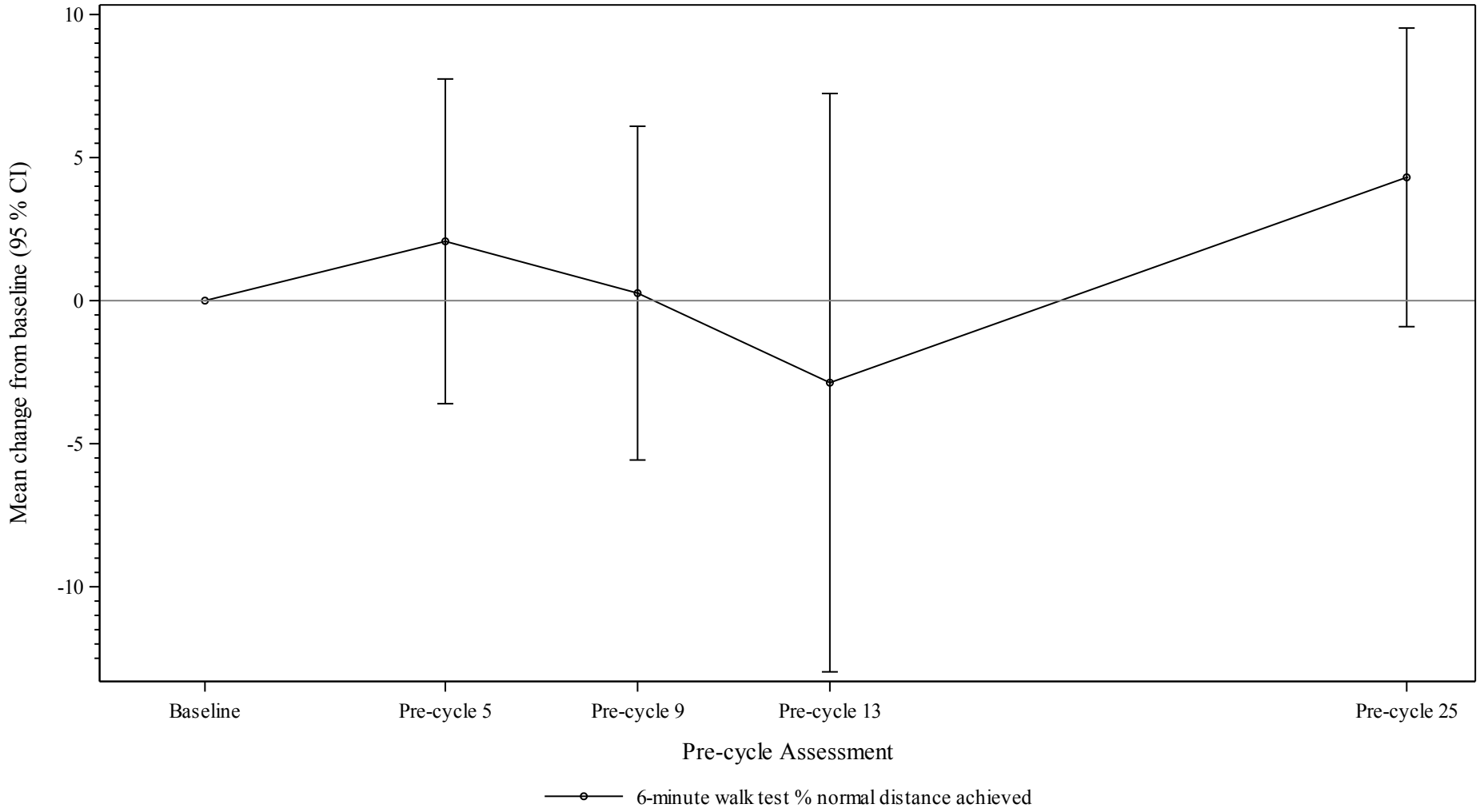
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.2 Endurance evaluation secondary outcome test score categories of change over time
Gender = Female (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 14



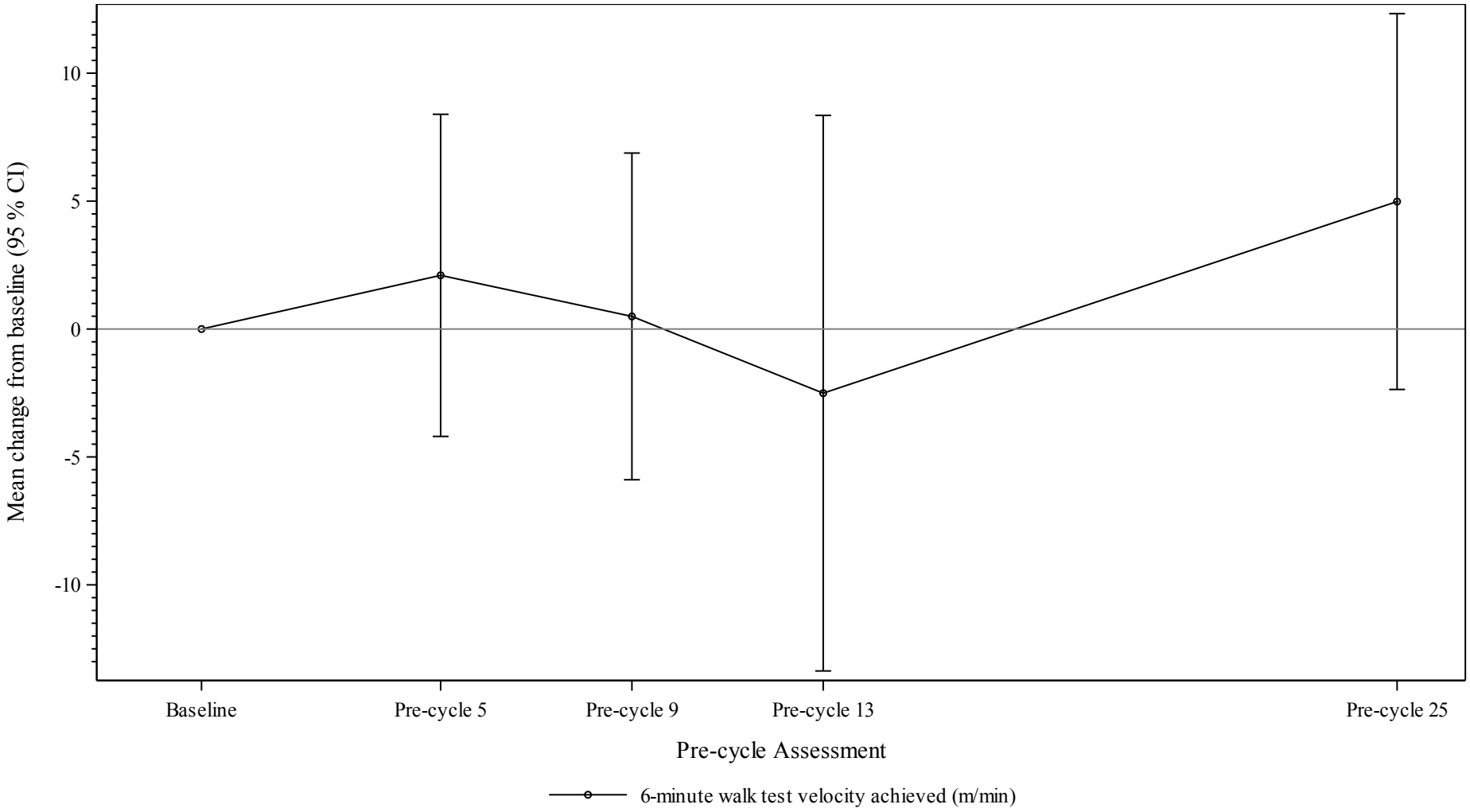
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.2 Endurance evaluation secondary outcome test score categories of change over time
Gender = Female (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 14



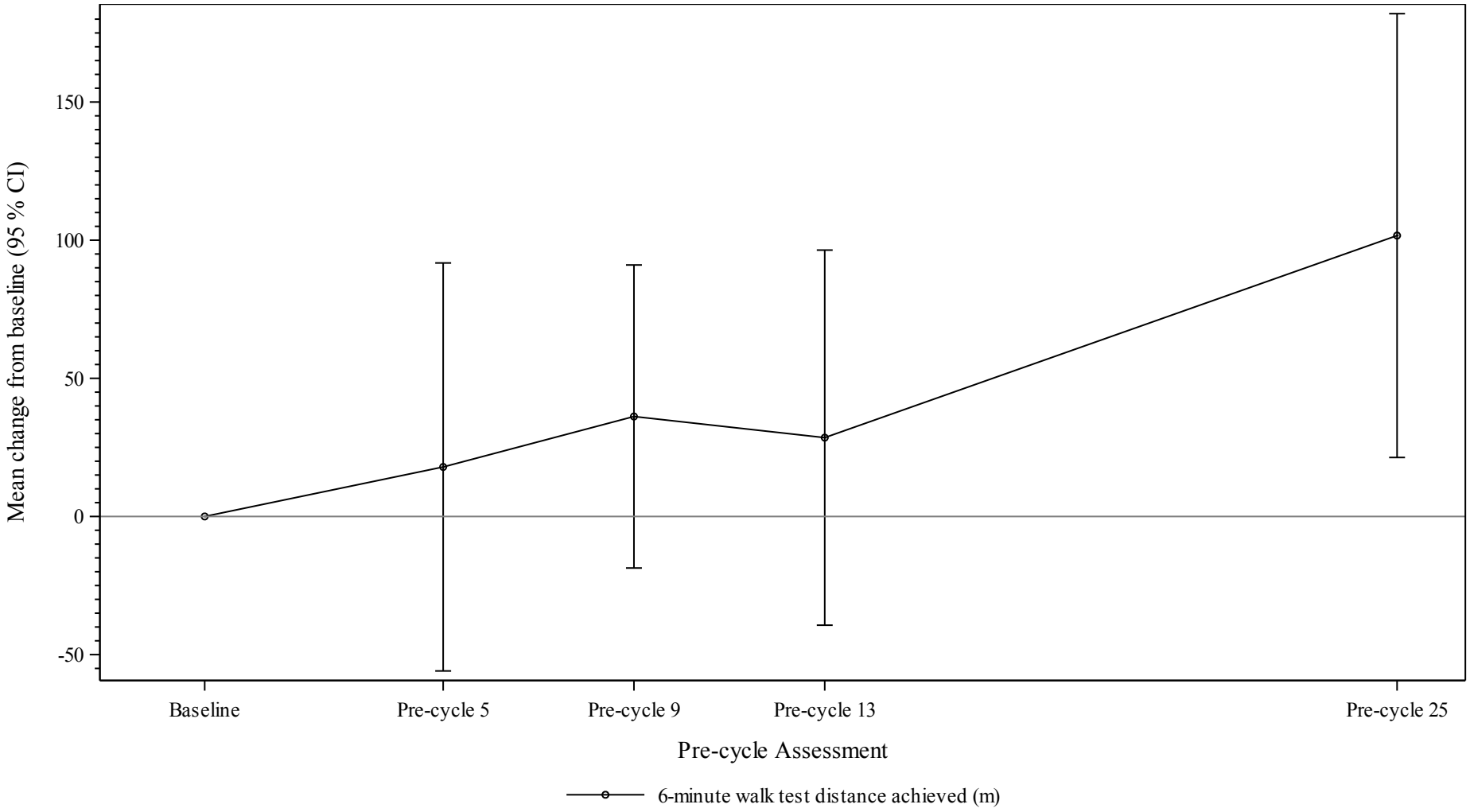
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.2 Endurance evaluation secondary outcome test score categories of change over time
Gender = Female (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 14



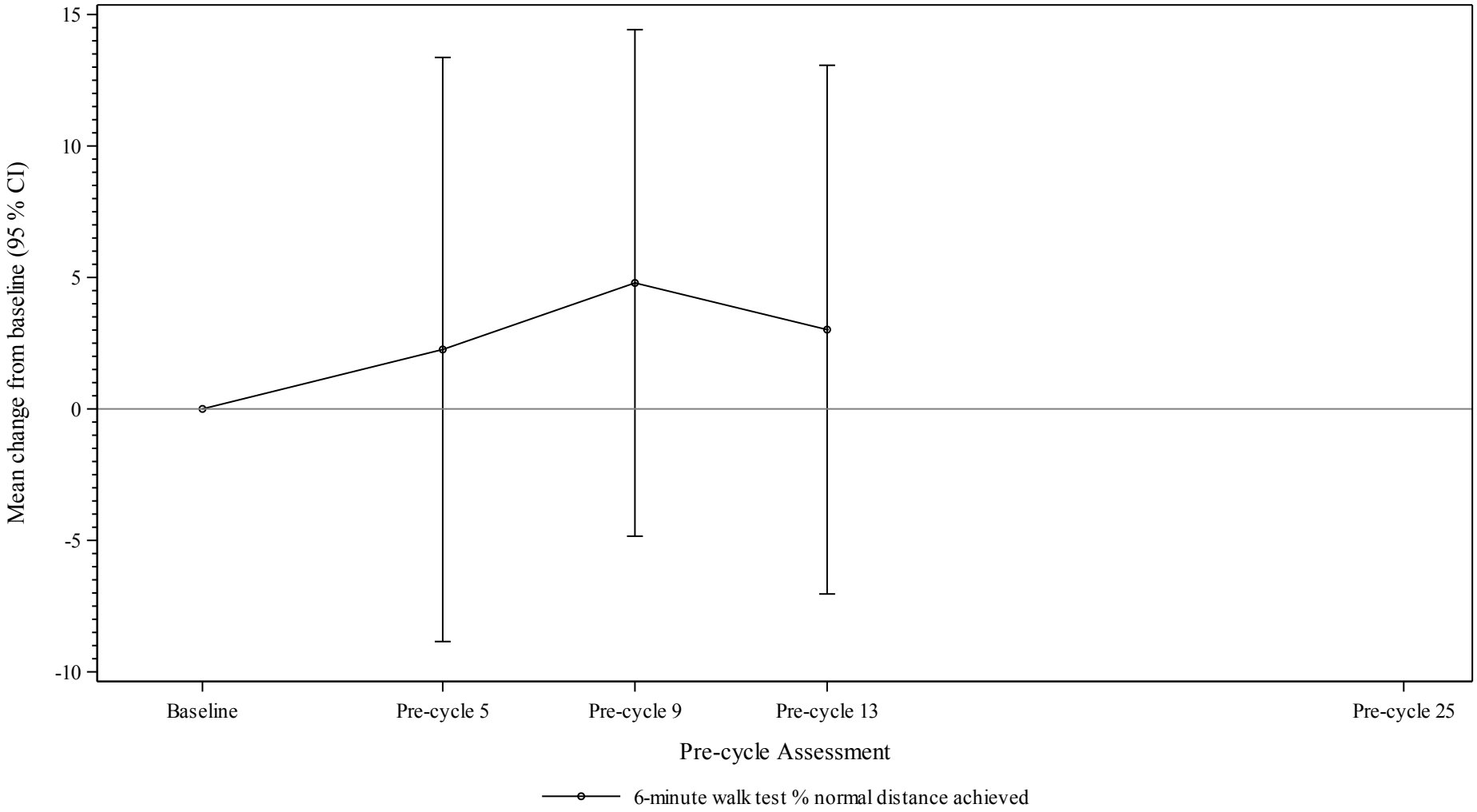
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.3 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 10



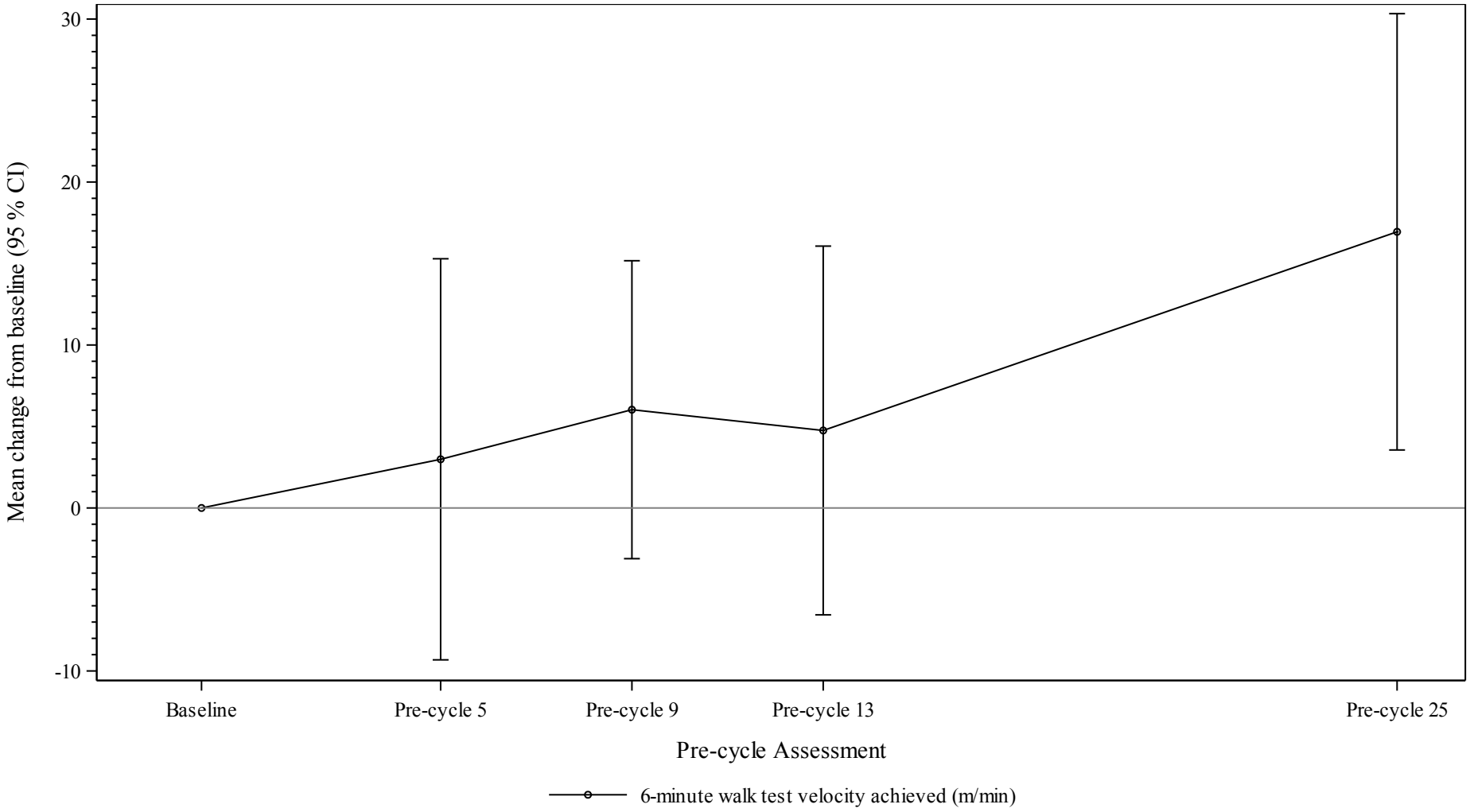
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.3 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 10



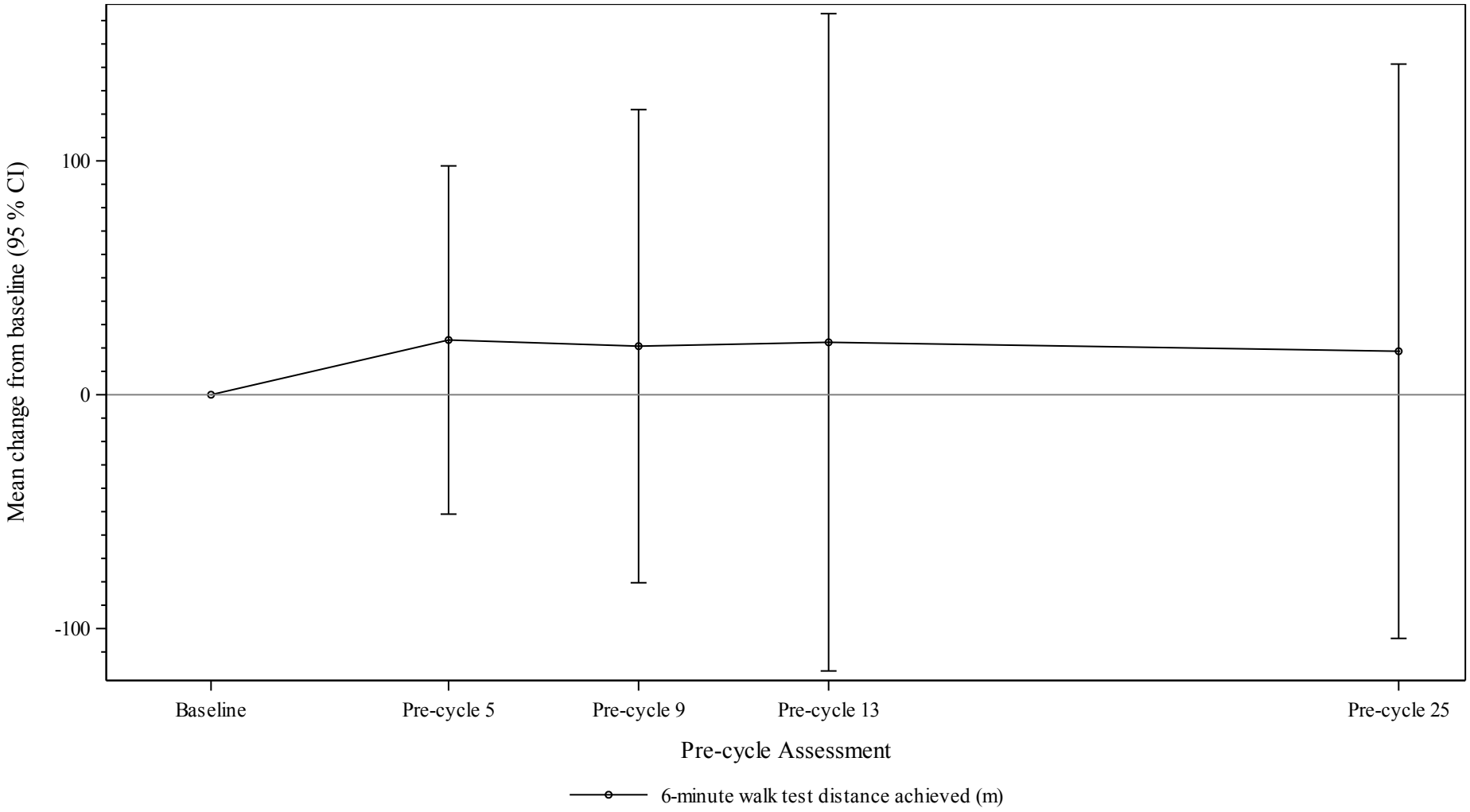
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.3 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 10



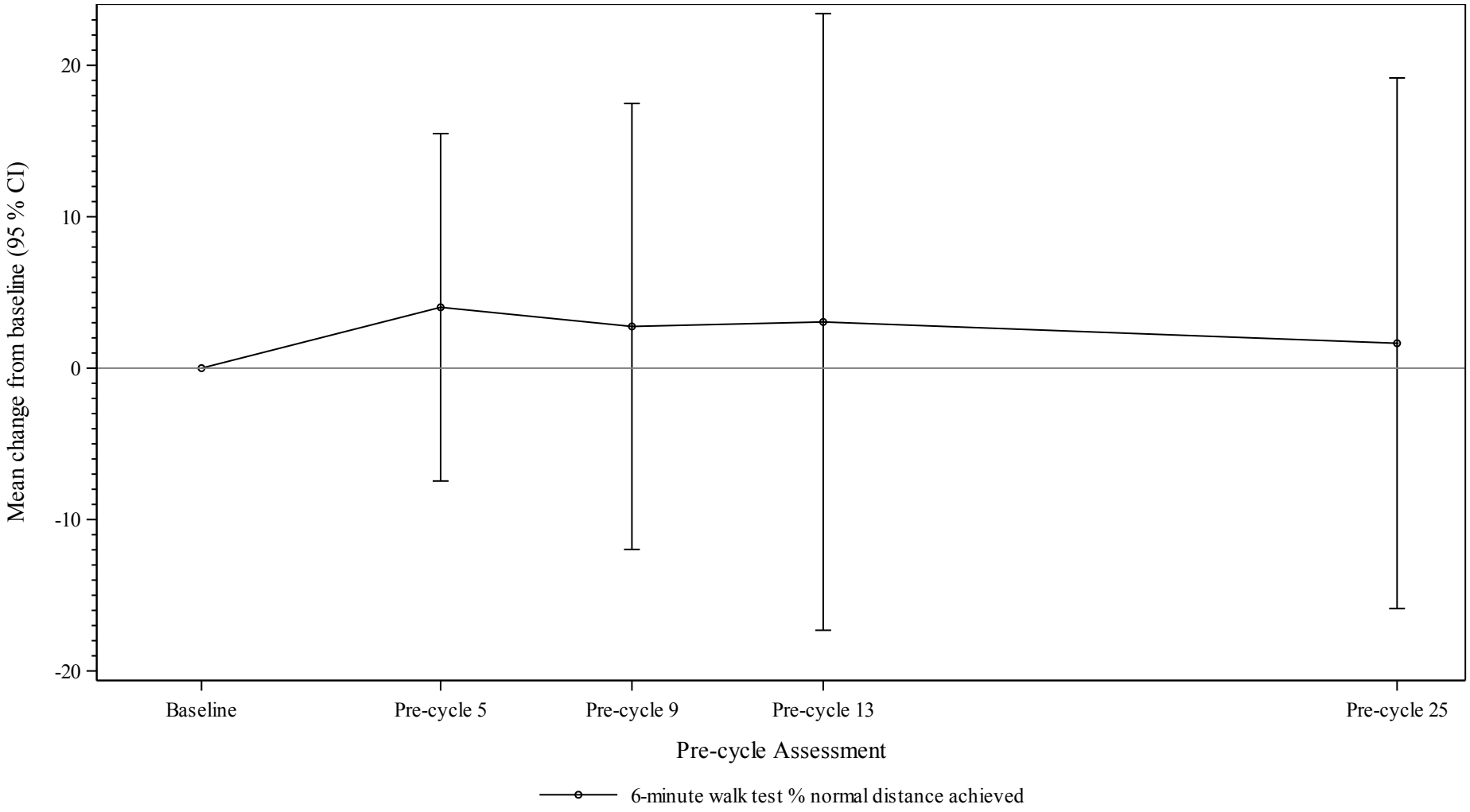
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.4 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Non-progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 8



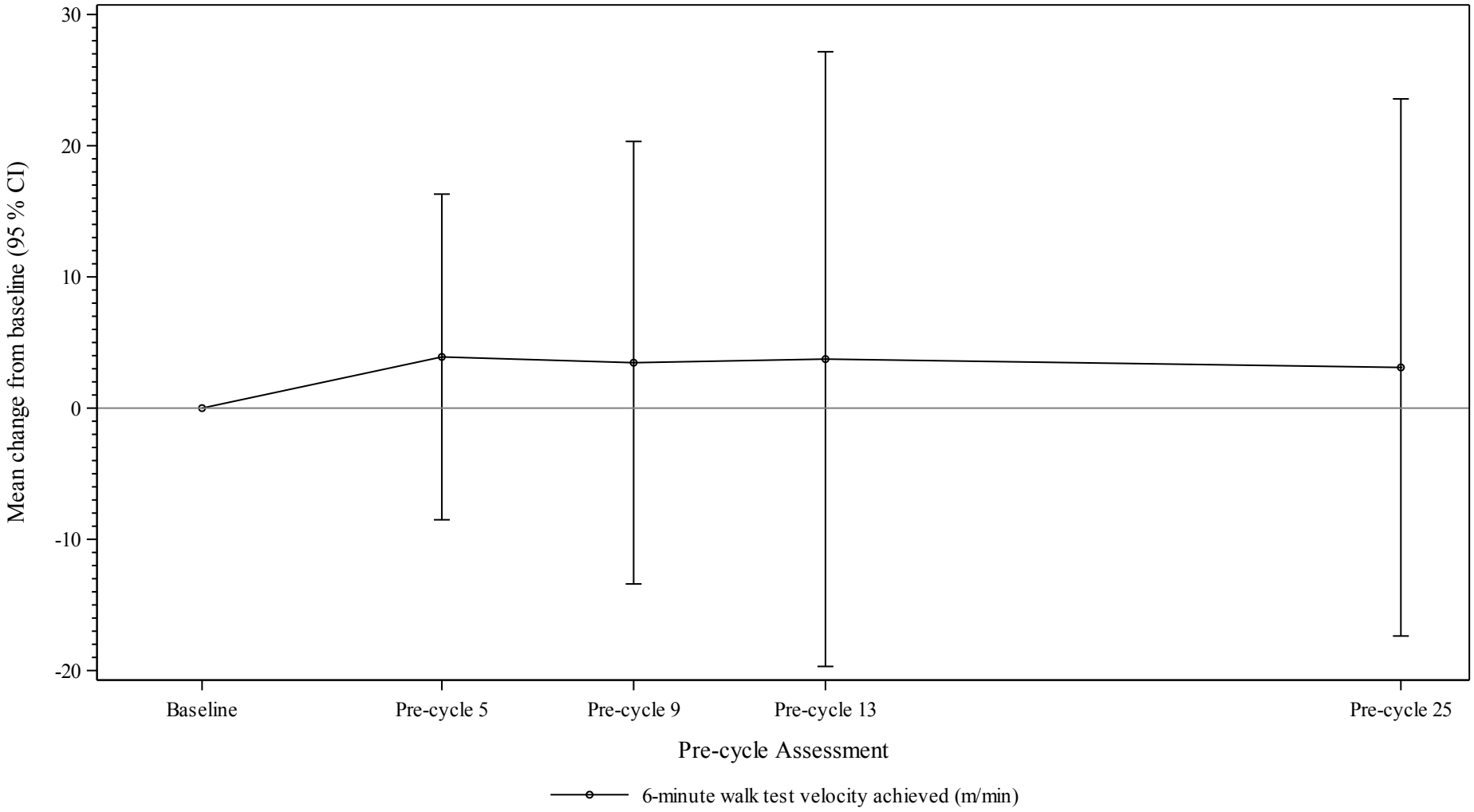
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.4 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Non-progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 8



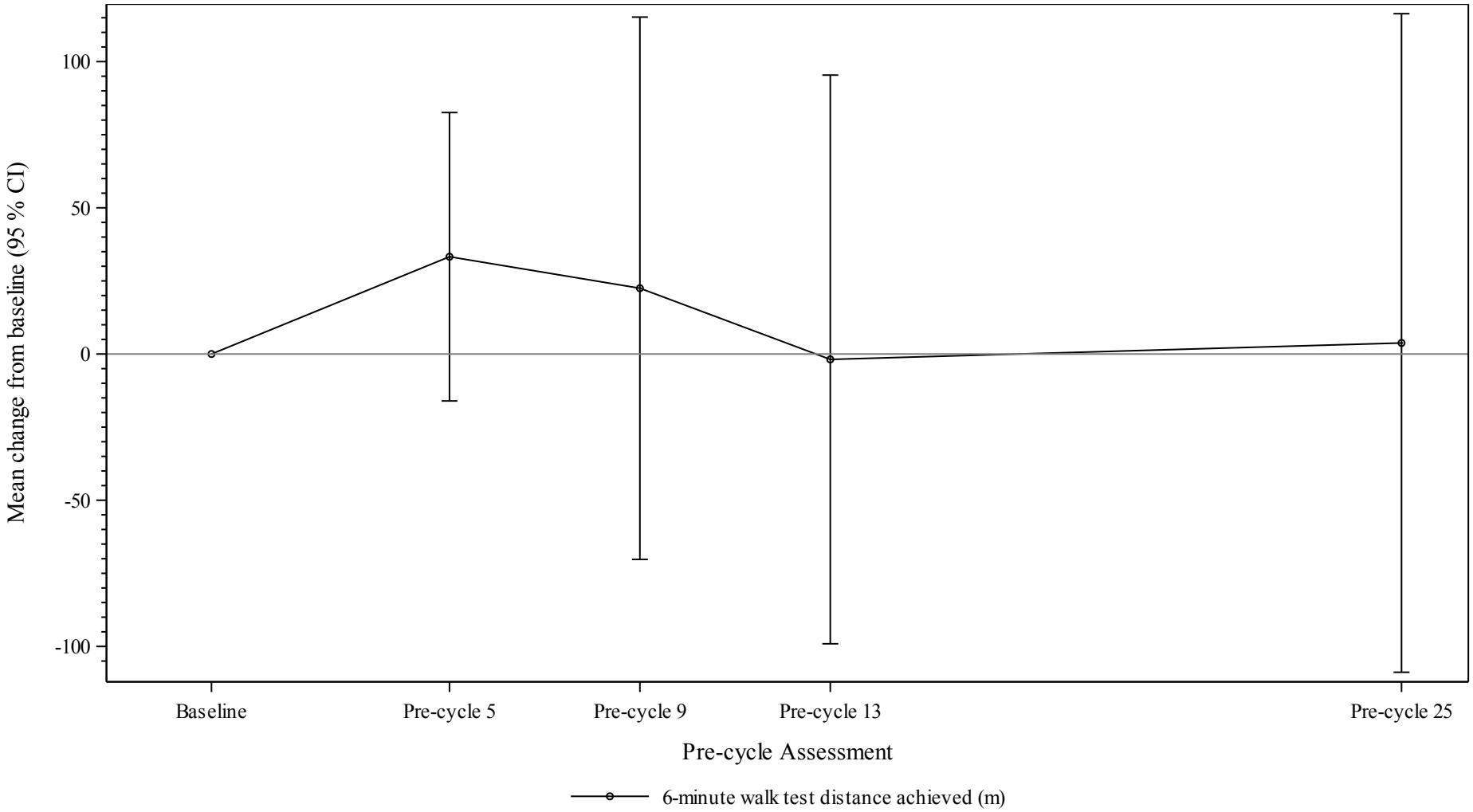
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.4 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Non-progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 8



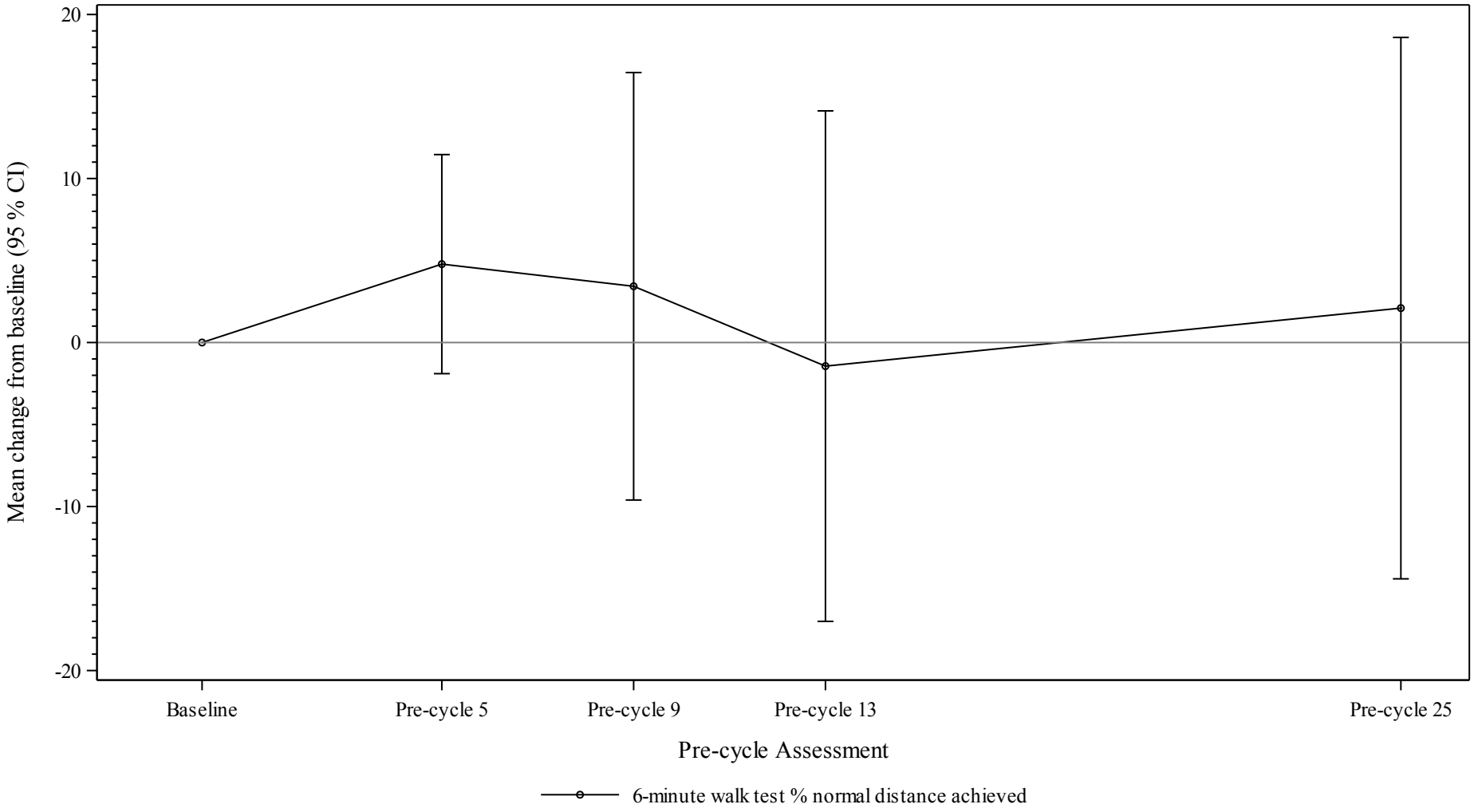
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.5 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 10



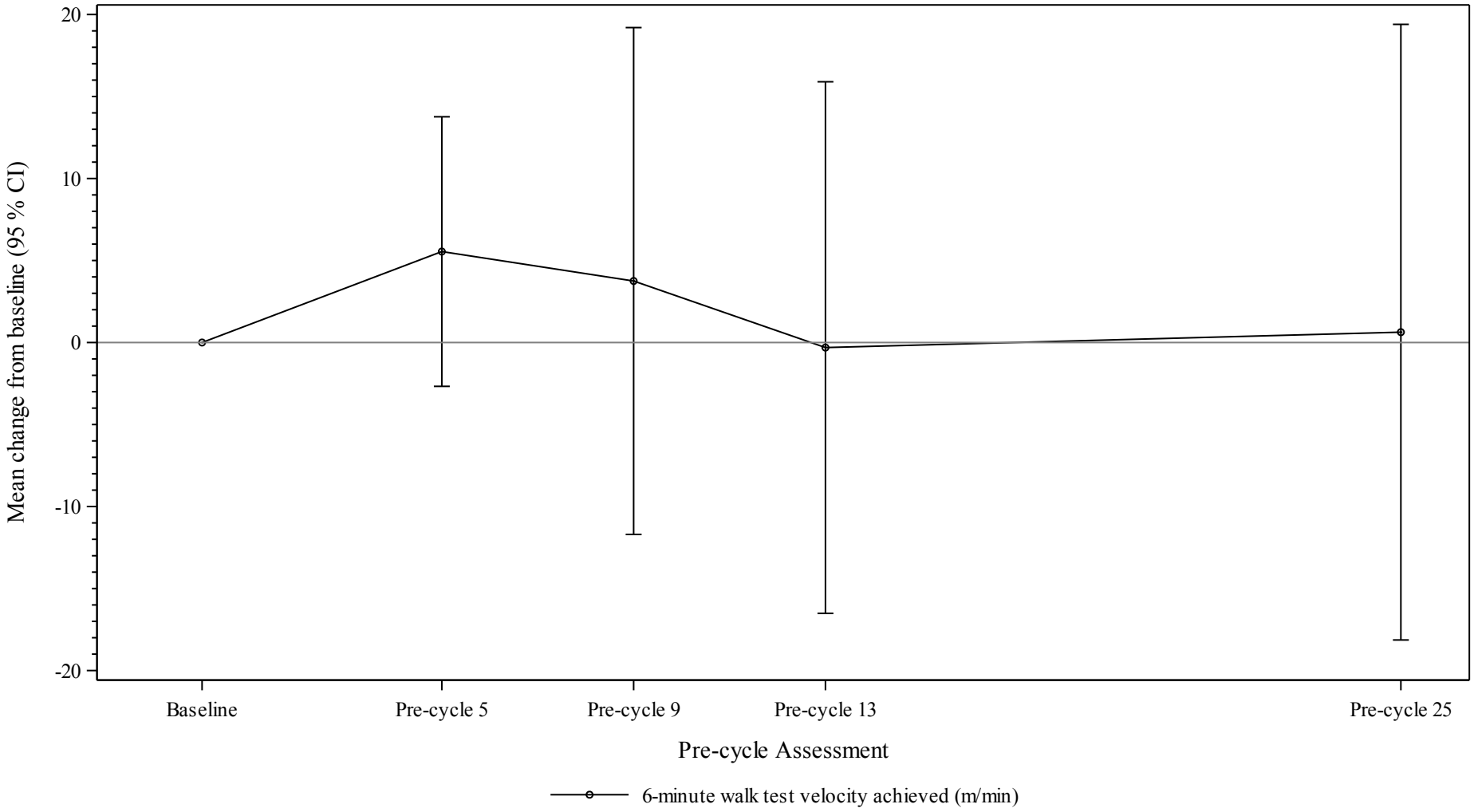
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.5 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 10



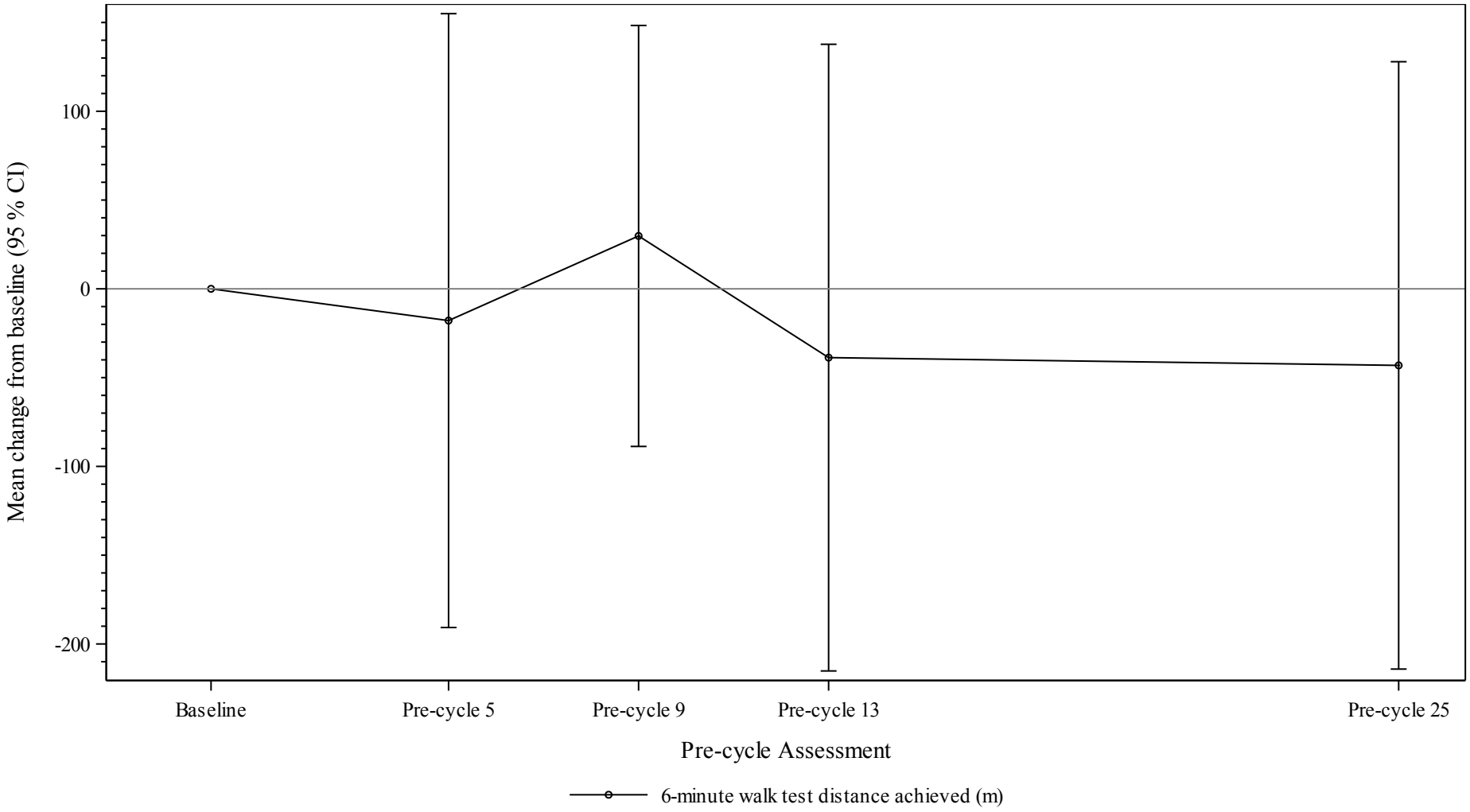
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.6.5 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 10



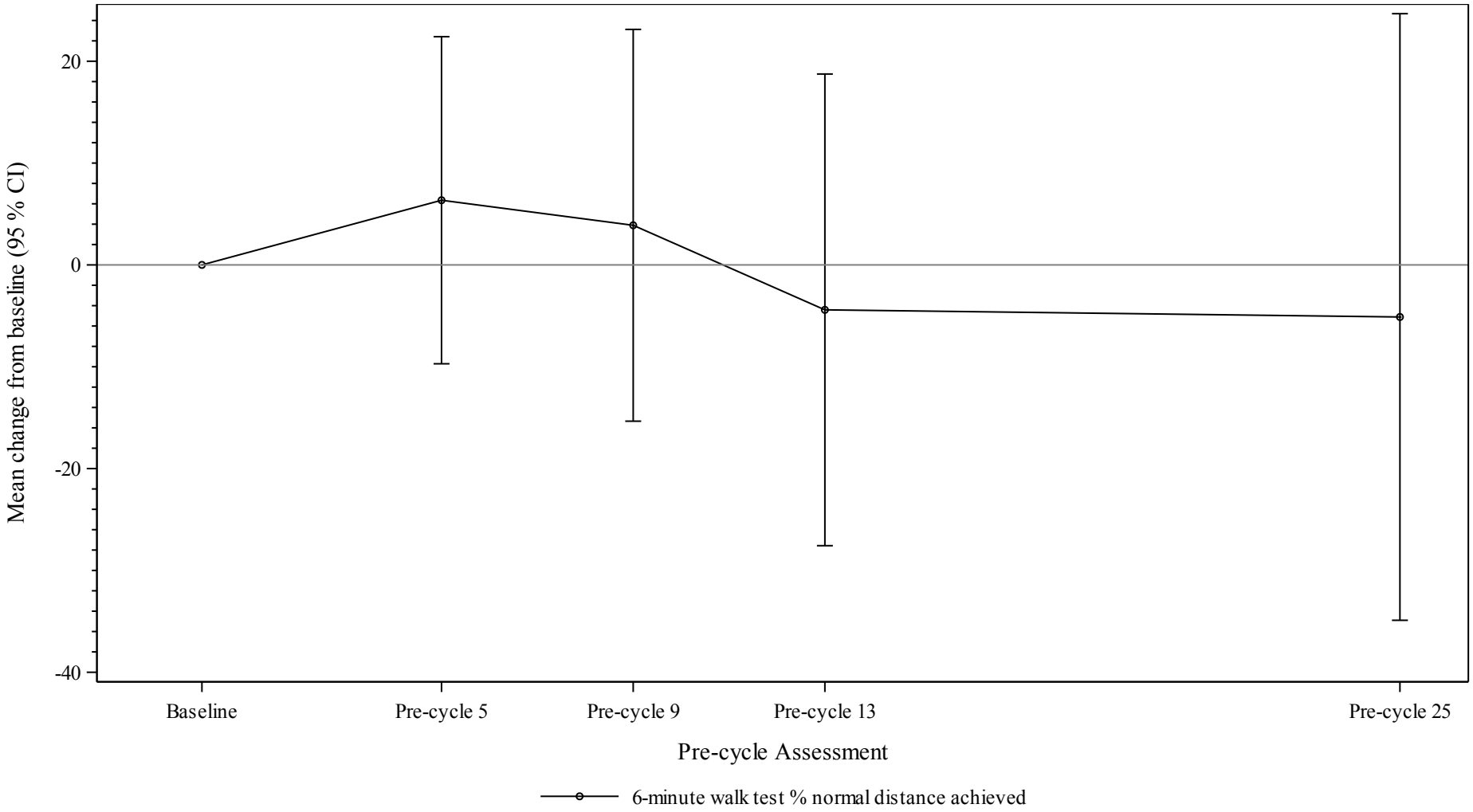
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.1 Endurance evaluation secondary outcome test score categories of change over time
Gender = Male (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 10



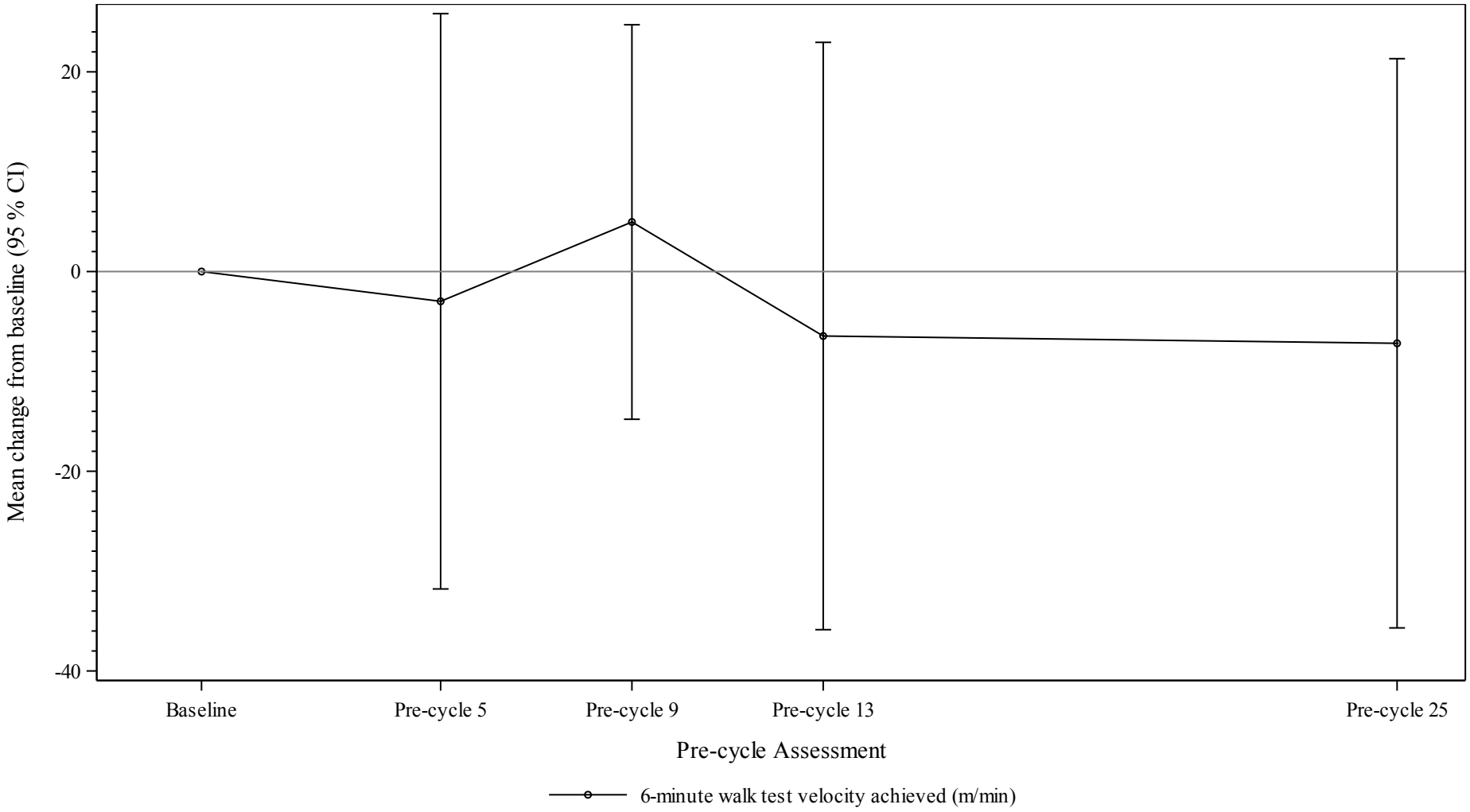
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.1 Endurance evaluation secondary outcome test score categories of change over time
Gender = Male (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 10



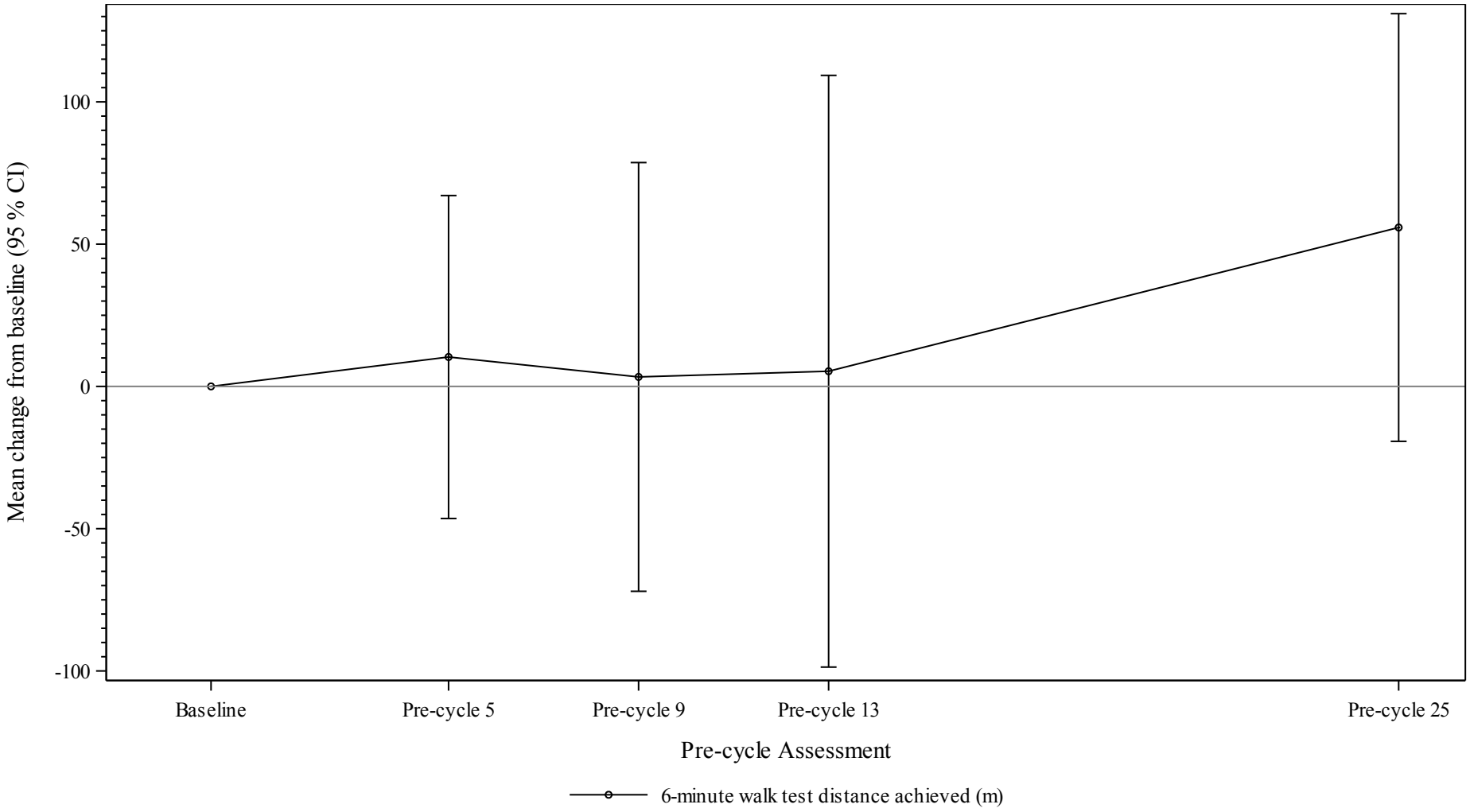
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.1 Endurance evaluation secondary outcome test score categories of change over time
Gender = Male (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 10



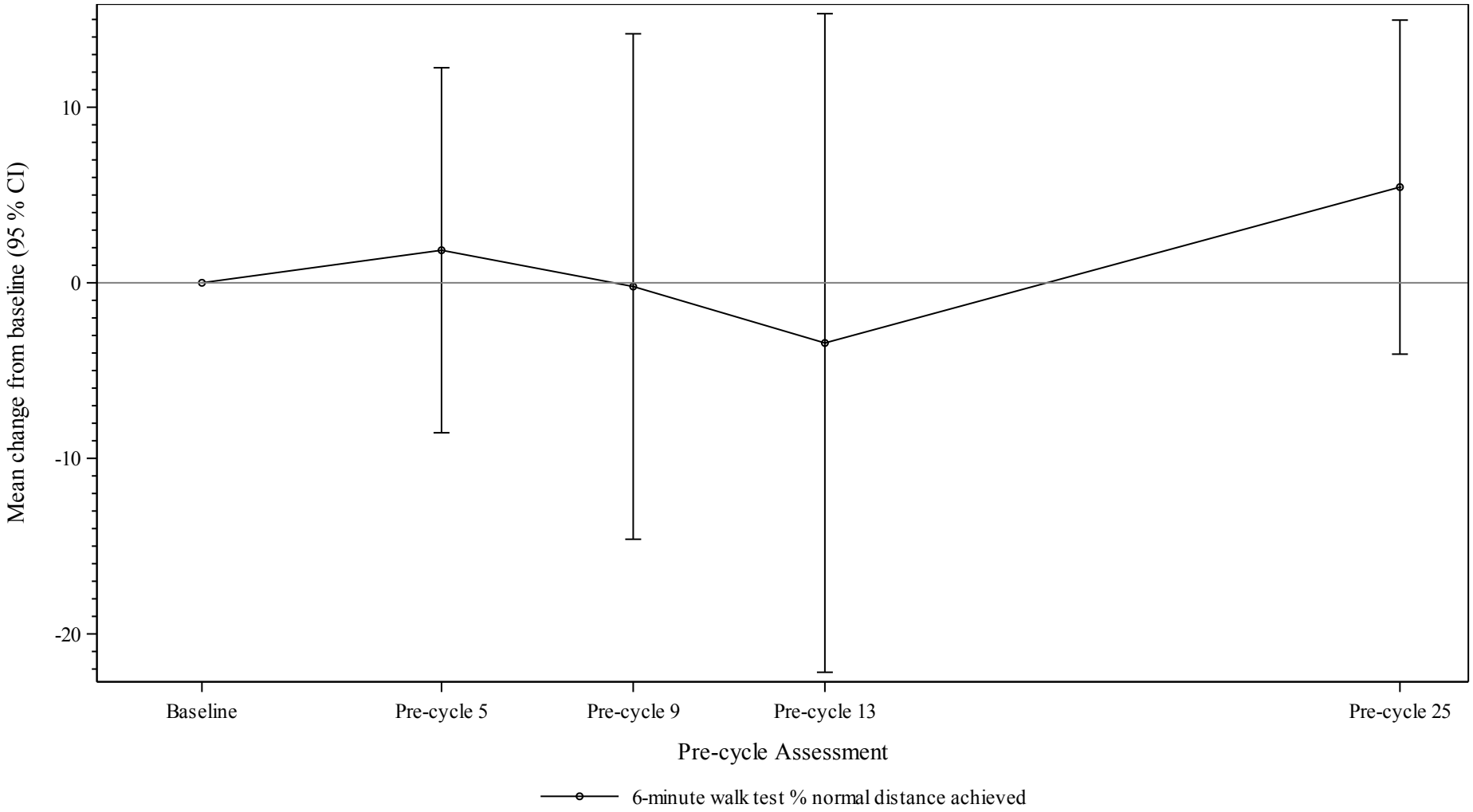
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.2 Endurance evaluation secondary outcome test score categories of change over time
Gender = Female (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 6



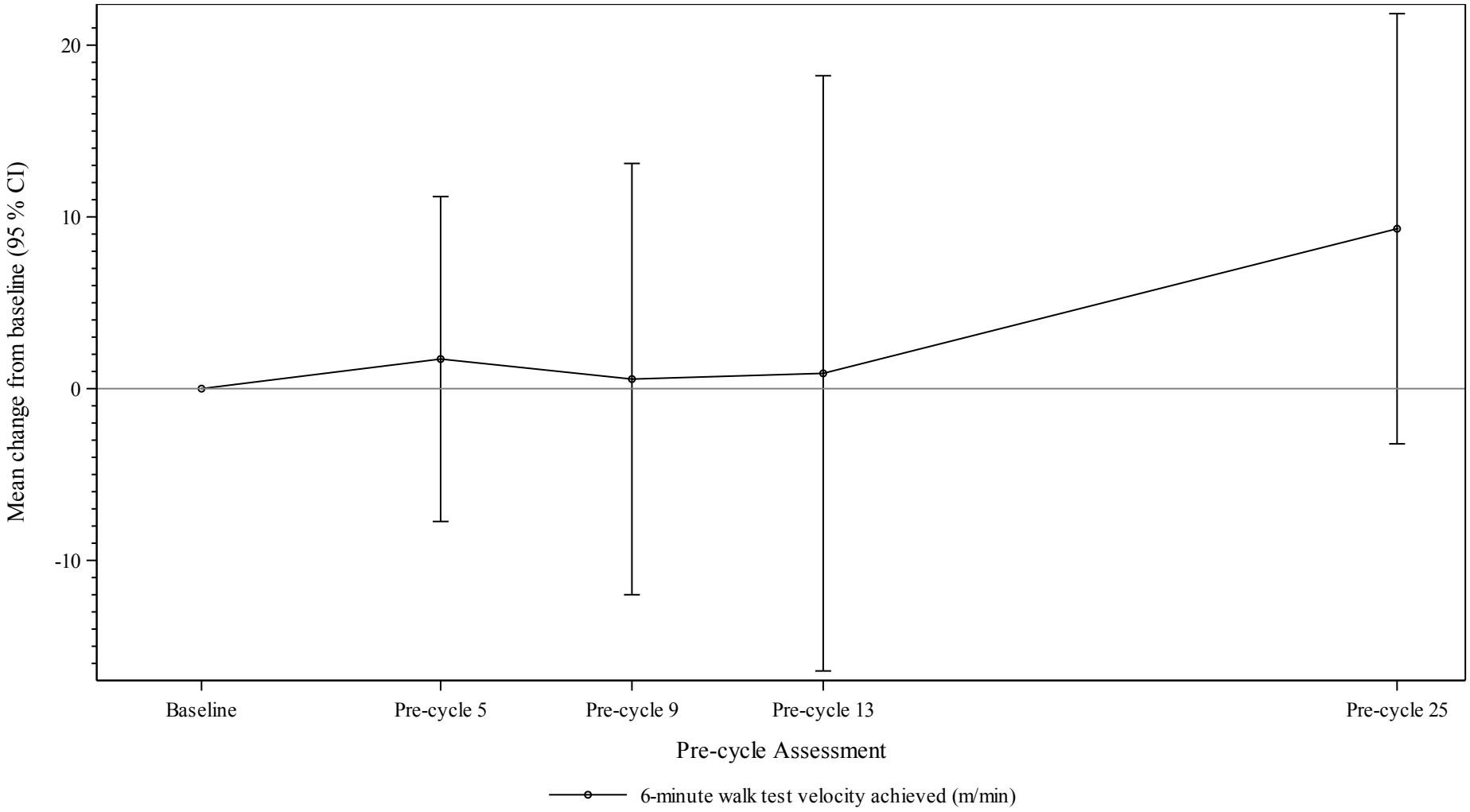
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.2 Endurance evaluation secondary outcome test score categories of change over time
Gender = Female (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 6



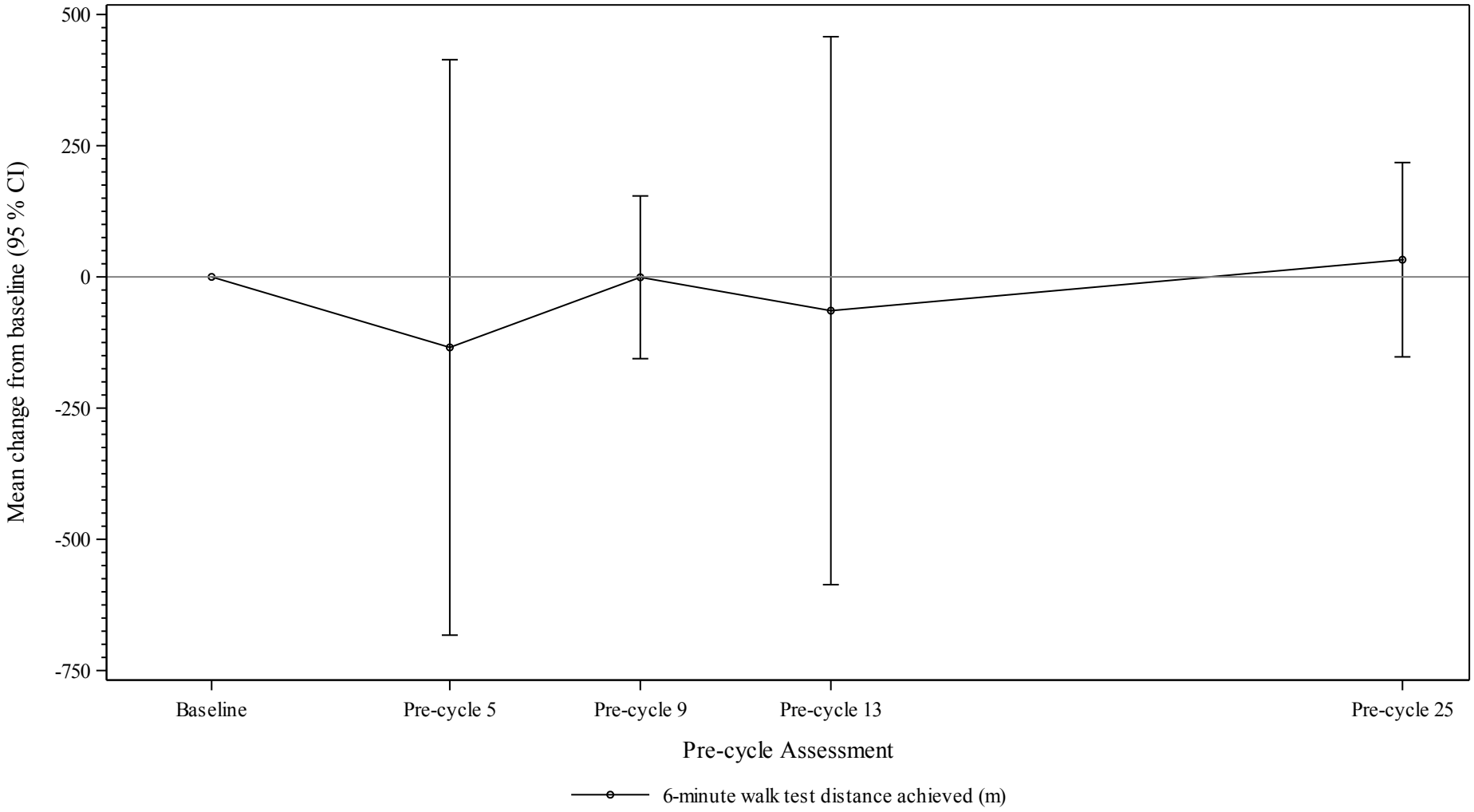
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.2 Endurance evaluation secondary outcome test score categories of change over time
Gender = Female (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 6



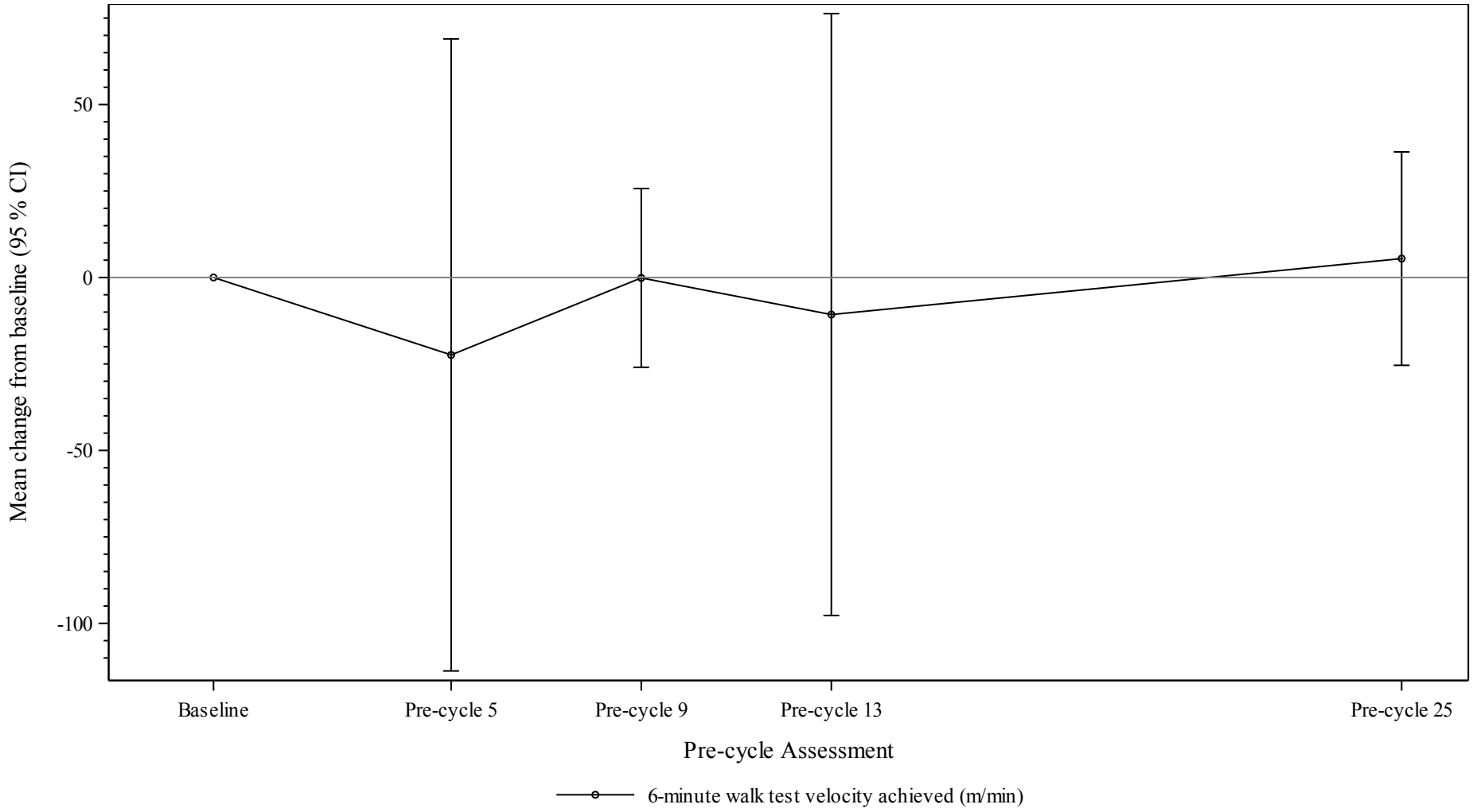
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.3 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 4



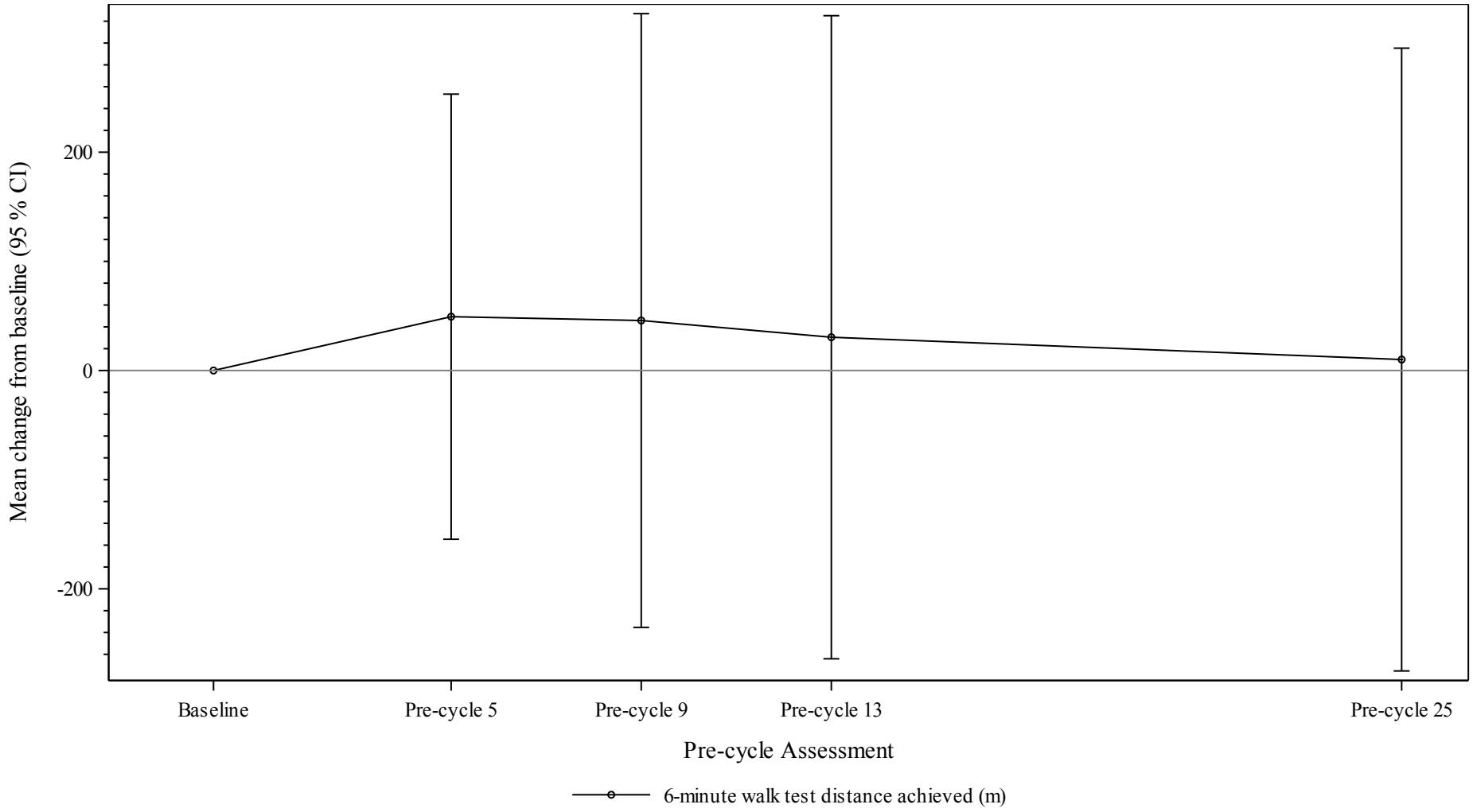
CI = Confidence interval.
Timepoints with <3 patients are omitted.
6-minute walk test % normal distance omitted owing to insufficient data.

Figure 2.11.2.7.3 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 4



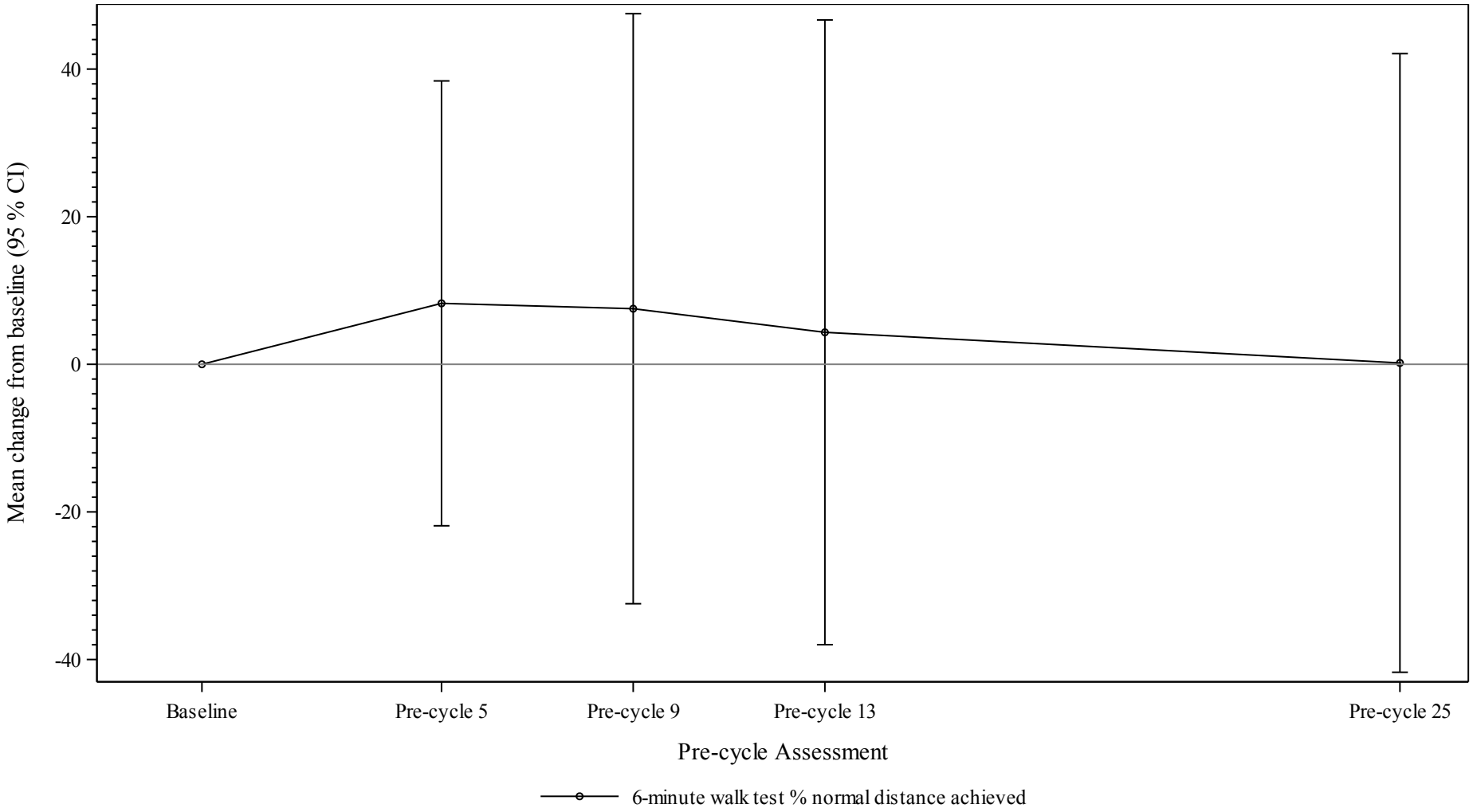
CI = Confidence interval.
Timepoints with <3 patients are omitted.
6-minute walk test % normal distance omitted owing to insufficient data.

Figure 2.11.2.7.4 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Non-progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 5



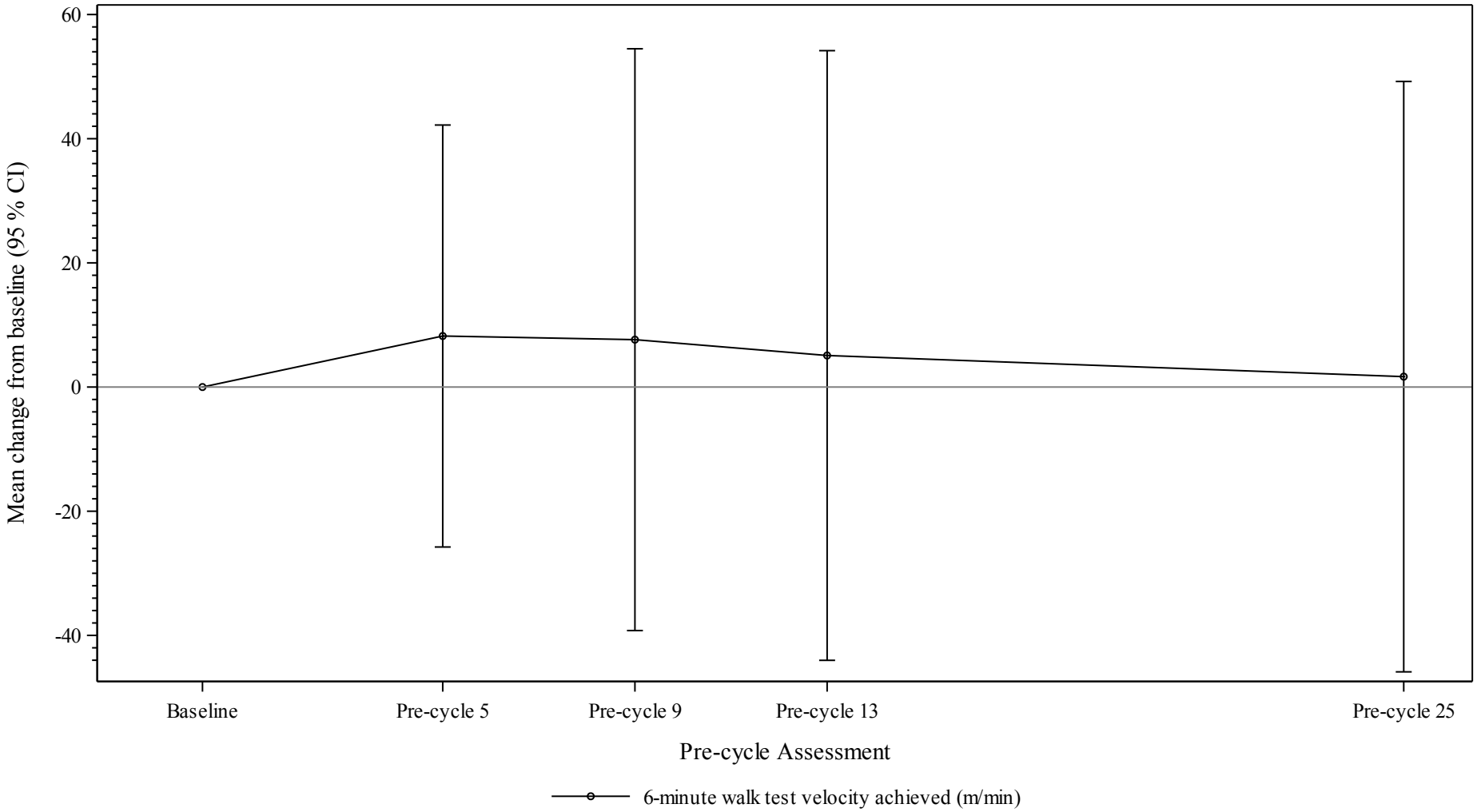
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.4 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Non-progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 5



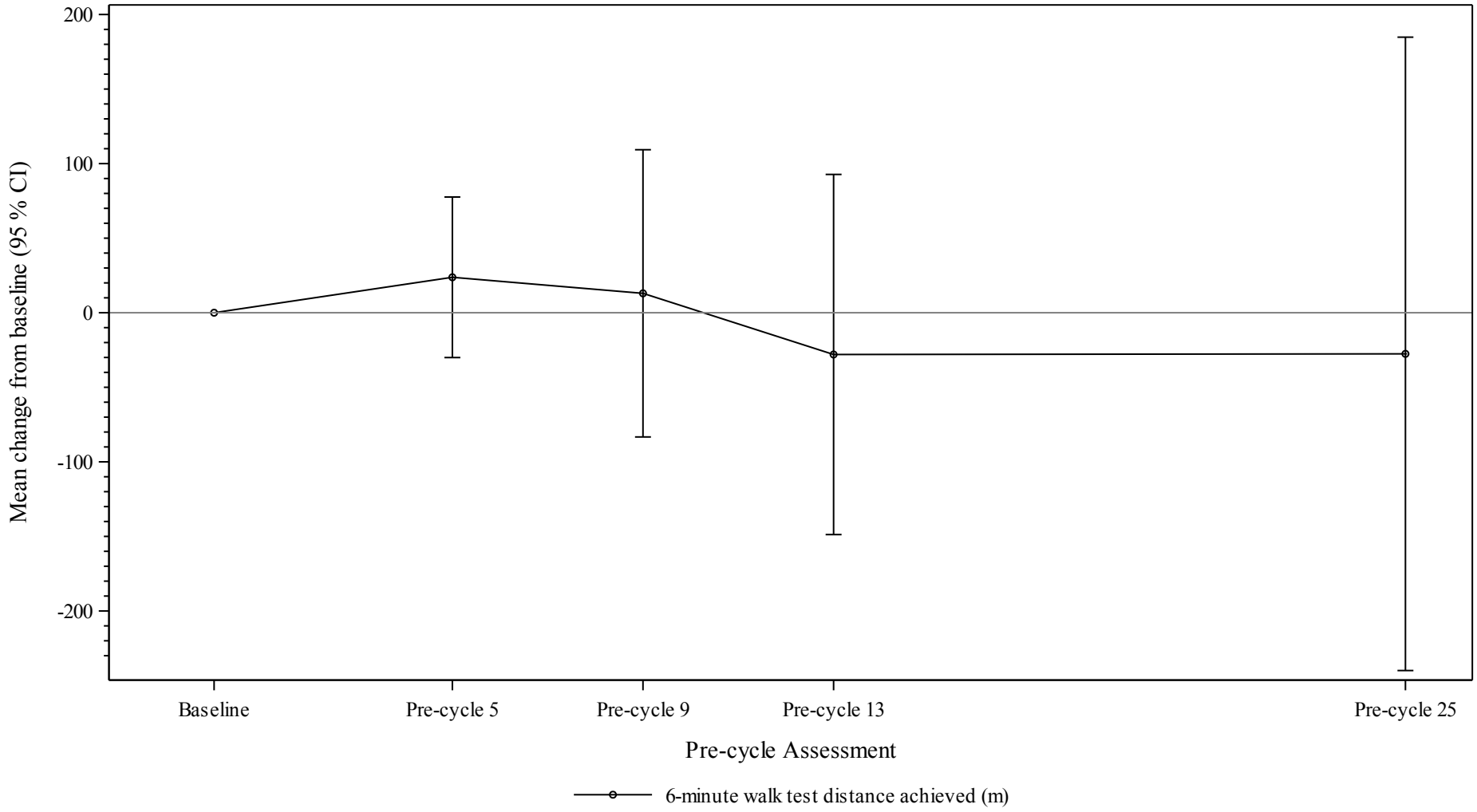
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.4 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Non-progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 5



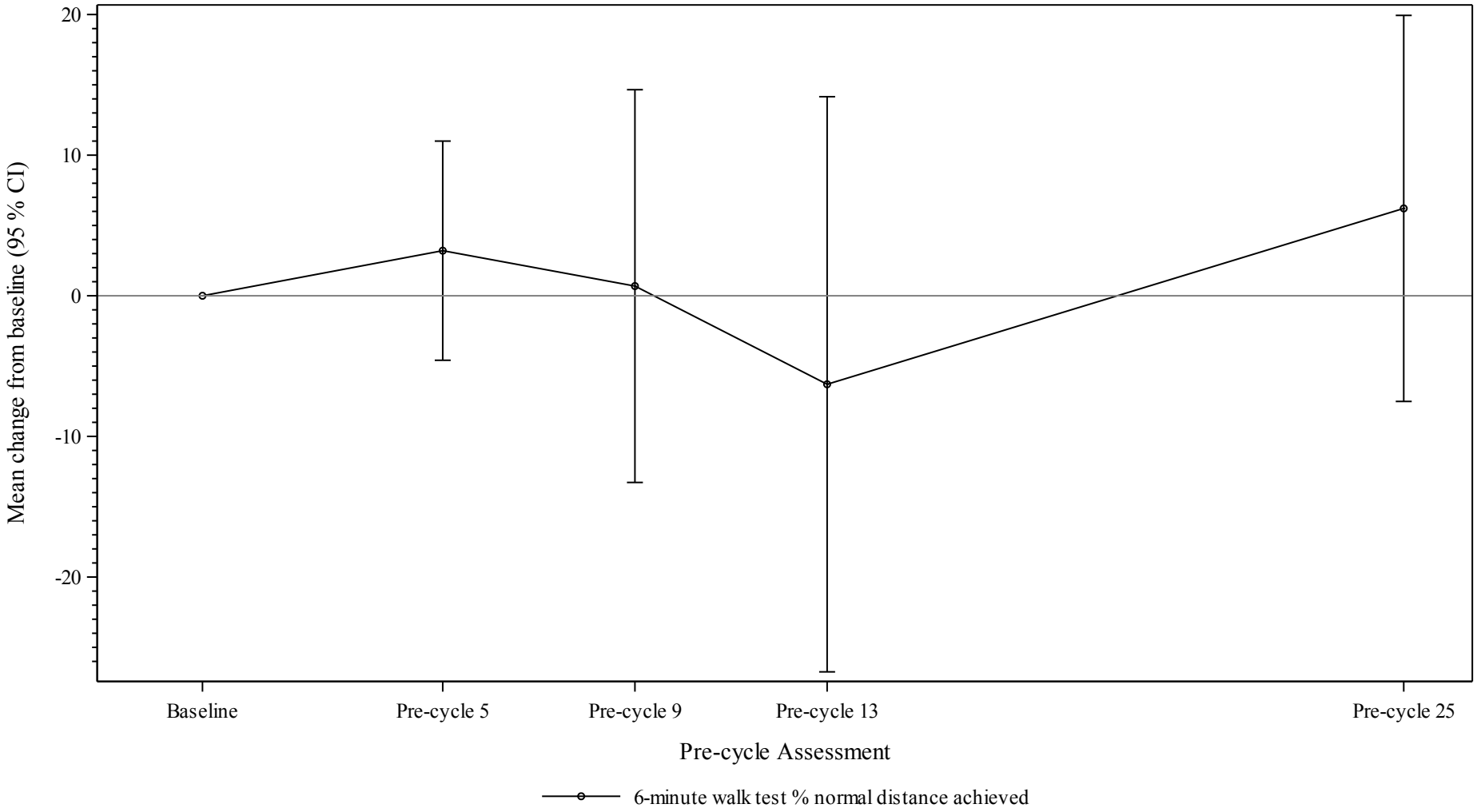
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.5 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Unknown (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 7



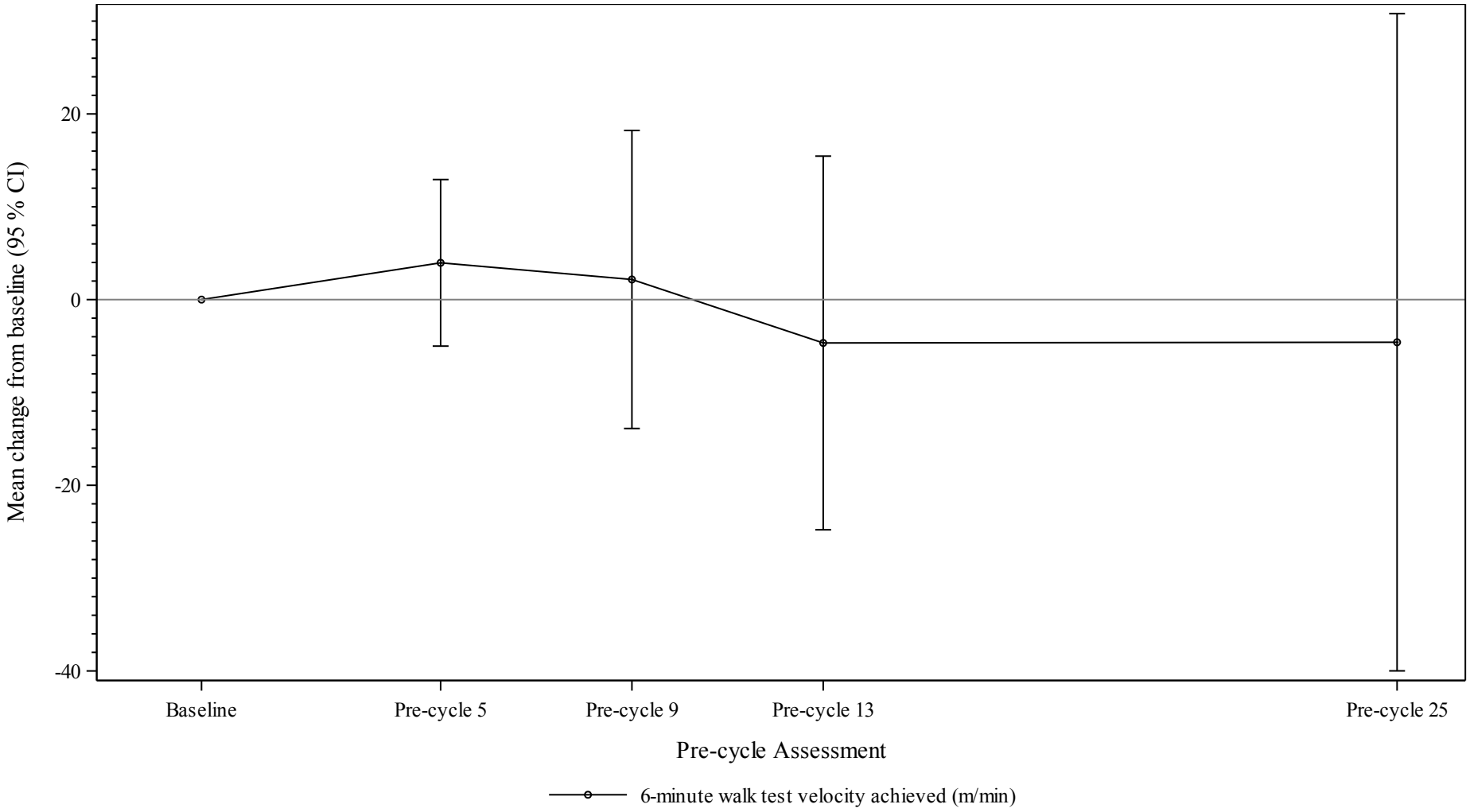
CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.5 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Unknown (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 7



CI = Confidence interval.
Timepoints with <3 patients are omitted.

Figure 2.11.2.7.5 Endurance evaluation secondary outcome test score categories of change over time
PN status at enrollment = Unknown (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, Data cut-off: 29th June 2018
N = 7



CI = Confidence interval.
Timepoints with <3 patients are omitted.

Table 2.12.1.1 PedsQL self-report score categories of overall change - percentage of patients with Improvement
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=34) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=31)	Categories of change - literature-based [d]			
		Improvement	23	74,2	55,4, 88,1
		No improvement	8	25,8	11,9, 44,6
Physical Functioning	Overall (N=31)	Categories of change - literature-based [d]			
		Improvement	18	58,1	39,1, 75,5
		No improvement	13	41,9	24,5, 60,9
Emotional Functioning	Overall (N=31)	Categories of change - literature-based [d]			
		Improvement	22	71,0	52,0, 85,8
		No improvement	9	29,0	14,2, 48,0
Social Functioning	Overall (N=31)	Categories of change - literature-based [d]			
		Improvement	18	58,1	39,1, 75,5
		No improvement	13	41,9	24,5, 60,9
School Functioning	Overall (N=27)	Categories of change - literature-based [d]			
		Improvement	18	66,7	46,0, 83,5
		No improvement	9	33,3	16,5, 54,0

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.1.2 PedsQL parent-report score categories of overall change - percentage of patients with Improvement
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=48)	Categories of change - literature-based [d]			
		Improvement	42	87,5	74,8, 95,3
		No improvement	6	12,5	4,7, 25,2
Physical Functioning	Overall (N=48)	Categories of change - literature-based [d]			
		Improvement	40	83,3	69,8, 92,5
		No improvement	8	16,7	7,5, 30,2
Emotional Functioning	Overall (N=48)	Categories of change - literature-based [d]			
		Improvement	40	83,3	69,8, 92,5
		No improvement	8	16,7	7,5, 30,2
Social Functioning	Overall (N=48)	Categories of change - literature-based [d]			
		Improvement	36	75,0	60,4, 86,4
		No improvement	12	25,0	13,6, 39,6
School Functioning	Overall (N=42)	Categories of change - literature-based [d]			
		Improvement	28	66,7	50,5, 80,4
		No improvement	14	33,3	19,6, 49,5

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement by >= 15 pts
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=34) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=31)	Categories of change [d]			
		Improvement	6	19,4	7,5, 37,5
		No improvement	25	80,6	62,5, 92,5
	Pre-cycle 5 (N=31)	Categories of change [d]			
		Improvement	6	19,4	7,5, 37,5
		No improvement	25	80,6	62,5, 92,5
	Pre-cycle 9 (N=31)	Categories of change [d]			
		Improvement	9	29,0	14,2, 48,0
		No improvement	22	71,0	52,0, 85,8
	Pre-cycle 13 (N=29)	Categories of change [d]			
		Improvement	7	24,1	10,3, 43,5
		No improvement	22	75,9	56,5, 89,7
	Pre-cycle 25 (N=23)	Categories of change [d]			
		Improvement	6	26,1	10,2, 48,4
		No improvement	17	73,9	51,6, 89,8
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Overall (N=31)	Categories of change [d]			
		Improvement	12	38,7	21,8, 57,8
		No improvement	19	61,3	42,2, 78,2

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement by >= 15 pts
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=34) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=31)	Categories of change [d]			
		Improvement	8	25,8	11,9, 44,6
		No improvement	23	74,2	55,4, 88,1
	Pre-cycle 5 (N=31)	Categories of change [d]			
		Improvement	8	25,8	11,9, 44,6
		No improvement	23	74,2	55,4, 88,1
	Pre-cycle 9 (N=31)	Categories of change [d]			
		Improvement	4	12,9	3,6, 29,8
		No improvement	27	87,1	70,2, 96,4
	Pre-cycle 13 (N=29)	Categories of change [d]			
		Improvement	10	34,5	17,9, 54,3
		No improvement	19	65,5	45,7, 82,1
	Pre-cycle 25 (N=23)	Categories of change [d]			
		Improvement	7	30,4	13,2, 52,9
		No improvement	16	69,6	47,1, 86,8
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Overall (N=31)	Categories of change [d]			
		Improvement	13	41,9	24,5, 60,9
		No improvement	18	58,1	39,1, 75,5

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement by >= 15 pts
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=34) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=31)	Categories of change [d]			
		Improvement	11	35,5	19,2, 54,6
		No improvement	20	64,5	45,4, 80,8
	Pre-cycle 5 (N=31)	Categories of change [d]			
		Improvement	10	32,3	16,7, 51,4
		No improvement	21	67,7	48,6, 83,3
	Pre-cycle 9 (N=31)	Categories of change [d]			
		Improvement	10	32,3	16,7, 51,4
		No improvement	21	67,7	48,6, 83,3
	Pre-cycle 13 (N=29)	Categories of change [d]			
		Improvement	11	37,9	20,7, 57,7
		No improvement	18	62,1	42,3, 79,3
	Pre-cycle 25 (N=23)	Categories of change [d]			
		Improvement	7	30,4	13,2, 52,9
		No improvement	16	69,6	47,1, 86,8
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6
	Overall (N=31)	Categories of change [d]			
		Improvement	17	54,8	36,0, 72,7
		No improvement	14	45,2	27,3, 64,0

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement by >= 15 pts
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=34) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=30)	Categories of change [d]			
		Improvement	10	33,3	17,3, 52,8
		No improvement	20	66,7	47,2, 82,7
	Pre-cycle 5 (N=31)	Categories of change [d]			
		Improvement	9	29,0	14,2, 48,0
		No improvement	22	71,0	52,0, 85,8
	Pre-cycle 9 (N=31)	Categories of change [d]			
		Improvement	8	25,8	11,9, 44,6
		No improvement	23	74,2	55,4, 88,1
	Pre-cycle 13 (N=29)	Categories of change [d]			
		Improvement	9	31,0	15,3, 50,8
		No improvement	20	69,0	49,2, 84,7
	Pre-cycle 25 (N=23)	Categories of change [d]			
		Improvement	7	30,4	13,2, 52,9
		No improvement	16	69,6	47,1, 86,8
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Overall (N=31)	Categories of change [d]			
		Improvement	15	48,4	30,2, 66,9
		No improvement	16	51,6	33,1, 69,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement by >= 15 pts
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=34) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=20)	Categories of change [d]			
		Improvement	7	35,0	15,4, 59,2
		No improvement	13	65,0	40,8, 84,6
	Pre-cycle 5 (N=17)	Categories of change [d]			
		Improvement	5	29,4	10,3, 56,0
		No improvement	12	70,6	44,0, 89,7
	Pre-cycle 9 (N=23)	Categories of change [d]			
		Improvement	8	34,8	16,4, 57,3
		No improvement	15	65,2	42,7, 83,6
	Pre-cycle 13 (N=23)	Categories of change [d]			
		Improvement	6	26,1	10,2, 48,4
		No improvement	17	73,9	51,6, 89,8
	Pre-cycle 25 (N=16)	Categories of change [d]			
		Improvement	3	18,8	4,0, 45,6
		No improvement	13	81,3	54,4, 96,0
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
	Overall (N=27)	Categories of change [d]			
		Improvement	14	51,9	31,9, 71,3
		No improvement	13	48,1	28,7, 68,1

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.1.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement by >= 15 pts
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=47)	Categories of change [d]			
		Improvement	17	36,2	22,7, 51,5
		No improvement	30	63,8	48,5, 77,3
	Pre-cycle 5 (N=47)	Categories of change [d]			
		Improvement	13	27,7	15,6, 42,6
		No improvement	34	72,3	57,4, 84,4
	Pre-cycle 9 (N=48)	Categories of change [d]			
		Improvement	18	37,5	24,0, 52,6
		No improvement	30	62,5	47,4, 76,0
	Pre-cycle 13 (N=45)	Categories of change [d]			
		Improvement	21	46,7	31,7, 62,1
		No improvement	24	53,3	37,9, 68,3
	Pre-cycle 25 (N=35)	Categories of change [d]			
		Improvement	18	51,4	34,0, 68,6
		No improvement	17	48,6	31,4, 66,0
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	4	80,0	28,4, 99,5
		No improvement	1	20,0	0,5, 71,6
	Overall (N=48)	Categories of change [d]			
		Improvement	34	70,8	55,9, 83,0
		No improvement	14	29,2	17,0, 44,1

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.1.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement by >= 15 pts
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=47)	Categories of change [d]			
		Improvement	15	31,9	19,1, 47,1
		No improvement	32	68,1	52,9, 80,9
	Pre-cycle 5 (N=47)	Categories of change [d]			
		Improvement	13	27,7	15,6, 42,6
		No improvement	34	72,3	57,4, 84,4
	Pre-cycle 9 (N=48)	Categories of change [d]			
		Improvement	20	41,7	27,6, 56,8
		No improvement	28	58,3	43,2, 72,4
	Pre-cycle 13 (N=45)	Categories of change [d]			
		Improvement	21	46,7	31,7, 62,1
		No improvement	24	53,3	37,9, 68,3
	Pre-cycle 25 (N=35)	Categories of change [d]			
		Improvement	20	57,1	39,4, 73,7
		No improvement	15	42,9	26,3, 60,6
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	4	80,0	28,4, 99,5
		No improvement	1	20,0	0,5, 71,6
	Overall (N=48)	Categories of change [d]			
		Improvement	35	72,9	58,2, 84,7
		No improvement	13	27,1	15,3, 41,8

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.1.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement by >= 15 pts
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=48)	Categories of change [d]			
		Improvement	22	45,8	31,4, 60,8
		No improvement	26	54,2	39,2, 68,6
	Pre-cycle 5 (N=47)	Categories of change [d]			
		Improvement	23	48,9	34,1, 63,9
		No improvement	24	51,1	36,1, 65,9
	Pre-cycle 9 (N=48)	Categories of change [d]			
		Improvement	25	52,1	37,2, 66,7
		No improvement	23	47,9	33,3, 62,8
	Pre-cycle 13 (N=45)	Categories of change [d]			
		Improvement	26	57,8	42,2, 72,3
		No improvement	19	42,2	27,7, 57,8
	Pre-cycle 25 (N=35)	Categories of change [d]			
		Improvement	19	54,3	36,6, 71,2
		No improvement	16	45,7	28,8, 63,4
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	4	80,0	28,4, 99,5
		No improvement	1	20,0	0,5, 71,6
	Overall (N=48)	Categories of change [d]			
		Improvement	37	77,1	62,7, 88,0
		No improvement	11	22,9	12,0, 37,3

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.1.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement by >= 15 pts
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=47)	Categories of change [d]			
		Improvement	22	46,8	32,1, 61,9
		No improvement	25	53,2	38,1, 67,9
	Pre-cycle 5 (N=47)	Categories of change [d]			
		Improvement	22	46,8	32,1, 61,9
		No improvement	25	53,2	38,1, 67,9
	Pre-cycle 9 (N=48)	Categories of change [d]			
		Improvement	19	39,6	25,8, 54,7
		No improvement	29	60,4	45,3, 74,2
	Pre-cycle 13 (N=45)	Categories of change [d]			
		Improvement	17	37,8	23,8, 53,5
		No improvement	28	62,2	46,5, 76,2
	Pre-cycle 25 (N=35)	Categories of change [d]			
		Improvement	13	37,1	21,5, 55,1
		No improvement	22	62,9	44,9, 78,5
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	4	80,0	28,4, 99,5
		No improvement	1	20,0	0,5, 71,6
	Overall (N=48)	Categories of change [d]			
		Improvement	31	64,6	49,5, 77,8
		No improvement	17	35,4	22,2, 50,5

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.1.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement by >= 15 pts
(Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=50) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=34)	Categories of change [d]			
		Improvement	9	26,5	12,9, 44,4
		No improvement	25	73,5	55,6, 87,1
	Pre-cycle 5 (N=27)	Categories of change [d]			
		Improvement	11	40,7	22,4, 61,2
		No improvement	16	59,3	38,8, 77,6
	Pre-cycle 9 (N=37)	Categories of change [d]			
		Improvement	14	37,8	22,5, 55,2
		No improvement	23	62,2	44,8, 77,5
	Pre-cycle 13 (N=37)	Categories of change [d]			
		Improvement	11	29,7	15,9, 47,0
		No improvement	26	70,3	53,0, 84,1
	Pre-cycle 25 (N=26)	Categories of change [d]			
		Improvement	7	26,9	11,6, 47,8
		No improvement	19	73,1	52,2, 88,4
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=42)	Categories of change [d]			
		Improvement	26	61,9	45,6, 76,4
		No improvement	16	38,1	23,6, 54,4

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.1.1 PedsQL self-report score categories of overall change - Gender = Male
- percentage of patients with Improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=19)	Categories of change - literature-based [d]			
		Improvement	16	84,2	60,4, 96,6
		No improvement	3	15,8	3,4, 39,6
Physical Functioning	Overall (N=19)	Categories of change - literature-based [d]			
		Improvement	10	52,6	28,9, 75,6
		No improvement	9	47,4	24,4, 71,1
Emotional Functioning	Overall (N=19)	Categories of change - literature-based [d]			
		Improvement	15	78,9	54,4, 93,9
		No improvement	4	21,1	6,1, 45,6
Social Functioning	Overall (N=19)	Categories of change - literature-based [d]			
		Improvement	13	68,4	43,4, 87,4
		No improvement	6	31,6	12,6, 56,6
School Functioning	Overall (N=16)	Categories of change - literature-based [d]			
		Improvement	13	81,3	54,4, 96,0
		No improvement	3	18,8	4,0, 45,6

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.2.1.2 PedsQL self-report score categories of overall change - Gender = Female
- percentage of patients with Improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=12)	Categories of change - literature-based [d]			
		Improvement	7	58,3	27,7, 84,8
		No improvement	5	41,7	15,2, 72,3
Physical Functioning	Overall (N=12)	Categories of change - literature-based [d]			
		Improvement	8	66,7	34,9, 90,1
		No improvement	4	33,3	9,9, 65,1
Emotional Functioning	Overall (N=12)	Categories of change - literature-based [d]			
		Improvement	7	58,3	27,7, 84,8
		No improvement	5	41,7	15,2, 72,3
Social Functioning	Overall (N=12)	Categories of change - literature-based [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8
School Functioning	Overall (N=11)	Categories of change - literature-based [d]			
		Improvement	5	45,5	16,7, 76,6
		No improvement	6	54,5	23,4, 83,3

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.2.1.3 PedsQL self-report score categories of overall change - PN status at enrollment = Progressive - percentage of patients with Improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=11)	Categories of change - literature-based [d]			
		Improvement	7	63,6	30,8, 89,1
		No improvement	4	36,4	10,9, 69,2
Physical Functioning	Overall (N=11)	Categories of change - literature-based [d]			
		Improvement	5	45,5	16,7, 76,6
		No improvement	6	54,5	23,4, 83,3
Emotional Functioning	Overall (N=11)	Categories of change - literature-based [d]			
		Improvement	8	72,7	39,0, 94,0
		No improvement	3	27,3	6,0, 61,0
Social Functioning	Overall (N=11)	Categories of change - literature-based [d]			
		Improvement	5	45,5	16,7, 76,6
		No improvement	6	54,5	23,4, 83,3
School Functioning	Overall (N=9)	Categories of change - literature-based [d]			
		Improvement	5	55,6	21,2, 86,3
		No improvement	4	44,4	13,7, 78,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.2.1.4 PedsQL self-report score categories of overall change - PN status at enrollment = Non-progressive - percentage of patients with Improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=10)	Categories of change - literature-based [d]			
		Improvement	8	80,0	44,4, 97,5
		No improvement	2	20,0	2,5, 55,6
Physical Functioning	Overall (N=10)	Categories of change - literature-based [d]			
		Improvement	6	60,0	26,2, 87,8
		No improvement	4	40,0	12,2, 73,8
Emotional Functioning	Overall (N=10)	Categories of change - literature-based [d]			
		Improvement	8	80,0	44,4, 97,5
		No improvement	2	20,0	2,5, 55,6
Social Functioning	Overall (N=10)	Categories of change - literature-based [d]			
		Improvement	7	70,0	34,8, 93,3
		No improvement	3	30,0	6,7, 65,2
School Functioning	Overall (N=10)	Categories of change - literature-based [d]			
		Improvement	8	80,0	44,4, 97,5
		No improvement	2	20,0	2,5, 55,6

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.2.1.5 PedsQL self-report score categories of overall change - PN status at enrollment = Unknown - percentage of patients with Improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=10)	Categories of change - literature-based [d]			
		Improvement	8	80,0	44,4, 97,5
		No improvement	2	20,0	2,5, 55,6
Physical Functioning	Overall (N=10)	Categories of change - literature-based [d]			
		Improvement	7	70,0	34,8, 93,3
		No improvement	3	30,0	6,7, 65,2
Emotional Functioning	Overall (N=10)	Categories of change - literature-based [d]			
		Improvement	6	60,0	26,2, 87,8
		No improvement	4	40,0	12,2, 73,8
Social Functioning	Overall (N=10)	Categories of change - literature-based [d]			
		Improvement	6	60,0	26,2, 87,8
		No improvement	4	40,0	12,2, 73,8
School Functioning	Overall (N=8)	Categories of change - literature-based [d]			
		Improvement	5	62,5	24,5, 91,5
		No improvement	3	37,5	8,5, 75,5

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.2.2.1 PedsQL parent-report score categories of overall change - Gender = Male
- percentage of patients with Improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=29)	Categories of change - literature-based [d]			
		Improvement	27	93,1	77,2, 99,2
		No improvement	2	6,9	0,8, 22,8
Physical Functioning	Overall (N=29)	Categories of change - literature-based [d]			
		Improvement	25	86,2	68,3, 96,1
		No improvement	4	13,8	3,9, 31,7
Emotional Functioning	Overall (N=29)	Categories of change - literature-based [d]			
		Improvement	24	82,8	64,2, 94,2
		No improvement	5	17,2	5,8, 35,8
Social Functioning	Overall (N=29)	Categories of change - literature-based [d]			
		Improvement	22	75,9	56,5, 89,7
		No improvement	7	24,1	10,3, 43,5
School Functioning	Overall (N=25)	Categories of change - literature-based [d]			
		Improvement	17	68,0	46,5, 85,1
		No improvement	8	32,0	14,9, 53,5

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.2.2.2 PedsQL parent-report score categories of overall change - Gender = Female
- percentage of patients with Improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=19)	Categories of change - literature-based [d]			
		Improvement	15	78,9	54,4, 93,9
		No improvement	4	21,1	6,1, 45,6
Physical Functioning	Overall (N=19)	Categories of change - literature-based [d]			
		Improvement	15	78,9	54,4, 93,9
		No improvement	4	21,1	6,1, 45,6
Emotional Functioning	Overall (N=19)	Categories of change - literature-based [d]			
		Improvement	16	84,2	60,4, 96,6
		No improvement	3	15,8	3,4, 39,6
Social Functioning	Overall (N=19)	Categories of change - literature-based [d]			
		Improvement	14	73,7	48,8, 90,9
		No improvement	5	26,3	9,1, 51,2
School Functioning	Overall (N=17)	Categories of change - literature-based [d]			
		Improvement	11	64,7	38,3, 85,8
		No improvement	6	35,3	14,2, 61,7

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.2.2.3 PedsQL parent-report score categories of overall change - PN status at enrollment = Progressive - percentage of patients with Improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=21)	Categories of change - literature-based [d]			
		Improvement	19	90,5	69,6, 98,8
		No improvement	2	9,5	1,2, 30,4
Physical Functioning	Overall (N=21)	Categories of change - literature-based [d]			
		Improvement	17	81,0	58,1, 94,6
		No improvement	4	19,0	5,4, 41,9
Emotional Functioning	Overall (N=21)	Categories of change - literature-based [d]			
		Improvement	18	85,7	63,7, 97,0
		No improvement	3	14,3	3,0, 36,3
Social Functioning	Overall (N=21)	Categories of change - literature-based [d]			
		Improvement	16	76,2	52,8, 91,8
		No improvement	5	23,8	8,2, 47,2
School Functioning	Overall (N=17)	Categories of change - literature-based [d]			
		Improvement	9	52,9	27,8, 77,0
		No improvement	8	47,1	23,0, 72,2

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.2.2.4 PedsQL parent-report score categories of overall change - PN status at enrollment = Non-progressive - percentage of patients with Improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=14)	Categories of change - literature-based [d]			
		Improvement	11	78,6	49,2, 95,3
		No improvement	3	21,4	4,7, 50,8
Physical Functioning	Overall (N=14)	Categories of change - literature-based [d]			
		Improvement	11	78,6	49,2, 95,3
		No improvement	3	21,4	4,7, 50,8
Emotional Functioning	Overall (N=14)	Categories of change - literature-based [d]			
		Improvement	10	71,4	41,9, 91,6
		No improvement	4	28,6	8,4, 58,1
Social Functioning	Overall (N=14)	Categories of change - literature-based [d]			
		Improvement	10	71,4	41,9, 91,6
		No improvement	4	28,6	8,4, 58,1
School Functioning	Overall (N=14)	Categories of change - literature-based [d]			
		Improvement	11	78,6	49,2, 95,3
		No improvement	3	21,4	4,7, 50,8

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.2.2.5 PedsQL parent-report score categories of overall change - PN status at enrollment = Unknown - percentage of patients with Improvement (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=13)	Categories of change - literature-based [d]			
		Improvement	12	92,3	64,0, 99,8
		No improvement	1	7,7	0,2, 36,0
Physical Functioning	Overall (N=13)	Categories of change - literature-based [d]			
		Improvement	12	92,3	64,0, 99,8
		No improvement	1	7,7	0,2, 36,0
Emotional Functioning	Overall (N=13)	Categories of change - literature-based [d]			
		Improvement	12	92,3	64,0, 99,8
		No improvement	1	7,7	0,2, 36,0
Social Functioning	Overall (N=13)	Categories of change - literature-based [d]			
		Improvement	10	76,9	46,2, 95,0
		No improvement	3	23,1	5,0, 53,8
School Functioning	Overall (N=11)	Categories of change - literature-based [d]			
		Improvement	8	72,7	39,0, 94,0
		No improvement	3	27,3	6,0, 61,0

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on literature (Varni et al, 2003): 4.36/6.66/8.94/8.36/9.12.

Table 2.12.2.3.1 PedsQL self-report score categories of change over time - Gender = Male
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=19)	Categories of change [d]			
		Improvement	3	15,8	3,4, 39,6
		No improvement	16	84,2	60,4, 96,6
	Pre-cycle 5 (N=19)	Categories of change [d]			
		Improvement	4	21,1	6,1, 45,6
		No improvement	15	78,9	54,4, 93,9
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	5	26,3	9,1, 51,2
		No improvement	14	73,7	48,8, 90,9
	Pre-cycle 13 (N=18)	Categories of change [d]			
		Improvement	4	22,2	6,4, 47,6
		No improvement	14	77,8	52,4, 93,6
	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	4	28,6	8,4, 58,1
		No improvement	10	71,4	41,9, 91,6
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Overall (N=19)	Categories of change [d]			
		Improvement	8	42,1	20,3, 66,5
		No improvement	11	57,9	33,5, 79,7

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.1 PedsQL self-report score categories of change over time - Gender = Male
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=19)	Categories of change [d]			
		Improvement	3	15,8	3,4, 39,6
		No improvement	16	84,2	60,4, 96,6
	Pre-cycle 5 (N=19)	Categories of change [d]			
		Improvement	4	21,1	6,1, 45,6
		No improvement	15	78,9	54,4, 93,9
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	2	10,5	1,3, 33,1
		No improvement	17	89,5	66,9, 98,7
	Pre-cycle 13 (N=18)	Categories of change [d]			
		Improvement	6	33,3	13,3, 59,0
		No improvement	12	66,7	41,0, 86,7
	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	4	28,6	8,4, 58,1
		No improvement	10	71,4	41,9, 91,6
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Overall (N=19)	Categories of change [d]			
		Improvement	8	42,1	20,3, 66,5
		No improvement	11	57,9	33,5, 79,7

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.1 PedsQL self-report score categories of change over time - Gender = Male
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=19)	Categories of change [d]			
		Improvement	7	36,8	16,3, 61,6
		No improvement	12	63,2	38,4, 83,7
	Pre-cycle 5 (N=19)	Categories of change [d]			
		Improvement	7	36,8	16,3, 61,6
		No improvement	12	63,2	38,4, 83,7
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	7	36,8	16,3, 61,6
		No improvement	12	63,2	38,4, 83,7
	Pre-cycle 13 (N=18)	Categories of change [d]			
		Improvement	8	44,4	21,5, 69,2
		No improvement	10	55,6	30,8, 78,5
	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	6	42,9	17,7, 71,1
		No improvement	8	57,1	28,9, 82,3
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6
	Overall (N=19)	Categories of change [d]			
		Improvement	12	63,2	38,4, 83,7
		No improvement	7	36,8	16,3, 61,6

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.1 PedsQL self-report score categories of change over time - Gender = Male
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=19)	Categories of change [d]			
		Improvement	7	36,8	16,3, 61,6
		No improvement	12	63,2	38,4, 83,7
	Pre-cycle 5 (N=19)	Categories of change [d]			
		Improvement	7	36,8	16,3, 61,6
		No improvement	12	63,2	38,4, 83,7
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	4	21,1	6,1, 45,6
		No improvement	15	78,9	54,4, 93,9
	Pre-cycle 13 (N=18)	Categories of change [d]			
		Improvement	5	27,8	9,7, 53,5
		No improvement	13	72,2	46,5, 90,3
	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	5	35,7	12,8, 64,9
		No improvement	9	64,3	35,1, 87,2
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60,2
		No improvement	4	100	39,8, 100
	Overall (N=19)	Categories of change [d]			
		Improvement	10	52,6	28,9, 75,6
		No improvement	9	47,4	24,4, 71,1

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.1 PedsQL self-report score categories of change over time - Gender = Male
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=15)	Categories of change [d]			
		Improvement	5	33,3	11,8, 61,6
		No improvement	10	66,7	38,4, 88,2
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 9 (N=13)	Categories of change [d]			
		Improvement	4	30,8	9,1, 61,4
		No improvement	9	69,2	38,6, 90,9
	Pre-cycle 13 (N=13)	Categories of change [d]			
		Improvement	3	23,1	5,0, 53,8
		No improvement	10	76,9	46,2, 95,0
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22,2	2,8, 60,0
		No improvement	7	77,8	40,0, 97,2
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
	Overall (N=16)	Categories of change [d]			
		Improvement	10	62,5	35,4, 84,8
		No improvement	6	37,5	15,2, 64,6

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.2 PedsQL self-report score categories of change over time - Gender = Female
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=12)	Categories of change [d]			
		Improvement	3	25,0	5,5, 57,2
		No improvement	9	75,0	42,8, 94,5
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	2	16,7	2,1, 48,4
		No improvement	10	83,3	51,6, 97,9
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22,2	2,8, 60,0
		No improvement	7	77,8	40,0, 97,2
	Overall (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.2 PedsQL self-report score categories of change over time - Gender = Female
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	2	16,7	2,1, 48,4
		No improvement	10	83,3	51,6, 97,9
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	3	33,3	7,5, 70,1
		No improvement	6	66,7	29,9, 92,5
	Overall (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.2 PedsQL self-report score categories of change over time - Gender = Female
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	3	25,0	5,5, 57,2
		No improvement	9	75,0	42,8, 94,5
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	3	25,0	5,5, 57,2
		No improvement	9	75,0	42,8, 94,5
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	1	11,1	0,3, 48,2
		No improvement	8	88,9	51,8, 99,7
	Overall (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.2 PedsQL self-report score categories of change over time - Gender = Female
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	2	16,7	2,1, 48,4
		No improvement	10	83,3	51,6, 97,9
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22,2	2,8, 60,0
		No improvement	7	77,8	40,0, 97,2
	Overall (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.2 PedsQL self-report score categories of change over time - Gender = Female
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=5)	Categories of change [d]			
		Improvement	2	40,0	5,3, 85,3
		No improvement	3	60,0	14,7, 94,7
	Pre-cycle 5 (N=7)	Categories of change [d]			
		Improvement	2	28,6	3,7, 71,0
		No improvement	5	71,4	29,0, 96,3
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Overall (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.3 PedsQL self-report score categories of change over time - PN status at enrollment = Progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
	Overall (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.3 PedsQL self-report score categories of change over time - PN status at enrollment = Progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	2	18,2	2,3, 51,8
		No improvement	9	81,8	48,2, 97,7
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	1	9,1	0,2, 41,3
		No improvement	10	90,9	58,7, 99,8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8
	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	2	33,3	4,3, 77,7
		No improvement	4	66,7	22,3, 95,7
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
	Overall (N=11)	Categories of change [d]			
		Improvement	5	45,5	16,7, 76,6
		No improvement	6	54,5	23,4, 83,3

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.3 PedsQL self-report score categories of change over time - PN status at enrollment = Progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	5	45,5	16,7, 76,6
		No improvement	6	54,5	23,4, 83,3
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	1	9,1	0,2, 41,3
		No improvement	10	90,9	58,7, 99,8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	2	66,7	9,4, 99,2
		No improvement	1	33,3	0,8, 90,6
	Overall (N=11)	Categories of change [d]			
		Improvement	6	54,5	23,4, 83,3
		No improvement	5	45,5	16,7, 76,6

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.3 PedsQL self-report score categories of change over time - PN status at enrollment = Progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45,9
		No improvement	6	100	54,1, 100
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Overall (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.3 PedsQL self-report score categories of change over time - PN status at enrollment = Progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=8)	Categories of change [d]			
		Improvement	3	37,5	8,5, 75,5
		No improvement	5	62,5	24,5, 91,5
	Pre-cycle 5 (N=7)	Categories of change [d]			
		Improvement	2	28,6	3,7, 71,0
		No improvement	5	71,4	29,0, 96,3
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	3	37,5	8,5, 75,5
		No improvement	5	62,5	24,5, 91,5
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	2	33,3	4,3, 77,7
		No improvement	4	66,7	22,3, 95,7
	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=9)	Categories of change [d]			
		Improvement	4	44,4	13,7, 78,8
		No improvement	5	55,6	21,2, 86,3

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.4 PedsQL self-report score categories of change over time - PN status at enrollment = Non-progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	2	22,2	2,8, 60,0
		No improvement	7	77,8	40,0, 97,2
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	3	33,3	7,5, 70,1
		No improvement	6	66,7	29,9, 92,5
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.4 PedsQL self-report score categories of change over time - PN status at enrollment = Non-progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33,3	7,5, 70,1
		No improvement	6	66,7	29,9, 92,5
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22,2	2,8, 60,0
		No improvement	7	77,8	40,0, 97,2
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.4 PedsQL self-report score categories of change over time - PN status at enrollment = Non-progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	6	60,0	26,2, 87,8
		No improvement	4	40,0	12,2, 73,8
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	7	70,0	34,8, 93,3
		No improvement	3	30,0	6,7, 65,2
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	6	66,7	29,9, 92,5
		No improvement	3	33,3	7,5, 70,1
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	4	44,4	13,7, 78,8
		No improvement	5	55,6	21,2, 86,3
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=10)	Categories of change [d]			
		Improvement	8	80,0	44,4, 97,5
		No improvement	2	20,0	2,5, 55,6

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.4 PedsQL self-report score categories of change over time - PN status at enrollment = Non-progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33,3	7,5, 70,1
		No improvement	6	66,7	29,9, 92,5
	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	4	44,4	13,7, 78,8
		No improvement	5	55,6	21,2, 86,3
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=10)	Categories of change [d]			
		Improvement	6	60,0	26,2, 87,8
		No improvement	4	40,0	12,2, 73,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.4 PedsQL self-report score categories of change over time - PN status at enrollment = Non-progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=8)	Categories of change [d]			
		Improvement	1	12,5	0,3, 52,7
		No improvement	7	87,5	47,3, 99,7
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	2	33,3	4,3, 77,7
		No improvement	4	66,7	22,3, 95,7
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	3	37,5	8,5, 75,5
		No improvement	5	62,5	24,5, 91,5
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	2	22,2	2,8, 60,0
		No improvement	7	77,8	40,0, 97,2
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=10)	Categories of change [d]			
		Improvement	6	60,0	26,2, 87,8
		No improvement	4	40,0	12,2, 73,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.5 PedsQL self-report score categories of change over time - PN status at enrollment = Unknown - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	1	10,0	0,3, 44,5
		No improvement	9	90,0	55,5, 99,7
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8
	Overall (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.5 PedsQL self-report score categories of change over time - PN status at enrollment = Unknown - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	3	37,5	8,5, 75,5
		No improvement	5	62,5	24,5, 91,5
	Overall (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.5 PedsQL self-report score categories of change over time - PN status at enrollment = Unknown - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30,8
		No improvement	10	100	69,2, 100
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8
	Overall (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.5 PedsQL self-report score categories of change over time - PN status at enrollment = Unknown - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=9)	Categories of change [d]			
		Improvement	4	44,4	13,7, 78,8
		No improvement	5	55,6	21,2, 86,3
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	2	20,0	2,5, 55,6
		No improvement	8	80,0	44,4, 97,5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	4	40,0	12,2, 73,8
		No improvement	6	60,0	26,2, 87,8
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	3	37,5	8,5, 75,5
		No improvement	5	62,5	24,5, 91,5
	Overall (N=10)	Categories of change [d]			
		Improvement	5	50,0	18,7, 81,3
		No improvement	5	50,0	18,7, 81,3

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.3.5 PedsQL self-report score categories of change over time - PN status at enrollment = Unknown - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6
	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	1	25,0	0,6, 80,6
		No improvement	3	75,0	19,4, 99,4
	Pre-cycle 9 (N=7)	Categories of change [d]			
		Improvement	2	28,6	3,7, 71,0
		No improvement	5	71,4	29,0, 96,3
	Pre-cycle 13 (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8
	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Overall (N=8)	Categories of change [d]			
		Improvement	4	50,0	15,7, 84,3
		No improvement	4	50,0	15,7, 84,3

[a] Children, ages 8-18 years at enrolment, completed self-report measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.1 PedsQL parent-report score categories of change over time - Gender = Male
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=29)	Categories of change [d]			
		Improvement	11	37,9	20,7, 57,7
		No improvement	18	62,1	42,3, 79,3
	Pre-cycle 5 (N=29)	Categories of change [d]			
		Improvement	8	27,6	12,7, 47,2
		No improvement	21	72,4	52,8, 87,3
	Pre-cycle 9 (N=29)	Categories of change [d]			
		Improvement	12	41,4	23,5, 61,1
		No improvement	17	58,6	38,9, 76,5
	Pre-cycle 13 (N=28)	Categories of change [d]			
		Improvement	11	39,3	21,5, 59,4
		No improvement	17	60,7	40,6, 78,5
	Pre-cycle 25 (N=20)	Categories of change [d]			
		Improvement	9	45,0	23,1, 68,5
		No improvement	11	55,0	31,5, 76,9
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6
	Overall (N=29)	Categories of change [d]			
		Improvement	22	75,9	56,5, 89,7
		No improvement	7	24,1	10,3, 43,5

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.1 PedsQL parent-report score categories of change over time - Gender = Male
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=29)	Categories of change [d]			
		Improvement	10	34,5	17,9, 54,3
		No improvement	19	65,5	45,7, 82,1
	Pre-cycle 5 (N=29)	Categories of change [d]			
		Improvement	9	31,0	15,3, 50,8
		No improvement	20	69,0	49,2, 84,7
	Pre-cycle 9 (N=29)	Categories of change [d]			
		Improvement	13	44,8	26,4, 64,3
		No improvement	16	55,2	35,7, 73,6
	Pre-cycle 13 (N=28)	Categories of change [d]			
		Improvement	10	35,7	18,6, 55,9
		No improvement	18	64,3	44,1, 81,4
	Pre-cycle 25 (N=20)	Categories of change [d]			
		Improvement	10	50,0	27,2, 72,8
		No improvement	10	50,0	27,2, 72,8
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6
	Overall (N=29)	Categories of change [d]			
		Improvement	21	72,4	52,8, 87,3
		No improvement	8	27,6	12,7, 47,2

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.1 PedsQL parent-report score categories of change over time - Gender = Male
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=29)	Categories of change [d]			
		Improvement	14	48,3	29,4, 67,5
		No improvement	15	51,7	32,5, 70,6
	Pre-cycle 5 (N=29)	Categories of change [d]			
		Improvement	15	51,7	32,5, 70,6
		No improvement	14	48,3	29,4, 67,5
	Pre-cycle 9 (N=29)	Categories of change [d]			
		Improvement	16	55,2	35,7, 73,6
		No improvement	13	44,8	26,4, 64,3
	Pre-cycle 13 (N=28)	Categories of change [d]			
		Improvement	15	53,6	33,9, 72,5
		No improvement	13	46,4	27,5, 66,1
	Pre-cycle 25 (N=20)	Categories of change [d]			
		Improvement	11	55,0	31,5, 76,9
		No improvement	9	45,0	23,1, 68,5
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6
	Overall (N=29)	Categories of change [d]			
		Improvement	23	79,3	60,3, 92,0
		No improvement	6	20,7	8,0, 39,7

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.1 PedsQL parent-report score categories of change over time - Gender = Male
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=29)	Categories of change [d]			
		Improvement	14	48,3	29,4, 67,5
		No improvement	15	51,7	32,5, 70,6
	Pre-cycle 5 (N=29)	Categories of change [d]			
		Improvement	16	55,2	35,7, 73,6
		No improvement	13	44,8	26,4, 64,3
	Pre-cycle 9 (N=29)	Categories of change [d]			
		Improvement	14	48,3	29,4, 67,5
		No improvement	15	51,7	32,5, 70,6
	Pre-cycle 13 (N=28)	Categories of change [d]			
		Improvement	10	35,7	18,6, 55,9
		No improvement	18	64,3	44,1, 81,4
	Pre-cycle 25 (N=20)	Categories of change [d]			
		Improvement	9	45,0	23,1, 68,5
		No improvement	11	55,0	31,5, 76,9
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6
	Overall (N=29)	Categories of change [d]			
		Improvement	21	72,4	52,8, 87,3
		No improvement	8	27,6	12,7, 47,2

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.1 PedsQL parent-report score categories of change over time - Gender = Male
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=23)	Categories of change [d]			
		Improvement	6	26,1	10,2, 48,4
		No improvement	17	73,9	51,6, 89,8
	Pre-cycle 5 (N=16)	Categories of change [d]			
		Improvement	6	37,5	15,2, 64,6
		No improvement	10	62,5	35,4, 84,8
	Pre-cycle 9 (N=21)	Categories of change [d]			
		Improvement	8	38,1	18,1, 61,6
		No improvement	13	61,9	38,4, 81,9
	Pre-cycle 13 (N=22)	Categories of change [d]			
		Improvement	6	27,3	10,7, 50,2
		No improvement	16	72,7	49,8, 89,3
	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	5	35,7	12,8, 64,9
		No improvement	9	64,3	35,1, 87,2
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=25)	Categories of change [d]			
		Improvement	16	64,0	42,5, 82,0
		No improvement	9	36,0	18,0, 57,5

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.2 PedsQL parent-report score categories of change over time - Gender = Female
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=18)	Categories of change [d]			
		Improvement	6	33,3	13,3, 59,0
		No improvement	12	66,7	41,0, 86,7
	Pre-cycle 5 (N=18)	Categories of change [d]			
		Improvement	5	27,8	9,7, 53,5
		No improvement	13	72,2	46,5, 90,3
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	6	31,6	12,6, 56,6
		No improvement	13	68,4	43,4, 87,4
	Pre-cycle 13 (N=17)	Categories of change [d]			
		Improvement	10	58,8	32,9, 81,6
		No improvement	7	41,2	18,4, 67,1
	Pre-cycle 25 (N=15)	Categories of change [d]			
		Improvement	9	60,0	32,3, 83,7
		No improvement	6	40,0	16,3, 67,7
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=19)	Categories of change [d]			
		Improvement	12	63,2	38,4, 83,7
		No improvement	7	36,8	16,3, 61,6

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.2 PedsQL parent-report score categories of change over time - Gender = Female
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=18)	Categories of change [d]			
		Improvement	5	27,8	9,7, 53,5
		No improvement	13	72,2	46,5, 90,3
	Pre-cycle 5 (N=18)	Categories of change [d]			
		Improvement	4	22,2	6,4, 47,6
		No improvement	14	77,8	52,4, 93,6
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	7	36,8	16,3, 61,6
		No improvement	12	63,2	38,4, 83,7
	Pre-cycle 13 (N=17)	Categories of change [d]			
		Improvement	11	64,7	38,3, 85,8
		No improvement	6	35,3	14,2, 61,7
	Pre-cycle 25 (N=15)	Categories of change [d]			
		Improvement	10	66,7	38,4, 88,2
		No improvement	5	33,3	11,8, 61,6
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=19)	Categories of change [d]			
		Improvement	14	73,7	48,8, 90,9
		No improvement	5	26,3	9,1, 51,2

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.2 PedsQL parent-report score categories of change over time - Gender = Female
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=19)	Categories of change [d]			
		Improvement	8	42,1	20,3, 66,5
		No improvement	11	57,9	33,5, 79,7
	Pre-cycle 5 (N=18)	Categories of change [d]			
		Improvement	8	44,4	21,5, 69,2
		No improvement	10	55,6	30,8, 78,5
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	9	47,4	24,4, 71,1
		No improvement	10	52,6	28,9, 75,6
	Pre-cycle 13 (N=17)	Categories of change [d]			
		Improvement	11	64,7	38,3, 85,8
		No improvement	6	35,3	14,2, 61,7
	Pre-cycle 25 (N=15)	Categories of change [d]			
		Improvement	8	53,3	26,6, 78,7
		No improvement	7	46,7	21,3, 73,4
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=19)	Categories of change [d]			
		Improvement	14	73,7	48,8, 90,9
		No improvement	5	26,3	9,1, 51,2

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.2 PedsQL parent-report score categories of change over time - Gender = Female
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=18)	Categories of change [d]			
		Improvement	8	44,4	21,5, 69,2
		No improvement	10	55,6	30,8, 78,5
	Pre-cycle 5 (N=18)	Categories of change [d]			
		Improvement	6	33,3	13,3, 59,0
		No improvement	12	66,7	41,0, 86,7
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	5	26,3	9,1, 51,2
		No improvement	14	73,7	48,8, 90,9
	Pre-cycle 13 (N=17)	Categories of change [d]			
		Improvement	7	41,2	18,4, 67,1
		No improvement	10	58,8	32,9, 81,6
	Pre-cycle 25 (N=15)	Categories of change [d]			
		Improvement	4	26,7	7,8, 55,1
		No improvement	11	73,3	44,9, 92,2
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=19)	Categories of change [d]			
		Improvement	10	52,6	28,9, 75,6
		No improvement	9	47,4	24,4, 71,1

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.2 PedsQL parent-report score categories of change over time - Gender = Female
- percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	3	27,3	6,0, 61,0
		No improvement	8	72,7	39,0, 94,0
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	5	45,5	16,7, 76,6
		No improvement	6	54,5	23,4, 83,3
	Pre-cycle 9 (N=16)	Categories of change [d]			
		Improvement	6	37,5	15,2, 64,6
		No improvement	10	62,5	35,4, 84,8
	Pre-cycle 13 (N=15)	Categories of change [d]			
		Improvement	5	33,3	11,8, 61,6
		No improvement	10	66,7	38,4, 88,2
	Pre-cycle 25 (N=12)	Categories of change [d]			
		Improvement	2	16,7	2,1, 48,4
		No improvement	10	83,3	51,6, 97,9
	Overall (N=17)	Categories of change [d]			
		Improvement	10	58,8	32,9, 81,6
		No improvement	7	41,2	18,4, 67,1

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.3 PedsQL parent-report score categories of change over time - PN status at enrollment = Progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=21)	Categories of change [d]			
		Improvement	9	42,9	21,8, 66,0
		No improvement	12	57,1	34,0, 78,2
	Pre-cycle 5 (N=20)	Categories of change [d]			
		Improvement	8	40,0	19,1, 63,9
		No improvement	12	60,0	36,1, 80,9
	Pre-cycle 9 (N=21)	Categories of change [d]			
		Improvement	10	47,6	25,7, 70,2
		No improvement	11	52,4	29,8, 74,3
	Pre-cycle 13 (N=20)	Categories of change [d]			
		Improvement	10	50,0	27,2, 72,8
		No improvement	10	50,0	27,2, 72,8
	Pre-cycle 25 (N=13)	Categories of change [d]			
		Improvement	7	53,8	25,1, 80,8
		No improvement	6	46,2	19,2, 74,9
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6
	Overall (N=21)	Categories of change [d]			
		Improvement	16	76,2	52,8, 91,8
		No improvement	5	23,8	8,2, 47,2

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.3 PedsQL parent-report score categories of change over time - PN status at enrollment = Progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=21)	Categories of change [d]			
		Improvement	9	42,9	21,8, 66,0
		No improvement	12	57,1	34,0, 78,2
	Pre-cycle 5 (N=20)	Categories of change [d]			
		Improvement	7	35,0	15,4, 59,2
		No improvement	13	65,0	40,8, 84,6
	Pre-cycle 9 (N=21)	Categories of change [d]			
		Improvement	8	38,1	18,1, 61,6
		No improvement	13	61,9	38,4, 81,9
	Pre-cycle 13 (N=20)	Categories of change [d]			
		Improvement	9	45,0	23,1, 68,5
		No improvement	11	55,0	31,5, 76,9
	Pre-cycle 25 (N=13)	Categories of change [d]			
		Improvement	8	61,5	31,6, 86,1
		No improvement	5	38,5	13,9, 68,4
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6
	Overall (N=21)	Categories of change [d]			
		Improvement	15	71,4	47,8, 88,7
		No improvement	6	28,6	11,3, 52,2

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.3 PedsQL parent-report score categories of change over time - PN status at enrollment = Progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=21)	Categories of change [d]			
		Improvement	12	57,1	34,0, 78,2
		No improvement	9	42,9	21,8, 66,0
	Pre-cycle 5 (N=20)	Categories of change [d]			
		Improvement	12	60,0	36,1, 80,9
		No improvement	8	40,0	19,1, 63,9
	Pre-cycle 9 (N=21)	Categories of change [d]			
		Improvement	14	66,7	43,0, 85,4
		No improvement	7	33,3	14,6, 57,0
	Pre-cycle 13 (N=20)	Categories of change [d]			
		Improvement	11	55,0	31,5, 76,9
		No improvement	9	45,0	23,1, 68,5
	Pre-cycle 25 (N=13)	Categories of change [d]			
		Improvement	8	61,5	31,6, 86,1
		No improvement	5	38,5	13,9, 68,4
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	3	75,0	19,4, 99,4
		No improvement	1	25,0	0,6, 80,6
	Overall (N=21)	Categories of change [d]			
		Improvement	18	85,7	63,7, 97,0
		No improvement	3	14,3	3,0, 36,3

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.3 PedsQL parent-report score categories of change over time - PN status at enrollment = Progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=21)	Categories of change [d]			
		Improvement	12	57,1	34,0, 78,2
		No improvement	9	42,9	21,8, 66,0
	Pre-cycle 5 (N=20)	Categories of change [d]			
		Improvement	12	60,0	36,1, 80,9
		No improvement	8	40,0	19,1, 63,9
	Pre-cycle 9 (N=21)	Categories of change [d]			
		Improvement	6	28,6	11,3, 52,2
		No improvement	15	71,4	47,8, 88,7
	Pre-cycle 13 (N=20)	Categories of change [d]			
		Improvement	9	45,0	23,1, 68,5
		No improvement	11	55,0	31,5, 76,9
	Pre-cycle 25 (N=13)	Categories of change [d]			
		Improvement	5	38,5	13,9, 68,4
		No improvement	8	61,5	31,6, 86,1
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	4	100	39,8, 100
		No improvement	0	0	0, 60,2
	Overall (N=21)	Categories of change [d]			
		Improvement	16	76,2	52,8, 91,8
		No improvement	5	23,8	8,2, 47,2

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.3 PedsQL parent-report score categories of change over time - PN status at enrollment = Progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=15)	Categories of change [d]			
		Improvement	3	20,0	4,3, 48,1
		No improvement	12	80,0	51,9, 95,7
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 9 (N=15)	Categories of change [d]			
		Improvement	7	46,7	21,3, 73,4
		No improvement	8	53,3	26,6, 78,7
	Pre-cycle 13 (N=14)	Categories of change [d]			
		Improvement	3	21,4	4,7, 50,8
		No improvement	11	78,6	49,2, 95,3
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	1	14,3	0,4, 57,9
		No improvement	6	85,7	42,1, 99,6
	Overall (N=17)	Categories of change [d]			
		Improvement	8	47,1	23,0, 72,2
		No improvement	9	52,9	27,8, 77,0

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.4 PedsQL parent-report score categories of change over time - PN status at enrollment = Non-progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=14)	Categories of change [d]			
		Improvement	4	28,6	8,4, 58,1
		No improvement	10	71,4	41,9, 91,6
	Pre-cycle 5 (N=14)	Categories of change [d]			
		Improvement	3	21,4	4,7, 50,8
		No improvement	11	78,6	49,2, 95,3
	Pre-cycle 9 (N=14)	Categories of change [d]			
		Improvement	4	28,6	8,4, 58,1
		No improvement	10	71,4	41,9, 91,6
	Pre-cycle 13 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 25 (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=14)	Categories of change [d]			
		Improvement	8	57,1	28,9, 82,3
		No improvement	6	42,9	17,7, 71,1

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.4 PedsQL parent-report score categories of change over time - PN status at enrollment = Non-progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=14)	Categories of change [d]			
		Improvement	3	21,4	4,7, 50,8
		No improvement	11	78,6	49,2, 95,3
	Pre-cycle 5 (N=14)	Categories of change [d]			
		Improvement	4	28,6	8,4, 58,1
		No improvement	10	71,4	41,9, 91,6
	Pre-cycle 9 (N=14)	Categories of change [d]			
		Improvement	7	50,0	23,0, 77,0
		No improvement	7	50,0	23,0, 77,0
	Pre-cycle 13 (N=12)	Categories of change [d]			
		Improvement	6	50,0	21,1, 78,9
		No improvement	6	50,0	21,1, 78,9
	Pre-cycle 25 (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=14)	Categories of change [d]			
		Improvement	10	71,4	41,9, 91,6
		No improvement	4	28,6	8,4, 58,1

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.4 PedsQL parent-report score categories of change over time - PN status at enrollment = Non-progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=14)	Categories of change [d]			
		Improvement	5	35,7	12,8, 64,9
		No improvement	9	64,3	35,1, 87,2
	Pre-cycle 5 (N=14)	Categories of change [d]			
		Improvement	4	28,6	8,4, 58,1
		No improvement	10	71,4	41,9, 91,6
	Pre-cycle 9 (N=14)	Categories of change [d]			
		Improvement	5	35,7	12,8, 64,9
		No improvement	9	64,3	35,1, 87,2
	Pre-cycle 13 (N=12)	Categories of change [d]			
		Improvement	7	58,3	27,7, 84,8
		No improvement	5	41,7	15,2, 72,3
	Pre-cycle 25 (N=12)	Categories of change [d]			
		Improvement	6	50,0	21,1, 78,9
		No improvement	6	50,0	21,1, 78,9
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=14)	Categories of change [d]			
		Improvement	8	57,1	28,9, 82,3
		No improvement	6	42,9	17,7, 71,1

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.4 PedsQL parent-report score categories of change over time - PN status at enrollment = Non-progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=14)	Categories of change [d]			
		Improvement	4	28,6	8,4, 58,1
		No improvement	10	71,4	41,9, 91,6
	Pre-cycle 5 (N=14)	Categories of change [d]			
		Improvement	4	28,6	8,4, 58,1
		No improvement	10	71,4	41,9, 91,6
	Pre-cycle 9 (N=14)	Categories of change [d]			
		Improvement	8	57,1	28,9, 82,3
		No improvement	6	42,9	17,7, 71,1
	Pre-cycle 13 (N=12)	Categories of change [d]			
		Improvement	3	25,0	5,5, 57,2
		No improvement	9	75,0	42,8, 94,5
	Pre-cycle 25 (N=12)	Categories of change [d]			
		Improvement	5	41,7	15,2, 72,3
		No improvement	7	58,3	27,7, 84,8
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=14)	Categories of change [d]			
		Improvement	8	57,1	28,9, 82,3
		No improvement	6	42,9	17,7, 71,1

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.4 PedsQL parent-report score categories of change over time - PN status at enrollment = Non-progressive - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=12)	Categories of change [d]			
		Improvement	3	25,0	5,5, 57,2
		No improvement	9	75,0	42,8, 94,5
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	5	55,6	21,2, 86,3
		No improvement	4	44,4	13,7, 78,8
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 13 (N=12)	Categories of change [d]			
		Improvement	3	25,0	5,5, 57,2
		No improvement	9	75,0	42,8, 94,5
	Pre-cycle 25 (N=11)	Categories of change [d]			
		Improvement	4	36,4	10,9, 69,2
		No improvement	7	63,6	30,8, 89,1
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=14)	Categories of change [d]			
		Improvement	10	71,4	41,9, 91,6
		No improvement	4	28,6	8,4, 58,1

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.5 PedsQL parent-report score categories of change over time - PN status at enrollment = Unknown - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 5 (N=13)	Categories of change [d]			
		Improvement	2	15,4	1,9, 45,4
		No improvement	11	84,6	54,6, 98,1
	Pre-cycle 9 (N=13)	Categories of change [d]			
		Improvement	4	30,8	9,1, 61,4
		No improvement	9	69,2	38,6, 90,9
	Pre-cycle 13 (N=13)	Categories of change [d]			
		Improvement	7	53,8	25,1, 80,8
		No improvement	6	46,2	19,2, 74,9
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	6	60,0	26,2, 87,8
		No improvement	4	40,0	12,2, 73,8
	Overall (N=13)	Categories of change [d]			
		Improvement	10	76,9	46,2, 95,0
		No improvement	3	23,1	5,0, 53,8

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.5 PedsQL parent-report score categories of change over time - PN status at enrollment = Unknown - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=12)	Categories of change [d]			
		Improvement	3	25,0	5,5, 57,2
		No improvement	9	75,0	42,8, 94,5
	Pre-cycle 5 (N=13)	Categories of change [d]			
		Improvement	2	15,4	1,9, 45,4
		No improvement	11	84,6	54,6, 98,1
	Pre-cycle 9 (N=13)	Categories of change [d]			
		Improvement	5	38,5	13,9, 68,4
		No improvement	8	61,5	31,6, 86,1
	Pre-cycle 13 (N=13)	Categories of change [d]			
		Improvement	6	46,2	19,2, 74,9
		No improvement	7	53,8	25,1, 80,8
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	7	70,0	34,8, 93,3
		No improvement	3	30,0	6,7, 65,2
	Overall (N=13)	Categories of change [d]			
		Improvement	10	76,9	46,2, 95,0
		No improvement	3	23,1	5,0, 53,8

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.5 PedsQL parent-report score categories of change over time - PN status at enrollment = Unknown - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=13)	Categories of change [d]			
		Improvement	5	38,5	13,9, 68,4
		No improvement	8	61,5	31,6, 86,1
	Pre-cycle 5 (N=13)	Categories of change [d]			
		Improvement	7	53,8	25,1, 80,8
		No improvement	6	46,2	19,2, 74,9
	Pre-cycle 9 (N=13)	Categories of change [d]			
		Improvement	6	46,2	19,2, 74,9
		No improvement	7	53,8	25,1, 80,8
	Pre-cycle 13 (N=13)	Categories of change [d]			
		Improvement	8	61,5	31,6, 86,1
		No improvement	5	38,5	13,9, 68,4
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	5	50,0	18,7, 81,3
		No improvement	5	50,0	18,7, 81,3
	Overall (N=13)	Categories of change [d]			
		Improvement	11	84,6	54,6, 98,1
		No improvement	2	15,4	1,9, 45,4

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.5 PedsQL parent-report score categories of change over time - PN status at enrollment = Unknown - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=12)	Categories of change [d]			
		Improvement	6	50,0	21,1, 78,9
		No improvement	6	50,0	21,1, 78,9
	Pre-cycle 5 (N=13)	Categories of change [d]			
		Improvement	6	46,2	19,2, 74,9
		No improvement	7	53,8	25,1, 80,8
	Pre-cycle 9 (N=13)	Categories of change [d]			
		Improvement	5	38,5	13,9, 68,4
		No improvement	8	61,5	31,6, 86,1
	Pre-cycle 13 (N=13)	Categories of change [d]			
		Improvement	5	38,5	13,9, 68,4
		No improvement	8	61,5	31,6, 86,1
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Overall (N=13)	Categories of change [d]			
		Improvement	7	53,8	25,1, 80,8
		No improvement	6	46,2	19,2, 74,9

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.2.4.5 PedsQL parent-report score categories of change over time - PN status at enrollment = Unknown - percentage of patients with Improvement by >= 15 pts (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]			
			Transformed Scores		
Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=7)	Categories of change [d]			
		Improvement	3	42,9	9,9, 81,6
		No improvement	4	57,1	18,4, 90,1
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	2	33,3	4,3, 77,7
		No improvement	4	66,7	22,3, 95,7
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30,0	6,7, 65,2
		No improvement	7	70,0	34,8, 93,3
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	5	45,5	16,7, 76,6
		No improvement	6	54,5	23,4, 83,3
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	2	25,0	3,2, 65,1
		No improvement	6	75,0	34,9, 96,8
	Overall (N=11)	Categories of change [d]			
		Improvement	8	72,7	39,0, 94,0
		No improvement	3	27,3	6,0, 61,0

[a] Parents or legal guardians of children 2-18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Percentages are based on the number of patients with a non-missing score at each analysis visit.
[c] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Categories (Total/Physical/Emotional/Social/School functioning) are based on MID=15 pts.

Table 2.12.3.1.1 PedsQL self-report scores over time and change from baseline over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=20)	75,49	17,833	81,13	48,6	95,7	4,8							
	Pre-cycle 3 (n=19)	79,35	14,826	84,78	48,9	97,8	9,5	19	4,64	12,807	5,43	-20,1	33,7	9,5
	Pre-cycle 5 (n=19)	80,10	14,968	84,78	42,4	97,8	9,5	19	5,38	16,472	5,37	-43,5	37,0	9,5
	Pre-cycle 9 (n=19)	79,95	14,400	84,72	46,7	96,7	9,5	19	5,24	15,825	3,26	-19,9	42,4	9,5
	Pre-cycle 13 (n=18)	82,93	17,832	89,67	45,7	100,0	14,3	18	7,08	15,297	8,15	-24,2	33,7	14,3
	Pre-cycle 25 (n=14)	90,89	9,285	94,57	71,7	100,0	33,3	14	9,85	14,452	7,19	-8,7	42,4	33,3
	Pre-cycle 37 (n=4)	88,95	10,242	92,57	73,9	96,7	81,0	4	9,95	10,598	6,70	1,1	25,3	81,0
Raw Total Score	Baseline (n=20)	3,02	0,713	3,25	1,9	3,8	4,8							
	Pre-cycle 3 (n=19)	3,17	0,593	3,39	2,0	3,9	9,5	19	0,19	0,512	0,22	-0,8	1,3	9,5
	Pre-cycle 5 (n=19)	3,20	0,599	3,39	1,7	3,9	9,5	19	0,22	0,659	0,21	-1,7	1,5	9,5
	Pre-cycle 9 (n=19)	3,20	0,576	3,39	1,9	3,9	9,5	19	0,21	0,633	0,13	-0,8	1,7	9,5
	Pre-cycle 13 (n=18)	3,32	0,713	3,59	1,8	4,0	14,3	18	0,28	0,612	0,33	-1,0	1,3	14,3
	Pre-cycle 25 (n=14)	3,64	0,371	3,78	2,9	4,0	33,3	14	0,39	0,578	0,29	-0,3	1,7	33,3
	Pre-cycle 37 (n=4)	3,56	0,410	3,70	3,0	3,9	81,0	4	0,40	0,424	0,27	0,0	1,0	81,0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.1 PedsQL self-report scores over time and change from baseline over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]											
		Absolute values						Change from baseline					
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Physical functioning	Baseline (n=20)	77,14	24,389	87,50	15,6	100,0	4,8							
	Pre-cycle 3 (n=19)	76,93	22,559	81,25	12,5	100,0	9,5	19	0,49	12,204	3,13	-25,0	18,8	9,5
	Pre-cycle 5 (n=19)	79,39	22,870	87,50	21,9	100,0	9,5	19	2,96	19,207	6,25	-56,3	34,4	9,5
	Pre-cycle 9 (n=19)	78,62	19,102	84,38	28,1	100,0	9,5	19	2,19	21,053	3,13	-37,5	65,6	9,5
	Pre-cycle 13 (n=18)	85,42	21,411	92,19	21,9	100,0	14,3	18	7,86	23,064	6,25	-46,9	68,8	14,3
	Pre-cycle 25 (n=14)	91,07	11,554	96,88	65,6	100,0	33,3	14	8,71	23,615	4,69	-31,3	59,4	33,3
	Pre-cycle 37 (n=4)	91,41	6,929	90,63	84,4	100,0	81,0	4	10,94	25,323	4,69	-12,5	46,9	81,0
Raw Physical functioning	Baseline (n=20)	3,09	0,976	3,50	0,6	4,0	4,8							
	Pre-cycle 3 (n=19)	3,08	0,902	3,25	0,5	4,0	9,5	19	0,02	0,488	0,13	-1,0	0,8	9,5
	Pre-cycle 5 (n=19)	3,18	0,915	3,50	0,9	4,0	9,5	19	0,12	0,768	0,25	-2,3	1,4	9,5
	Pre-cycle 9 (n=19)	3,14	0,764	3,38	1,1	4,0	9,5	19	0,09	0,842	0,13	-1,5	2,6	9,5
	Pre-cycle 13 (n=18)	3,42	0,856	3,69	0,9	4,0	14,3	18	0,31	0,923	0,25	-1,9	2,8	14,3
	Pre-cycle 25 (n=14)	3,64	0,462	3,88	2,6	4,0	33,3	14	0,35	0,945	0,19	-1,3	2,4	33,3
	Pre-cycle 37 (n=4)	3,66	0,277	3,63	3,4	4,0	81,0	4	0,44	1,013	0,19	-0,5	1,9	81,0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.1 PedsQL self-report scores over time and change from baseline over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Emotional functioning	Baseline (n=20)	78,50	18,289	85,00	45,0	100,0	4,8							
	Pre-cycle 3 (n=19)	88,42	11,553	95,00	65,0	100,0	9,5	19	11,05	18,751	10,00	-15,0	55,0	9,5
	Pre-cycle 5 (n=19)	82,11	16,526	85,00	40,0	100,0	9,5	19	4,74	21,633	5,00	-45,0	55,0	9,5
	Pre-cycle 9 (n=19)	83,95	17,287	90,00	50,0	100,0	9,5	19	6,58	20,619	10,00	-35,0	55,0	9,5
	Pre-cycle 13 (n=18)	85,28	18,979	92,50	45,0	100,0	14,3	18	6,11	22,199	10,00	-35,0	55,0	14,3
	Pre-cycle 25 (n=14)	92,50	11,223	95,00	60,0	100,0	33,3	14	10,71	16,036	10,00	-20,0	55,0	33,3
	Pre-cycle 37 (n=4)	95,00	10,000	100,00	80,0	100,0	81,0	4	16,25	14,361	15,00	0,0	35,0	81,0
Raw Emotional functioning	Baseline (n=20)	3,14	0,732	3,40	1,8	4,0	4,8							
	Pre-cycle 3 (n=19)	3,54	0,462	3,80	2,6	4,0	9,5	19	0,44	0,750	0,40	-0,6	2,2	9,5
	Pre-cycle 5 (n=19)	3,28	0,661	3,40	1,6	4,0	9,5	19	0,19	0,865	0,20	-1,8	2,2	9,5
	Pre-cycle 9 (n=19)	3,36	0,691	3,60	2,0	4,0	9,5	19	0,26	0,825	0,40	-1,4	2,2	9,5
	Pre-cycle 13 (n=18)	3,41	0,759	3,70	1,8	4,0	14,3	18	0,24	0,888	0,40	-1,4	2,2	14,3
	Pre-cycle 25 (n=14)	3,70	0,449	3,80	2,4	4,0	33,3	14	0,43	0,641	0,40	-0,8	2,2	33,3
	Pre-cycle 37 (n=4)	3,80	0,400	4,00	3,2	4,0	81,0	4	0,65	0,574	0,60	0,0	1,4	81,0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.1 PedsQL self-report scores over time and change from baseline over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Social functioning	Baseline (n=20)	76,75	19,418	80,00	30,0	100,0	4,8							
	Pre-cycle 3 (n=19)	80,79	18,125	85,00	30,0	100,0	9,5	19	4,21	20,225	5,00	-35,0	35,0	9,5
	Pre-cycle 5 (n=19)	83,42	17,484	90,00	45,0	100,0	9,5	19	6,84	17,417	10,00	-35,0	35,0	9,5
	Pre-cycle 9 (n=19)	80,79	16,772	85,00	55,0	100,0	9,5	19	4,21	17,422	5,00	-30,0	35,0	9,5
	Pre-cycle 13 (n=18)	81,67	27,279	92,50	15,0	100,0	14,3	18	3,33	19,704	5,00	-45,0	40,0	14,3
	Pre-cycle 25 (n=14)	93,93	11,125	100,00	65,0	100,0	33,3	14	8,21	12,951	10,00	-15,0	35,0	33,3
	Pre-cycle 37 (n=4)	83,75	22,500	95,00	50,0	95,0	81,0	4	-3,75	8,539	-2,50	-15,0	5,0	81,0
Raw Social functioning	Baseline (n=20)	3,07	0,777	3,20	1,2	4,0	4,8							
	Pre-cycle 3 (n=19)	3,23	0,725	3,40	1,2	4,0	9,5	19	0,17	0,809	0,20	-1,4	1,4	9,5
	Pre-cycle 5 (n=19)	3,34	0,699	3,60	1,8	4,0	9,5	19	0,27	0,697	0,40	-1,4	1,4	9,5
	Pre-cycle 9 (n=19)	3,23	0,671	3,40	2,2	4,0	9,5	19	0,17	0,697	0,20	-1,2	1,4	9,5
	Pre-cycle 13 (n=18)	3,27	1,091	3,70	0,6	4,0	14,3	18	0,13	0,788	0,20	-1,8	1,6	14,3
	Pre-cycle 25 (n=14)	3,76	0,445	4,00	2,6	4,0	33,3	14	0,33	0,518	0,40	-0,6	1,4	33,3
	Pre-cycle 37 (n=4)	3,35	0,900	3,80	2,0	3,8	81,0	4	-0,15	0,342	-0,10	-0,6	0,2	81,0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.1 PedsQL self-report scores over time and change from baseline over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
School functioning score	Baseline (n=17)	68,24	24,170	80,00	15,0	95,0	19,0							
	Pre-cycle 3 (n=18)	71,67	18,471	72,50	35,0	100,0	14,3	15	5,00	18,613	0,00	-20,0	45,0	28,6
	Pre-cycle 5 (n=13)	76,54	19,620	80,00	25,0	100,0	38,1	10	6,50	24,614	2,50	-30,0	50,0	52,4
	Pre-cycle 9 (n=15)	75,00	13,758	80,00	50,0	95,0	28,6	13	7,69	26,030	5,00	-40,0	70,0	38,1
	Pre-cycle 13 (n=15)	75,67	20,254	80,00	25,0	100,0	28,6	13	7,31	17,031	10,00	-25,0	45,0	38,1
	Pre-cycle 25 (n=11)	85,91	14,632	90,00	55,0	100,0	47,6	9	9,44	21,279	5,00	-20,0	50,0	57,1
	Pre-cycle 37 (n=3)	81,67	16,073	75,00	70,0	100,0	85,7	2	NC	NC	NC	-10,0	15,0	90,5
Raw School functioning score	Baseline (n=17)	2,73	0,967	3,20	0,6	3,8	19,0							
	Pre-cycle 3 (n=18)	2,87	0,739	2,90	1,4	4,0	14,3	15	0,20	0,745	0,00	-0,8	1,8	28,6
	Pre-cycle 5 (n=13)	3,06	0,785	3,20	1,0	4,0	38,1	10	0,26	0,985	0,10	-1,2	2,0	52,4
	Pre-cycle 9 (n=15)	3,00	0,550	3,20	2,0	3,8	28,6	13	0,31	1,041	0,20	-1,6	2,8	38,1
	Pre-cycle 13 (n=15)	3,03	0,810	3,20	1,0	4,0	28,6	13	0,29	0,681	0,40	-1,0	1,8	38,1
	Pre-cycle 25 (n=11)	3,44	0,585	3,60	2,2	4,0	47,6	9	0,38	0,851	0,20	-0,8	2,0	57,1
	Pre-cycle 37 (n=3)	3,27	0,643	3,00	2,8	4,0	85,7	2	NC	NC	NC	-0,4	0,6	90,5

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.2 PedsQL self-report scores over time and change from baseline over time - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=13)	71,48	24,998	83,70	13,0	96,7	0,0							
	Pre-cycle 3 (n=12)	80,38	12,217	80,43	55,6	95,8	7,7	12	10,58	18,187	5,04	-4,8	57,8	7,7
	Pre-cycle 5 (n=12)	74,22	17,882	79,89	44,4	94,6	7,7	12	4,42	13,851	-1,09	-13,8	35,9	7,7
	Pre-cycle 9 (n=12)	76,03	19,769	82,61	32,6	97,2	7,7	12	6,23	15,893	2,96	-17,4	34,8	7,7
	Pre-cycle 13 (n=11)	74,04	19,537	78,26	30,4	98,9	15,4	11	6,09	20,972	4,35	-22,3	53,3	15,4
	Pre-cycle 25 (n=9)	75,22	16,124	79,17	34,8	91,3	30,8	9	3,77	19,112	-5,43	-15,2	43,5	30,8
Raw Total Score	Baseline (n=13)	2,86	1,000	3,35	0,5	3,9	0,0							
	Pre-cycle 3 (n=12)	3,22	0,489	3,22	2,2	3,8	7,7	12	0,42	0,727	0,20	-0,2	2,3	7,7
	Pre-cycle 5 (n=12)	2,97	0,715	3,20	1,8	3,8	7,7	12	0,18	0,554	-0,04	-0,6	1,4	7,7
	Pre-cycle 9 (n=12)	3,04	0,791	3,30	1,3	3,9	7,7	12	0,25	0,636	0,12	-0,7	1,4	7,7
	Pre-cycle 13 (n=11)	2,96	0,781	3,13	1,2	4,0	15,4	11	0,24	0,839	0,17	-0,9	2,1	15,4
	Pre-cycle 25 (n=9)	3,01	0,645	3,17	1,4	3,7	30,8	9	0,15	0,764	-0,22	-0,6	1,7	30,8

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.2 PedsQL self-report scores over time and change from baseline over time - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Physical functioning	Baseline (n=13)	72,84	21,401	81,25	28,1	96,9	0,0							
	Pre-cycle 3 (n=12)	79,69	12,885	82,81	59,4	93,8	7,7	12	8,85	18,504	9,38	-25,0	40,6	7,7
	Pre-cycle 5 (n=12)	72,14	15,679	78,13	34,4	87,5	7,7	12	1,30	17,346	1,56	-28,1	28,1	7,7
	Pre-cycle 9 (n=12)	74,03	18,846	83,26	43,8	93,8	7,7	12	3,20	13,647	7,81	-18,8	21,9	7,7
	Pre-cycle 13 (n=11)	73,58	18,507	71,88	37,5	100,0	15,4	11	4,83	17,364	9,38	-25,0	31,3	15,4
	Pre-cycle 25 (n=9)	76,74	14,914	75,00	53,1	100,0	30,8	9	5,21	23,123	-3,13	-15,6	53,1	30,8
Raw Physical functioning	Baseline (n=13)	2,91	0,856	3,25	1,1	3,9	0,0							
	Pre-cycle 3 (n=12)	3,19	0,515	3,31	2,4	3,8	7,7	12	0,35	0,740	0,38	-1,0	1,6	7,7
	Pre-cycle 5 (n=12)	2,89	0,627	3,13	1,4	3,5	7,7	12	0,05	0,694	0,06	-1,1	1,1	7,7
	Pre-cycle 9 (n=12)	2,96	0,754	3,33	1,8	3,8	7,7	12	0,13	0,546	0,31	-0,8	0,9	7,7
	Pre-cycle 13 (n=11)	2,94	0,740	2,88	1,5	4,0	15,4	11	0,19	0,695	0,38	-1,0	1,3	15,4
	Pre-cycle 25 (n=9)	3,07	0,597	3,00	2,1	4,0	30,8	9	0,21	0,925	-0,13	-0,6	2,1	30,8

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.2 PedsQL self-report scores over time and change from baseline over time - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]											
		Absolute values						Change from baseline					
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Emotional functioning	Baseline (n=13)	71,92	28,762	85,00	5,0	100,0	0,0							
	Pre-cycle 3 (n=12)	81,25	19,203	87,50	45,0	100,0	7,7	12	9,58	25,357	2,50	-25,0	75,0	7,7
	Pre-cycle 5 (n=12)	77,08	19,477	82,50	40,0	100,0	7,7	12	5,42	22,508	0,00	-20,0	65,0	7,7
	Pre-cycle 9 (n=12)	83,33	18,007	85,00	40,0	100,0	7,7	12	11,67	23,290	0,00	-15,0	65,0	7,7
	Pre-cycle 13 (n=11)	80,00	20,736	90,00	50,0	100,0	15,4	11	9,55	33,798	-5,00	-35,0	95,0	15,4
	Pre-cycle 25 (n=9)	75,00	26,810	85,00	25,0	100,0	30,8	9	-0,56	29,416	-5,00	-45,0	65,0	30,8
Raw Emotional functioning	Baseline (n=13)	2,88	1,150	3,40	0,2	4,0	0,0							
	Pre-cycle 3 (n=12)	3,25	0,768	3,50	1,8	4,0	7,7	12	0,38	1,014	0,10	-1,0	3,0	7,7
	Pre-cycle 5 (n=12)	3,08	0,779	3,30	1,6	4,0	7,7	12	0,22	0,900	0,00	-0,8	2,6	7,7
	Pre-cycle 9 (n=12)	3,33	0,720	3,40	1,6	4,0	7,7	12	0,47	0,932	0,00	-0,6	2,6	7,7
	Pre-cycle 13 (n=11)	3,20	0,829	3,60	2,0	4,0	15,4	11	0,38	1,352	-0,20	-1,4	3,8	15,4
	Pre-cycle 25 (n=9)	3,00	1,072	3,40	1,0	4,0	30,8	9	-0,02	1,177	-0,20	-1,8	2,6	30,8

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.2 PedsQL self-report scores over time and change from baseline over time - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Social functioning	Baseline (n=13)	74,62	29,330	85,00	0,0	100,0	0,0							
	Pre-cycle 3 (n=11)	80,91	17,003	85,00	50,0	100,0	15,4	11	9,55	21,030	5,00	-10,0	65,0	15,4
	Pre-cycle 5 (n=12)	77,08	23,880	85,00	30,0	100,0	7,7	12	4,58	12,332	0,00	-10,0	35,0	7,7
	Pre-cycle 9 (n=12)	76,25	26,382	87,50	25,0	100,0	7,7	12	3,75	17,073	5,00	-25,0	30,0	7,7
	Pre-cycle 13 (n=11)	78,64	22,923	85,00	30,0	100,0	15,4	11	8,18	27,953	5,00	-35,0	65,0	15,4
	Pre-cycle 25 (n=9)	77,22	18,893	80,00	35,0	100,0	30,8	9	1,67	19,365	0,00	-25,0	40,0	30,8
Raw Social functioning	Baseline (n=13)	2,98	1,173	3,40	0,0	4,0	0,0							
	Pre-cycle 3 (n=11)	3,24	0,680	3,40	2,0	4,0	15,4	11	0,38	0,841	0,20	-0,4	2,6	15,4
	Pre-cycle 5 (n=12)	3,08	0,955	3,40	1,2	4,0	7,7	12	0,18	0,493	0,00	-0,4	1,4	7,7
	Pre-cycle 9 (n=12)	3,05	1,055	3,50	1,0	4,0	7,7	12	0,15	0,683	0,20	-1,0	1,2	7,7
	Pre-cycle 13 (n=11)	3,15	0,917	3,40	1,2	4,0	15,4	11	0,33	1,118	0,20	-1,4	2,6	15,4
	Pre-cycle 25 (n=9)	3,09	0,756	3,20	1,4	4,0	30,8	9	0,07	0,775	0,00	-1,0	1,6	30,8

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.2 PedsQL self-report scores over time and change from baseline over time - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=13) [a]											
		Absolute values						Change from baseline					
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
School functioning score	Baseline (n=11)	63,18	32,960	70,00	10,0	100,0	15,4							
	Pre-cycle 3 (n=6)	80,00	17,607	85,00	50,0	100,0	53,8	5	14,00	15,572	10,00	0,0	35,0	61,5
	Pre-cycle 5 (n=8)	72,50	26,322	80,00	30,0	95,0	38,5	7	5,00	15,275	-5,00	-10,0	30,0	46,2
	Pre-cycle 9 (n=11)	69,55	25,735	80,00	5,0	95,0	15,4	10	8,50	19,156	-2,50	-10,0	35,0	23,1
	Pre-cycle 13 (n=10)	63,00	31,552	65,00	0,0	100,0	23,1	10	2,00	16,364	0,00	-20,0	35,0	23,1
	Pre-cycle 25 (n=8)	70,00	31,168	77,50	0,0	100,0	38,5	7	2,14	14,392	0,00	-15,0	25,0	46,2
Raw School functioning score	Baseline (n=11)	2,53	1,318	2,80	0,4	4,0	15,4							
	Pre-cycle 3 (n=6)	3,20	0,704	3,40	2,0	4,0	53,8	5	0,56	0,623	0,40	0,0	1,4	61,5
	Pre-cycle 5 (n=8)	2,90	1,053	3,20	1,2	3,8	38,5	7	0,20	0,611	-0,20	-0,4	1,2	46,2
	Pre-cycle 9 (n=11)	2,78	1,029	3,20	0,2	3,8	15,4	10	0,34	0,766	-0,10	-0,4	1,4	23,1
	Pre-cycle 13 (n=10)	2,52	1,262	2,60	0,0	4,0	23,1	10	0,08	0,655	0,00	-0,8	1,4	23,1
	Pre-cycle 25 (n=8)	2,80	1,247	3,10	0,0	4,0	38,5	7	0,09	0,576	0,00	-0,6	1,0	46,2

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.3 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Progressive
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=11)	71,89	27,182	85,87	13,0	95,7	0,0							
	Pre-cycle 3 (n=11)	78,15	14,830	75,00	48,9	97,8	0,0	11	6,26	22,996	0,30	-20,1	57,8	0,0
	Pre-cycle 5 (n=11)	75,61	18,346	84,78	42,4	93,5	0,0	11	3,73	22,431	-0,30	-43,5	37,0	0,0
	Pre-cycle 9 (n=11)	75,86	16,112	78,26	47,8	95,7	0,0	11	3,98	17,116	1,39	-19,9	34,8	0,0
	Pre-cycle 13 (n=10)	77,21	18,251	75,72	51,1	100,0	9,1	10	7,16	23,461	5,43	-24,2	53,3	9,1
	Pre-cycle 25 (n=6)	91,24	8,906	95,65	79,2	98,6	45,5	6	6,96	12,496	4,20	-5,3	30,6	45,5
	Pre-cycle 37 (n=3)	86,35	10,811	91,67	73,9	93,5	72,7	3	10,73	12,839	5,80	1,1	25,3	72,7
Raw Total Score	Baseline (n=11)	2,88	1,087	3,43	0,5	3,8	0,0							
	Pre-cycle 3 (n=11)	3,13	0,593	3,00	2,0	3,9	0,0	11	0,25	0,920	0,01	-0,8	2,3	0,0
	Pre-cycle 5 (n=11)	3,02	0,734	3,39	1,7	3,7	0,0	11	0,15	0,897	-0,01	-1,7	1,5	0,0
	Pre-cycle 9 (n=11)	3,03	0,644	3,13	1,9	3,8	0,0	11	0,16	0,685	0,06	-0,8	1,4	0,0
	Pre-cycle 13 (n=10)	3,09	0,730	3,03	2,0	4,0	9,1	10	0,29	0,938	0,22	-1,0	2,1	9,1
	Pre-cycle 25 (n=6)	3,65	0,356	3,83	3,2	3,9	45,5	6	0,28	0,500	0,17	-0,2	1,2	45,5
	Pre-cycle 37 (n=3)	3,45	0,432	3,67	3,0	3,7	72,7	3	0,43	0,514	0,23	0,0	1,0	72,7

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.3 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Physical functioning	Baseline (n=11)	78,33	24,886	92,86	28,1	100,0	0,0							
	Pre-cycle 3 (n=11)	78,33	17,698	78,13	37,5	100,0	0,0	11	0,00	18,435	-3,13	-25,0	40,6	0,0
	Pre-cycle 5 (n=11)	78,13	21,515	84,38	40,6	100,0	0,0	11	-0,20	24,948	3,13	-56,3	34,4	0,0
	Pre-cycle 9 (n=11)	76,99	17,858	78,13	43,8	100,0	0,0	11	-1,34	14,463	3,13	-25,0	21,9	0,0
	Pre-cycle 13 (n=10)	80,63	18,622	89,06	50,0	100,0	9,1	10	3,84	24,292	1,56	-46,9	31,3	9,1
	Pre-cycle 25 (n=6)	93,23	13,752	100,00	65,6	100,0	45,5	6	7,81	29,761	3,13	-31,3	59,4	45,5
	Pre-cycle 37 (n=3)	90,63	8,268	87,50	84,4	100,0	72,7	3	13,54	30,352	6,25	-12,5	46,9	72,7
Raw Physical functioning	Baseline (n=11)	3,13	0,995	3,71	1,1	4,0	0,0							
	Pre-cycle 3 (n=11)	3,13	0,708	3,13	1,5	4,0	0,0	11	0,00	0,737	-0,13	-1,0	1,6	0,0
	Pre-cycle 5 (n=11)	3,13	0,861	3,38	1,6	4,0	0,0	11	-0,01	0,998	0,13	-2,3	1,4	0,0
	Pre-cycle 9 (n=11)	3,08	0,714	3,13	1,8	4,0	0,0	11	-0,05	0,579	0,13	-1,0	0,9	0,0
	Pre-cycle 13 (n=10)	3,23	0,745	3,56	2,0	4,0	9,1	10	0,15	0,972	0,06	-1,9	1,3	9,1
	Pre-cycle 25 (n=6)	3,73	0,550	4,00	2,6	4,0	45,5	6	0,31	1,190	0,13	-1,3	2,4	45,5
	Pre-cycle 37 (n=3)	3,63	0,331	3,50	3,4	4,0	72,7	3	0,54	1,214	0,25	-0,5	1,9	72,7

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.3 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Emotional functioning	Baseline (n=11)	70,91	27,822	80,00	5,0	100,0	0,0							
	Pre-cycle 3 (n=11)	86,82	11,890	90,00	65,0	100,0	0,0	11	15,91	26,816	5,00	-15,0	75,0	0,0
	Pre-cycle 5 (n=11)	74,55	17,671	75,00	40,0	100,0	0,0	11	3,64	28,818	0,00	-45,0	65,0	0,0
	Pre-cycle 9 (n=11)	76,82	15,211	85,00	55,0	95,0	0,0	11	5,91	22,228	5,00	-25,0	65,0	0,0
	Pre-cycle 13 (n=10)	80,00	19,437	82,50	45,0	100,0	9,1	10	10,50	35,547	10,00	-35,0	95,0	9,1
	Pre-cycle 25 (n=6)	89,17	14,634	95,00	60,0	100,0	45,5	6	6,67	6,831	7,50	-5,0	15,0	45,5
	Pre-cycle 37 (n=3)	93,33	11,547	100,00	80,0	100,0	72,7	3	16,67	17,559	15,00	0,0	35,0	72,7
Raw Emotional functioning	Baseline (n=11)	2,84	1,113	3,20	0,2	4,0	0,0							
	Pre-cycle 3 (n=11)	3,47	0,476	3,60	2,6	4,0	0,0	11	0,64	1,073	0,20	-0,6	3,0	0,0
	Pre-cycle 5 (n=11)	2,98	0,707	3,00	1,6	4,0	0,0	11	0,15	1,153	0,00	-1,8	2,6	0,0
	Pre-cycle 9 (n=11)	3,07	0,608	3,40	2,2	3,8	0,0	11	0,24	0,889	0,20	-1,0	2,6	0,0
	Pre-cycle 13 (n=10)	3,20	0,777	3,30	1,8	4,0	9,1	10	0,42	1,422	0,40	-1,4	3,8	9,1
	Pre-cycle 25 (n=6)	3,57	0,585	3,80	2,4	4,0	45,5	6	0,27	0,273	0,30	-0,2	0,6	45,5
	Pre-cycle 37 (n=3)	3,73	0,462	4,00	3,2	4,0	72,7	3	0,67	0,702	0,60	0,0	1,4	72,7

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.3 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Social functioning	Baseline (n=11)	72,27	33,194	90,00	0,0	100,0	0,0							
	Pre-cycle 3 (n=11)	76,82	20,649	80,00	30,0	100,0	0,0	11	4,55	29,619	0,00	-35,0	65,0	0,0
	Pre-cycle 5 (n=11)	76,82	23,798	90,00	35,0	100,0	0,0	11	4,55	21,267	0,00	-35,0	35,0	0,0
	Pre-cycle 9 (n=11)	77,27	25,036	90,00	25,0	100,0	0,0	11	5,00	20,248	5,00	-30,0	35,0	0,0
	Pre-cycle 13 (n=10)	73,00	33,764	90,00	15,0	100,0	9,1	10	3,00	30,386	-2,50	-45,0	65,0	9,1
	Pre-cycle 25 (n=6)	92,50	14,053	100,00	65,0	100,0	45,5	6	0,83	6,646	0,00	-10,0	10,0	45,5
	Pre-cycle 37 (n=3)	80,00	25,981	95,00	50,0	95,0	72,7	3	-5,00	10,000	-5,00	-15,0	5,0	72,7
Raw Social functioning	Baseline (n=11)	2,89	1,328	3,60	0,0	4,0	0,0							
	Pre-cycle 3 (n=11)	3,07	0,826	3,20	1,2	4,0	0,0	11	0,18	1,185	0,00	-1,4	2,6	0,0
	Pre-cycle 5 (n=11)	3,07	0,952	3,60	1,4	4,0	0,0	11	0,18	0,851	0,00	-1,4	1,4	0,0
	Pre-cycle 9 (n=11)	3,09	1,001	3,60	1,0	4,0	0,0	11	0,20	0,810	0,20	-1,2	1,4	0,0
	Pre-cycle 13 (n=10)	2,92	1,351	3,60	0,6	4,0	9,1	10	0,12	1,215	-0,10	-1,8	2,6	9,1
	Pre-cycle 25 (n=6)	3,70	0,562	4,00	2,6	4,0	45,5	6	0,03	0,266	0,00	-0,4	0,4	45,5
	Pre-cycle 37 (n=3)	3,20	1,039	3,80	2,0	3,8	72,7	3	-0,20	0,400	-0,20	-0,6	0,2	72,7

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.3 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
School functioning score	Baseline (n=9)	61,11	35,424	85,00	10,0	95,0	18,2							
	Pre-cycle 3 (n=10)	70,50	17,552	70,00	45,0	100,0	9,1	8	6,88	22,190	2,50	-20,0	45,0	27,3
	Pre-cycle 5 (n=9)	69,44	25,055	75,00	25,0	95,0	18,2	7	5,00	25,331	0,00	-30,0	50,0	36,4
	Pre-cycle 9 (n=9)	68,33	17,678	60,00	45,0	90,0	18,2	8	13,13	33,052	5,00	-40,0	70,0	27,3
	Pre-cycle 13 (n=8)	70,63	25,834	75,00	25,0	100,0	27,3	6	10,00	27,203	10,00	-25,0	45,0	45,5
	Pre-cycle 25 (n=3)	91,67	2,887	90,00	90,0	95,0	72,7	2	NC	NC	NC	-5,0	5,0	81,8
	Pre-cycle 37 (n=2)	NC	NC	NC	70,0	75,0	81,8	1	NC	NC	NC	-10,0	-10,0	90,9
Raw School functioning score	Baseline (n=9)	2,44	1,417	3,40	0,4	3,8	18,2							
	Pre-cycle 3 (n=10)	2,82	0,702	2,80	1,8	4,0	9,1	8	0,28	0,888	0,10	-0,8	1,8	27,3
	Pre-cycle 5 (n=9)	2,78	1,002	3,00	1,0	3,8	18,2	7	0,20	1,013	0,00	-1,2	2,0	36,4
	Pre-cycle 9 (n=9)	2,73	0,707	2,40	1,8	3,6	18,2	8	0,53	1,322	0,20	-1,6	2,8	27,3
	Pre-cycle 13 (n=8)	2,83	1,033	3,00	1,0	4,0	27,3	6	0,40	1,088	0,40	-1,0	1,8	45,5
	Pre-cycle 25 (n=3)	3,67	0,115	3,60	3,6	3,8	72,7	2	NC	NC	NC	-0,2	0,2	81,8
	Pre-cycle 37 (n=2)	NC	NC	NC	2,8	3,0	81,8	1	NC	NC	NC	-0,4	-0,4	90,9

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.4 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=11)	78,29	16,463	83,70	50,0	96,7	0,0							
	Pre-cycle 3 (n=10)	83,75	11,831	88,59	61,4	96,6	9,1	10	6,80	7,697	6,99	-4,3	22,8	9,1
	Pre-cycle 5 (n=10)	84,49	9,042	84,75	68,1	97,8	9,1	10	7,54	10,810	4,86	-5,9	27,8	9,1
	Pre-cycle 9 (n=10)	86,61	8,003	86,96	72,8	97,2	9,1	10	9,65	17,082	7,07	-17,4	42,4	9,1
	Pre-cycle 13 (n=9)	90,94	6,853	92,39	78,3	98,9	18,2	9	11,47	10,213	8,70	2,2	33,7	18,2
	Pre-cycle 25 (n=9)	88,63	9,422	91,30	72,8	100,0	18,2	9	9,16	17,350	9,78	-10,9	42,4	18,2
	Pre-cycle 37 (n=1)	NC	NC	NC	96,7	96,7	90,9	1	NC	NC	NC	7,6	7,6	90,9
Raw Total Score	Baseline (n=11)	3,13	0,659	3,35	2,0	3,9	0,0							
	Pre-cycle 3 (n=10)	3,35	0,473	3,54	2,5	3,9	9,1	10	0,27	0,308	0,28	-0,2	0,9	9,1
	Pre-cycle 5 (n=10)	3,38	0,362	3,39	2,7	3,9	9,1	10	0,30	0,432	0,19	-0,2	1,1	9,1
	Pre-cycle 9 (n=10)	3,46	0,320	3,48	2,9	3,9	9,1	10	0,39	0,683	0,28	-0,7	1,7	9,1
	Pre-cycle 13 (n=9)	3,64	0,274	3,70	3,1	4,0	18,2	9	0,46	0,409	0,35	0,1	1,3	18,2
	Pre-cycle 25 (n=9)	3,55	0,377	3,65	2,9	4,0	18,2	9	0,37	0,694	0,39	-0,4	1,7	18,2
	Pre-cycle 37 (n=1)	NC	NC	NC	3,9	3,9	90,9	1	NC	NC	NC	0,3	0,3	90,9

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.4 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Physical functioning	Baseline (n=11)	79,55	21,073	90,63	31,3	96,9	0,0							
	Pre-cycle 3 (n=10)	84,06	14,617	87,50	50,0	100,0	9,1	10	6,25	9,200	4,69	-12,5	18,8	9,1
	Pre-cycle 5 (n=10)	84,29	12,858	87,50	59,4	100,0	9,1	10	6,47	10,032	6,25	-4,0	28,1	9,1
	Pre-cycle 9 (n=10)	86,25	11,986	89,06	59,4	96,9	9,1	10	8,44	25,856	6,25	-37,5	65,6	9,1
	Pre-cycle 13 (n=9)	95,14	5,658	96,88	84,4	100,0	18,2	9	14,93	21,354	9,38	0,0	68,8	18,2
	Pre-cycle 25 (n=9)	89,24	7,512	90,63	78,1	100,0	18,2	9	9,03	20,279	6,25	-12,5	53,1	18,2
	Pre-cycle 37 (n=1)	NC	NC	NC	93,8	93,8	90,9	1	NC	NC	NC	3,1	3,1	90,9
Raw Physical functioning	Baseline (n=11)	3,18	0,843	3,63	1,3	3,9	0,0							
	Pre-cycle 3 (n=10)	3,36	0,585	3,50	2,0	4,0	9,1	10	0,25	0,368	0,19	-0,5	0,8	9,1
	Pre-cycle 5 (n=10)	3,37	0,514	3,50	2,4	4,0	9,1	10	0,26	0,401	0,25	-0,2	1,1	9,1
	Pre-cycle 9 (n=10)	3,45	0,479	3,56	2,4	3,9	9,1	10	0,34	1,034	0,25	-1,5	2,6	9,1
	Pre-cycle 13 (n=9)	3,81	0,226	3,88	3,4	4,0	18,2	9	0,60	0,854	0,38	0,0	2,8	18,2
	Pre-cycle 25 (n=9)	3,57	0,300	3,63	3,1	4,0	18,2	9	0,36	0,811	0,25	-0,5	2,1	18,2
	Pre-cycle 37 (n=1)	NC	NC	NC	3,8	3,8	90,9	1	NC	NC	NC	0,1	0,1	90,9

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.4 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Emotional functioning	Baseline (n=11)	73,64	18,040	80,00	45,0	100,0	0,0							
	Pre-cycle 3 (n=10)	85,50	18,775	95,00	45,0	100,0	9,1	10	12,00	20,303	10,00	-25,0	55,0	9,1
	Pre-cycle 5 (n=10)	88,00	14,757	92,50	55,0	100,0	9,1	10	14,50	19,358	15,00	-15,0	55,0	9,1
	Pre-cycle 9 (n=10)	92,50	10,607	100,00	70,0	100,0	9,1	10	19,00	18,227	15,00	0,0	55,0	9,1
	Pre-cycle 13 (n=9)	93,33	11,456	100,00	65,0	100,0	18,2	9	16,67	19,039	15,00	-5,0	55,0	18,2
	Pre-cycle 25 (n=9)	85,00	25,249	95,00	25,0	100,0	18,2	9	8,33	25,860	10,00	-45,0	55,0	18,2
	Pre-cycle 37 (n=1)	NC	NC	NC	100,0	100,0	90,9	1	NC	NC	NC	15,0	15,0	90,9
Raw Emotional functioning	Baseline (n=11)	2,95	0,722	3,20	1,8	4,0	0,0							
	Pre-cycle 3 (n=10)	3,42	0,751	3,80	1,8	4,0	9,1	10	0,48	0,812	0,40	-1,0	2,2	9,1
	Pre-cycle 5 (n=10)	3,52	0,590	3,70	2,2	4,0	9,1	10	0,58	0,774	0,60	-0,6	2,2	9,1
	Pre-cycle 9 (n=10)	3,70	0,424	4,00	2,8	4,0	9,1	10	0,76	0,729	0,60	0,0	2,2	9,1
	Pre-cycle 13 (n=9)	3,73	0,458	4,00	2,6	4,0	18,2	9	0,67	0,762	0,60	-0,2	2,2	18,2
	Pre-cycle 25 (n=9)	3,40	1,010	3,80	1,0	4,0	18,2	9	0,33	1,034	0,40	-1,8	2,2	18,2
	Pre-cycle 37 (n=1)	NC	NC	NC	4,0	4,0	90,9	1	NC	NC	NC	0,6	0,6	90,9

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.4 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Social functioning	Baseline (n=11)	83,64	16,446	85,00	45,0	100,0	0,0							
	Pre-cycle 3 (n=10)	86,00	13,703	90,00	65,0	100,0	9,1	10	4,00	13,904	2,50	-15,0	30,0	9,1
	Pre-cycle 5 (n=10)	87,50	12,304	87,50	65,0	100,0	9,1	10	5,50	10,916	5,00	-10,0	20,0	9,1
	Pre-cycle 9 (n=10)	85,00	12,910	87,50	60,0	100,0	9,1	10	3,00	13,984	2,50	-15,0	30,0	9,1
	Pre-cycle 13 (n=9)	91,11	11,667	95,00	65,0	100,0	18,2	9	5,00	10,607	10,00	-15,0	15,0	18,2
	Pre-cycle 25 (n=9)	93,89	9,930	100,00	75,0	100,0	18,2	9	7,78	12,019	10,00	-15,0	20,0	18,2
	Pre-cycle 37 (n=1)	NC	NC	NC	95,0	95,0	90,9	1	NC	NC	NC	0,0	0,0	90,9
Raw Social functioning	Baseline (n=11)	3,35	0,658	3,40	1,8	4,0	0,0							
	Pre-cycle 3 (n=10)	3,44	0,548	3,60	2,6	4,0	9,1	10	0,16	0,556	0,10	-0,6	1,2	9,1
	Pre-cycle 5 (n=10)	3,50	0,492	3,50	2,6	4,0	9,1	10	0,22	0,437	0,20	-0,4	0,8	9,1
	Pre-cycle 9 (n=10)	3,40	0,516	3,50	2,4	4,0	9,1	10	0,12	0,559	0,10	-0,6	1,2	9,1
	Pre-cycle 13 (n=9)	3,64	0,467	3,80	2,6	4,0	18,2	9	0,20	0,424	0,40	-0,6	0,6	18,2
	Pre-cycle 25 (n=9)	3,76	0,397	4,00	3,0	4,0	18,2	9	0,31	0,481	0,40	-0,6	0,8	18,2
	Pre-cycle 37 (n=1)	NC	NC	NC	3,8	3,8	90,9	1	NC	NC	NC	0,0	0,0	90,9

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.4 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=11) [a]											
		Absolute values						Change from baseline					
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
School functioning score	Baseline (n=10)	74,00	19,692	80,00	40,0	100,0	9,1							
	Pre-cycle 3 (n=8)	75,63	21,454	82,50	35,0	95,0	27,3	8	1,88	13,346	0,00	-20,0	25,0	27,3
	Pre-cycle 5 (n=6)	79,17	17,151	77,50	55,0	100,0	45,5	6	5,00	17,029	0,00	-15,0	30,0	45,5
	Pre-cycle 9 (n=8)	80,00	4,629	80,00	75,0	85,0	27,3	8	6,25	16,637	-2,50	-10,0	35,0	27,3
	Pre-cycle 13 (n=9)	81,67	17,500	90,00	55,0	100,0	18,2	9	7,22	5,652	5,00	0,0	15,0	18,2
	Pre-cycle 25 (n=8)	86,88	13,611	90,00	65,0	100,0	27,3	8	8,13	24,044	5,00	-20,0	50,0	27,3
	Pre-cycle 37 (n=1)	NC	NC	NC	100,0	100,0	90,9	1	NC	NC	NC	15,0	15,0	90,9
Raw School functioning score	Baseline (n=10)	2,96	0,788	3,20	1,6	4,0	9,1							
	Pre-cycle 3 (n=8)	3,03	0,858	3,30	1,4	3,8	27,3	8	0,08	0,534	0,00	-0,8	1,0	27,3
	Pre-cycle 5 (n=6)	3,17	0,686	3,10	2,2	4,0	45,5	6	0,20	0,681	0,00	-0,6	1,2	45,5
	Pre-cycle 9 (n=8)	3,20	0,185	3,20	3,0	3,4	27,3	8	0,25	0,665	-0,10	-0,4	1,4	27,3
	Pre-cycle 13 (n=9)	3,27	0,700	3,60	2,2	4,0	18,2	9	0,29	0,226	0,20	0,0	0,6	18,2
	Pre-cycle 25 (n=8)	3,48	0,544	3,60	2,6	4,0	27,3	8	0,33	0,962	0,20	-0,8	2,0	27,3
	Pre-cycle 37 (n=1)	NC	NC	NC	4,0	4,0	90,9	1	NC	NC	NC	0,6	0,6	90,9

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.5 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=11)	71,56	18,032	73,91	40,2	91,3	8,3							
	Pre-cycle 3 (n=10)	77,50	14,562	80,98	50,0	95,8	16,7	10	7,81	10,625	6,04	-4,8	31,5	16,7
	Pre-cycle 5 (n=10)	73,58	18,331	80,98	44,4	90,2	16,7	10	3,89	9,567	5,50	-13,8	15,2	16,7
	Pre-cycle 9 (n=10)	73,09	20,940	76,93	32,6	96,7	16,7	10	3,40	12,894	4,65	-17,4	20,7	16,7
	Pre-cycle 13 (n=10)	71,66	22,469	78,71	30,4	100,0	16,7	10	1,97	15,507	7,07	-22,3	22,2	16,7
	Pre-cycle 25 (n=8)	75,54	18,410	79,35	34,8	98,9	33,3	8	5,96	19,292	2,72	-15,2	43,5	33,3
Raw Total Score	Baseline (n=11)	2,86	0,721	2,96	1,6	3,7	8,3							
	Pre-cycle 3 (n=10)	3,10	0,582	3,24	2,0	3,8	16,7	10	0,31	0,425	0,24	-0,2	1,3	16,7
	Pre-cycle 5 (n=10)	2,94	0,733	3,24	1,8	3,6	16,7	10	0,16	0,383	0,22	-0,6	0,6	16,7
	Pre-cycle 9 (n=10)	2,92	0,838	3,08	1,3	3,9	16,7	10	0,14	0,516	0,19	-0,7	0,8	16,7
	Pre-cycle 13 (n=10)	2,87	0,899	3,15	1,2	4,0	16,7	10	0,08	0,620	0,28	-0,9	0,9	16,7
	Pre-cycle 25 (n=8)	3,02	0,736	3,17	1,4	4,0	33,3	8	0,24	0,772	0,11	-0,6	1,7	33,3

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.5 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Physical functioning	Baseline (n=11)	68,47	23,446	75,00	15,6	90,6	8,3							
	Pre-cycle 3 (n=10)	71,56	24,046	79,69	12,5	93,8	16,7	10	5,31	16,864	7,81	-25,0	37,5	16,7
	Pre-cycle 5 (n=10)	67,19	23,304	71,88	21,9	100,0	16,7	10	0,94	16,928	6,25	-28,1	21,9	16,7
	Pre-cycle 9 (n=10)	67,28	21,978	68,75	28,1	93,8	16,7	10	1,03	12,425	7,81	-18,8	12,5	16,7
	Pre-cycle 13 (n=10)	68,44	24,538	70,31	21,9	100,0	16,7	10	2,19	15,870	9,38	-25,0	18,8	16,7
	Pre-cycle 25 (n=8)	75,39	16,657	71,88	53,1	100,0	33,3	8	5,08	23,322	-3,13	-15,6	53,1	33,3
Raw Physical functioning	Baseline (n=11)	2,74	0,938	3,00	0,6	3,6	8,3							
	Pre-cycle 3 (n=10)	2,86	0,962	3,19	0,5	3,8	16,7	10	0,21	0,675	0,31	-1,0	1,5	16,7
	Pre-cycle 5 (n=10)	2,69	0,932	2,88	0,9	4,0	16,7	10	0,04	0,677	0,25	-1,1	0,9	16,7
	Pre-cycle 9 (n=10)	2,69	0,879	2,75	1,1	3,8	16,7	10	0,04	0,497	0,31	-0,8	0,5	16,7
	Pre-cycle 13 (n=10)	2,74	0,982	2,81	0,9	4,0	16,7	10	0,09	0,635	0,38	-1,0	0,8	16,7
	Pre-cycle 25 (n=8)	3,02	0,666	2,88	2,1	4,0	33,3	8	0,20	0,933	-0,13	-0,6	2,1	33,3

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.5 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Emotional functioning	Baseline (n=11)	83,18	21,711	90,00	30,0	100,0	8,3							
	Pre-cycle 3 (n=10)	84,50	15,714	87,50	55,0	100,0	16,7	10	3,00	13,375	0,00	-10,0	35,0	16,7
	Pre-cycle 5 (n=10)	78,50	18,864	85,00	40,0	95,0	16,7	10	-3,00	9,189	-2,50	-20,0	10,0	16,7
	Pre-cycle 9 (n=10)	82,50	21,890	90,00	40,0	100,0	16,7	10	1,00	21,448	0,00	-35,0	45,0	16,7
	Pre-cycle 13 (n=10)	77,50	23,124	87,50	50,0	100,0	16,7	10	-4,00	19,551	-5,00	-35,0	25,0	16,7
	Pre-cycle 25 (n=8)	83,75	19,955	90,00	40,0	100,0	33,3	8	3,75	27,484	-7,50	-20,0	65,0	33,3
Raw Emotional functioning	Baseline (n=11)	3,33	0,868	3,60	1,2	4,0	8,3							
	Pre-cycle 3 (n=10)	3,38	0,629	3,50	2,2	4,0	16,7	10	0,12	0,535	0,00	-0,4	1,4	16,7
	Pre-cycle 5 (n=10)	3,14	0,755	3,40	1,6	3,8	16,7	10	-0,12	0,368	-0,10	-0,8	0,4	16,7
	Pre-cycle 9 (n=10)	3,30	0,876	3,60	1,6	4,0	16,7	10	0,04	0,858	0,00	-1,4	1,8	16,7
	Pre-cycle 13 (n=10)	3,10	0,925	3,50	2,0	4,0	16,7	10	-0,16	0,782	-0,20	-1,4	1,0	16,7
	Pre-cycle 25 (n=8)	3,35	0,798	3,60	1,6	4,0	33,3	8	0,15	1,099	-0,30	-0,8	2,6	33,3

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.5 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]												
		Absolute values						Change from baseline						
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Social functioning	Baseline (n=11)	71,82	16,774	75,00	35,0	95,0	8,3							
	Pre-cycle 3 (n=9)	80,00	17,321	85,00	50,0	100,0	25,0	9	10,56	12,360	10,00	-10,0	30,0	25,0
	Pre-cycle 5 (n=10)	79,00	22,086	85,00	30,0	100,0	16,7	10	8,00	12,953	5,00	-5,0	35,0	16,7
	Pre-cycle 9 (n=10)	75,00	22,485	82,50	35,0	100,0	16,7	10	4,00	17,607	7,50	-25,0	35,0	16,7
	Pre-cycle 13 (n=10)	78,50	23,576	87,50	30,0	100,0	16,7	10	7,50	24,181	10,00	-35,0	35,0	16,7
	Pre-cycle 25 (n=8)	76,25	19,594	80,00	35,0	100,0	33,3	8	6,88	23,443	7,50	-25,0	40,0	33,3
Raw Social functioning	Baseline (n=11)	2,87	0,671	3,00	1,4	3,8	8,3							
	Pre-cycle 3 (n=9)	3,20	0,693	3,40	2,0	4,0	25,0	9	0,42	0,494	0,40	-0,4	1,2	25,0
	Pre-cycle 5 (n=10)	3,16	0,883	3,40	1,2	4,0	16,7	10	0,32	0,518	0,20	-0,2	1,4	16,7
	Pre-cycle 9 (n=10)	3,00	0,899	3,30	1,4	4,0	16,7	10	0,16	0,704	0,30	-1,0	1,4	16,7
	Pre-cycle 13 (n=10)	3,14	0,943	3,50	1,2	4,0	16,7	10	0,30	0,967	0,40	-1,4	1,4	16,7
	Pre-cycle 25 (n=8)	3,05	0,784	3,20	1,4	4,0	33,3	8	0,28	0,938	0,30	-1,0	1,6	33,3

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.1.5 PedsQL self-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=12) [a]											
		Absolute values						Change from baseline					
PedsQL self report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
School functioning score	Baseline (n=9)	62,78	27,170	55,00	15,0	100,0	25,0							
	Pre-cycle 3 (n=6)	76,67	17,224	77,50	50,0	100,0	50,0	4	18,75	14,930	20,00	0,0	35,0	66,7
	Pre-cycle 5 (n=6)	79,17	22,675	85,00	35,0	95,0	50,0	4	8,75	22,500	2,50	-10,0	40,0	66,7
	Pre-cycle 9 (n=9)	70,56	27,776	80,00	5,0	95,0	25,0	7	4,29	15,924	-5,00	-10,0	30,0	41,7
	Pre-cycle 13 (n=8)	58,13	29,753	65,00	0,0	100,0	33,3	8	-1,25	15,059	-2,50	-20,0	25,0	33,3
	Pre-cycle 25 (n=8)	66,88	30,815	77,50	0,0	95,0	33,3	6	5,83	13,197	7,50	-15,0	25,0	50,0
Raw School functioning score	Baseline (n=9)	2,51	1,087	2,20	0,6	4,0	25,0							
	Pre-cycle 3 (n=6)	3,07	0,689	3,10	2,0	4,0	50,0	4	0,75	0,597	0,80	0,0	1,4	66,7
	Pre-cycle 5 (n=6)	3,17	0,907	3,40	1,4	3,8	50,0	4	0,35	0,900	0,10	-0,4	1,6	66,7
	Pre-cycle 9 (n=9)	2,82	1,111	3,20	0,2	3,8	25,0	7	0,17	0,637	-0,20	-0,4	1,2	41,7
	Pre-cycle 13 (n=8)	2,33	1,190	2,60	0,0	4,0	33,3	8	-0,05	0,602	-0,10	-0,8	1,0	33,3
	Pre-cycle 25 (n=8)	2,68	1,233	3,10	0,0	3,8	33,3	6	0,23	0,528	0,30	-0,6	1,0	50,0

[a] Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.1 PedsQL parent-report scores over time and change from baseline over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=30)	62,67	18,605	63,07	31,9	98,9	0,0							
	Pre-cycle 3 (n=29)	70,23	14,705	69,57	42,4	100,0	3,3	29	8,43	12,371	10,87	-21,7	30,4	3,3
	Pre-cycle 5 (n=29)	72,49	15,194	76,09	45,7	94,6	3,3	29	10,69	11,598	10,71	-15,6	45,7	3,3
	Pre-cycle 9 (n=29)	71,39	16,216	70,65	40,2	95,7	3,3	29	9,59	16,174	10,87	-23,9	37,5	3,3
	Pre-cycle 13 (n=28)	73,82	17,004	76,63	39,1	98,9	6,7	28	11,41	14,846	10,87	-10,9	43,2	6,7
	Pre-cycle 25 (n=20)	77,12	15,645	78,56	54,3	100,0	33,3	20	12,03	19,393	11,41	-29,0	53,3	33,3
	Pre-cycle 37 (n=4)	76,34	14,849	79,32	56,5	90,2	86,7	4	19,70	9,123	20,44	8,6	29,3	86,7
Raw Total Score	Baseline (n=30)	2,51	0,744	2,52	1,3	4,0	0,0							
	Pre-cycle 3 (n=29)	2,81	0,588	2,78	1,7	4,0	3,3	29	0,34	0,495	0,43	-0,9	1,2	3,3
	Pre-cycle 5 (n=29)	2,90	0,608	3,04	1,8	3,8	3,3	29	0,43	0,464	0,43	-0,6	1,8	3,3
	Pre-cycle 9 (n=29)	2,86	0,649	2,83	1,6	3,8	3,3	29	0,38	0,647	0,43	-1,0	1,5	3,3
	Pre-cycle 13 (n=28)	2,95	0,680	3,07	1,6	4,0	6,7	28	0,46	0,594	0,43	-0,4	1,7	6,7
	Pre-cycle 25 (n=20)	3,08	0,626	3,14	2,2	4,0	33,3	20	0,48	0,776	0,46	-1,2	2,1	33,3
	Pre-cycle 37 (n=4)	3,05	0,594	3,17	2,3	3,6	86,7	4	0,79	0,365	0,82	0,3	1,2	86,7

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.1 PedsQL parent-report scores over time and change from baseline over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Physical functioning	Baseline (n=30)	62,92	26,879	68,75	9,4	100,0	0,0							
	Pre-cycle 3 (n=29)	71,55	22,893	75,00	18,8	100,0	3,3	29	9,91	15,892	9,38	-31,3	43,8	3,3
	Pre-cycle 5 (n=29)	72,52	22,448	78,13	21,9	100,0	3,3	29	10,88	17,690	12,50	-18,8	75,0	3,3
	Pre-cycle 9 (n=29)	70,69	25,159	75,00	12,5	100,0	3,3	29	9,05	23,790	12,50	-71,9	43,8	3,3
	Pre-cycle 13 (n=28)	73,55	22,861	78,13	18,8	100,0	6,7	28	10,83	18,409	9,38	-12,5	53,1	6,7
	Pre-cycle 25 (n=20)	77,66	24,127	84,38	0,0	100,0	33,3	20	10,00	23,000	12,50	-31,3	71,9	33,3
	Pre-cycle 37 (n=4)	75,78	20,788	78,13	50,0	96,9	86,7	4	13,28	6,929	15,63	3,1	18,8	86,7
Raw Physical functioning	Baseline (n=30)	2,52	1,075	2,75	0,4	4,0	0,0							
	Pre-cycle 3 (n=29)	2,86	0,916	3,00	0,8	4,0	3,3	29	0,40	0,636	0,38	-1,3	1,8	3,3
	Pre-cycle 5 (n=29)	2,90	0,898	3,13	0,9	4,0	3,3	29	0,44	0,708	0,50	-0,8	3,0	3,3
	Pre-cycle 9 (n=29)	2,83	1,006	3,00	0,5	4,0	3,3	29	0,36	0,952	0,50	-2,9	1,8	3,3
	Pre-cycle 13 (n=28)	2,94	0,914	3,13	0,8	4,0	6,7	28	0,43	0,736	0,38	-0,5	2,1	6,7
	Pre-cycle 25 (n=20)	3,11	0,965	3,38	0,0	4,0	33,3	20	0,40	0,920	0,50	-1,3	2,9	33,3
	Pre-cycle 37 (n=4)	3,03	0,832	3,13	2,0	3,9	86,7	4	0,53	0,277	0,63	0,1	0,8	86,7

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.1 PedsQL parent-report scores over time and change from baseline over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Emotional functioning	Baseline (n=30)	68,17	20,781	70,00	25,0	100,0	0,0							
	Pre-cycle 3 (n=29)	77,41	16,509	75,00	50,0	100,0	3,3	29	10,17	19,015	10,00	-35,0	50,0	3,3
	Pre-cycle 5 (n=29)	77,59	16,883	75,00	45,0	100,0	3,3	29	10,34	17,057	15,00	-35,0	40,0	3,3
	Pre-cycle 9 (n=29)	80,17	19,109	85,00	25,0	100,0	3,3	29	12,93	21,938	15,00	-40,0	50,0	3,3
	Pre-cycle 13 (n=28)	83,21	15,469	85,00	40,0	100,0	6,7	28	15,71	19,038	15,00	-25,0	55,0	6,7
	Pre-cycle 25 (n=20)	84,50	17,006	90,00	55,0	100,0	33,3	20	18,50	23,792	17,50	-20,0	55,0	33,3
	Pre-cycle 37 (n=4)	82,50	17,559	82,50	65,0	100,0	86,7	4	25,00	28,868	25,00	-10,0	60,0	86,7
Raw Emotional functioning	Baseline (n=30)	2,73	0,831	2,80	1,0	4,0	0,0							
	Pre-cycle 3 (n=29)	3,10	0,660	3,00	2,0	4,0	3,3	29	0,41	0,761	0,40	-1,4	2,0	3,3
	Pre-cycle 5 (n=29)	3,10	0,675	3,00	1,8	4,0	3,3	29	0,41	0,682	0,60	-1,4	1,6	3,3
	Pre-cycle 9 (n=29)	3,21	0,764	3,40	1,0	4,0	3,3	29	0,52	0,878	0,60	-1,6	2,0	3,3
	Pre-cycle 13 (n=28)	3,33	0,619	3,40	1,6	4,0	6,7	28	0,63	0,762	0,60	-1,0	2,2	6,7
	Pre-cycle 25 (n=20)	3,38	0,680	3,60	2,2	4,0	33,3	20	0,74	0,952	0,70	-0,8	2,2	33,3
	Pre-cycle 37 (n=4)	3,30	0,702	3,30	2,6	4,0	86,7	4	1,00	1,155	1,00	-0,4	2,4	86,7

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.1 PedsQL parent-report scores over time and change from baseline over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Social functioning	Baseline (n=30)	58,17	24,086	55,00	15,0	100,0	0,0							
	Pre-cycle 3 (n=29)	66,38	21,082	65,00	30,0	100,0	3,3	29	8,97	15,945	10,00	-40,0	35,0	3,3
	Pre-cycle 5 (n=29)	70,52	21,059	75,00	15,0	100,0	3,3	29	13,10	22,417	15,00	-25,0	80,0	3,3
	Pre-cycle 9 (n=29)	67,41	23,131	70,00	20,0	100,0	3,3	29	10,00	20,354	10,00	-40,0	50,0	3,3
	Pre-cycle 13 (n=28)	68,75	25,554	70,00	20,0	100,0	6,7	28	10,71	20,580	5,00	-20,0	55,0	6,7
	Pre-cycle 25 (n=20)	73,25	20,214	72,50	35,0	100,0	33,3	20	10,75	24,563	5,00	-30,0	60,0	33,3
	Pre-cycle 37 (n=4)	67,50	25,000	65,00	40,0	100,0	86,7	4	21,25	14,361	20,00	5,0	40,0	86,7
Raw Social functioning	Baseline (n=30)	2,33	0,963	2,20	0,6	4,0	0,0							
	Pre-cycle 3 (n=29)	2,66	0,843	2,60	1,2	4,0	3,3	29	0,36	0,638	0,40	-1,6	1,4	3,3
	Pre-cycle 5 (n=29)	2,82	0,842	3,00	0,6	4,0	3,3	29	0,52	0,897	0,60	-1,0	3,2	3,3
	Pre-cycle 9 (n=29)	2,70	0,925	2,80	0,8	4,0	3,3	29	0,40	0,814	0,40	-1,6	2,0	3,3
	Pre-cycle 13 (n=28)	2,75	1,022	2,80	0,8	4,0	6,7	28	0,43	0,823	0,20	-0,8	2,2	6,7
	Pre-cycle 25 (n=20)	2,93	0,809	2,90	1,4	4,0	33,3	20	0,43	0,983	0,20	-1,2	2,4	33,3
	Pre-cycle 37 (n=4)	2,70	1,000	2,60	1,6	4,0	86,7	4	0,85	0,574	0,80	0,2	1,6	86,7

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.1 PedsQL parent-report scores over time and change from baseline over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=30) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
School functioning score	Baseline (n=26)	62,12	19,695	65,83	8,3	95,0	13,3							
	Pre-cycle 3 (n=27)	64,26	18,898	60,00	25,0	100,0	10,0	23	1,01	20,380	0,00	-30,0	40,0	23,3
	Pre-cycle 5 (n=20)	67,42	19,152	67,50	30,0	100,0	33,3	16	8,33	19,963	5,00	-25,0	41,7	46,7
	Pre-cycle 9 (n=24)	66,25	18,903	65,00	33,3	95,0	20,0	21	5,24	19,524	10,00	-45,0	30,0	30,0
	Pre-cycle 13 (n=24)	67,43	22,029	75,00	20,0	100,0	20,0	22	4,70	15,750	2,50	-25,0	35,0	26,7
	Pre-cycle 25 (n=16)	73,13	22,500	72,50	25,0	100,0	46,7	14	7,74	22,528	5,00	-41,7	50,0	53,3
	Pre-cycle 37 (n=3)	78,33	18,930	70,00	65,0	100,0	90,0	1	NC	NC	NC	25,0	25,0	96,7
Raw School functioning score	Baseline (n=26)	2,48	0,788	2,63	0,3	3,8	13,3							
	Pre-cycle 3 (n=27)	2,57	0,756	2,40	1,0	4,0	10,0	23	0,04	0,815	0,00	-1,2	1,6	23,3
	Pre-cycle 5 (n=20)	2,70	0,766	2,70	1,2	4,0	33,3	16	0,33	0,799	0,20	-1,0	1,7	46,7
	Pre-cycle 9 (n=24)	2,65	0,756	2,60	1,3	3,8	20,0	21	0,21	0,781	0,40	-1,8	1,2	30,0
	Pre-cycle 13 (n=24)	2,70	0,881	3,00	0,8	4,0	20,0	22	0,19	0,630	0,10	-1,0	1,4	26,7
	Pre-cycle 25 (n=16)	2,93	0,900	2,90	1,0	4,0	46,7	14	0,31	0,901	0,20	-1,7	2,0	53,3
	Pre-cycle 37 (n=3)	3,13	0,757	2,80	2,6	4,0	90,0	1	NC	NC	NC	1,0	1,0	96,7

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.2 PedsQL parent-report scores over time and change from baseline over time - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=20)	57,98	19,379	58,15	20,7	88,0	0,0							
	Pre-cycle 3 (n=18)	66,13	17,169	65,76	39,1	97,2	10,0	18	8,71	17,221	4,89	-17,4	43,7	10,0
	Pre-cycle 5 (n=18)	62,71	19,070	64,67	25,0	88,9	10,0	18	6,15	16,375	2,60	-19,6	45,9	10,0
	Pre-cycle 9 (n=19)	67,60	19,556	70,65	34,8	98,9	5,0	19	10,23	16,502	10,03	-20,7	58,7	5,0
	Pre-cycle 13 (n=17)	72,54	12,685	75,00	52,8	94,6	15,0	17	15,52	18,441	18,48	-14,1	57,6	15,0
	Pre-cycle 25 (n=15)	71,63	18,039	73,91	34,8	91,7	25,0	15	14,69	24,080	17,39	-22,8	68,5	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	65,2	65,2	95,0	1	NC	NC	NC	26,3	26,3	95,0
Raw Total Score	Baseline (n=20)	2,32	0,775	2,33	0,8	3,5	0,0							
	Pre-cycle 3 (n=18)	2,65	0,687	2,63	1,6	3,9	10,0	18	0,35	0,689	0,20	-0,7	1,7	10,0
	Pre-cycle 5 (n=18)	2,51	0,763	2,59	1,0	3,6	10,0	18	0,25	0,655	0,10	-0,8	1,8	10,0
	Pre-cycle 9 (n=19)	2,70	0,782	2,83	1,4	4,0	5,0	19	0,41	0,660	0,40	-0,8	2,3	5,0
	Pre-cycle 13 (n=17)	2,90	0,507	3,00	2,1	3,8	15,0	17	0,62	0,738	0,74	-0,6	2,3	15,0
	Pre-cycle 25 (n=15)	2,87	0,722	2,96	1,4	3,7	25,0	15	0,59	0,963	0,70	-0,9	2,7	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	2,6	2,6	95,0	1	NC	NC	NC	1,1	1,1	95,0

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.2 PedsQL parent-report scores over time and change from baseline over time - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Physical functioning	Baseline (n=20)	57,03	23,317	54,69	21,9	100,0	0,0							
	Pre-cycle 3 (n=18)	64,76	19,407	67,19	34,4	96,9	10,0	18	9,55	20,770	9,38	-25,0	43,8	10,0
	Pre-cycle 5 (n=18)	57,64	21,363	57,81	21,9	90,6	10,0	18	2,08	18,658	0,00	-28,1	43,8	10,0
	Pre-cycle 9 (n=19)	68,49	22,442	75,00	28,1	100,0	5,0	19	13,06	21,949	9,38	-21,9	71,9	5,0
	Pre-cycle 13 (n=17)	72,61	18,340	75,00	40,6	100,0	15,0	17	18,75	22,069	21,88	-25,0	65,6	15,0
	Pre-cycle 25 (n=15)	78,54	21,124	87,50	25,0	100,0	25,0	15	25,00	24,493	28,13	-28,1	71,9	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	68,8	68,8	95,0	1	NC	NC	NC	34,4	34,4	95,0
Raw Physical functioning	Baseline (n=20)	2,28	0,933	2,19	0,9	4,0	0,0							
	Pre-cycle 3 (n=18)	2,59	0,776	2,69	1,4	3,9	10,0	18	0,38	0,831	0,38	-1,0	1,8	10,0
	Pre-cycle 5 (n=18)	2,31	0,855	2,31	0,9	3,6	10,0	18	0,08	0,746	0,00	-1,1	1,8	10,0
	Pre-cycle 9 (n=19)	2,74	0,898	3,00	1,1	4,0	5,0	19	0,52	0,878	0,38	-0,9	2,9	5,0
	Pre-cycle 13 (n=17)	2,90	0,734	3,00	1,6	4,0	15,0	17	0,75	0,883	0,88	-1,0	2,6	15,0
	Pre-cycle 25 (n=15)	3,14	0,845	3,50	1,0	4,0	25,0	15	1,00	0,980	1,13	-1,1	2,9	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	2,8	2,8	95,0	1	NC	NC	NC	1,4	1,4	95,0

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.2 PedsQL parent-report scores over time and change from baseline over time - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Emotional functioning	Baseline (n=20)	60,00	21,704	62,50	15,0	90,0	0,0							
	Pre-cycle 3 (n=19)	72,89	20,502	75,00	30,0	100,0	5,0	19	12,89	18,583	10,00	-15,0	50,0	5,0
	Pre-cycle 5 (n=18)	71,11	23,736	75,00	30,0	100,0	10,0	18	11,94	20,229	7,50	-20,0	50,0	10,0
	Pre-cycle 9 (n=19)	74,47	20,876	75,00	35,0	100,0	5,0	19	14,47	23,740	10,00	-30,0	75,0	5,0
	Pre-cycle 13 (n=17)	80,59	15,800	80,00	55,0	100,0	15,0	17	20,29	24,589	15,00	-20,0	70,0	15,0
	Pre-cycle 25 (n=15)	74,00	21,481	75,00	40,0	100,0	25,0	15	13,33	25,542	15,00	-25,0	70,0	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	80,0	80,0	95,0	1	NC	NC	NC	30,0	30,0	95,0
Raw Emotional functioning	Baseline (n=20)	2,40	0,868	2,50	0,6	3,6	0,0							
	Pre-cycle 3 (n=19)	2,92	0,820	3,00	1,2	4,0	5,0	19	0,52	0,743	0,40	-0,6	2,0	5,0
	Pre-cycle 5 (n=18)	2,84	0,949	3,00	1,2	4,0	10,0	18	0,48	0,809	0,30	-0,8	2,0	10,0
	Pre-cycle 9 (n=19)	2,98	0,835	3,00	1,4	4,0	5,0	19	0,58	0,950	0,40	-1,2	3,0	5,0
	Pre-cycle 13 (n=17)	3,22	0,632	3,20	2,2	4,0	15,0	17	0,81	0,984	0,60	-0,8	2,8	15,0
	Pre-cycle 25 (n=15)	2,96	0,859	3,00	1,6	4,0	25,0	15	0,53	1,022	0,60	-1,0	2,8	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	3,2	3,2	95,0	1	NC	NC	NC	1,2	1,2	95,0

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.2 PedsQL parent-report scores over time and change from baseline over time - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Social functioning	Baseline (n=20)	57,38	25,411	60,00	10,0	100,0	0,0							
	Pre-cycle 3 (n=18)	65,56	22,745	65,00	15,0	100,0	10,0	18	6,53	21,337	7,50	-30,0	35,0	10,0
	Pre-cycle 5 (n=18)	64,44	23,319	67,50	15,0	100,0	10,0	18	8,47	17,928	0,00	-20,0	45,0	10,0
	Pre-cycle 9 (n=19)	63,95	26,330	75,00	25,0	100,0	5,0	19	6,71	23,718	5,00	-35,0	65,0	5,0
	Pre-cycle 13 (n=17)	71,18	20,956	75,00	40,0	100,0	15,0	17	13,38	25,965	5,00	-30,0	70,0	15,0
	Pre-cycle 25 (n=15)	64,67	26,013	70,00	25,0	100,0	25,0	15	7,83	32,056	10,00	-45,0	85,0	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	50,0	50,0	95,0	1	NC	NC	NC	15,0	15,0	95,0
Raw Social functioning	Baseline (n=20)	2,30	1,016	2,40	0,4	4,0	0,0							
	Pre-cycle 3 (n=18)	2,62	0,910	2,60	0,6	4,0	10,0	18	0,26	0,853	0,30	-1,2	1,4	10,0
	Pre-cycle 5 (n=18)	2,58	0,933	2,70	0,6	4,0	10,0	18	0,34	0,717	0,00	-0,8	1,8	10,0
	Pre-cycle 9 (n=19)	2,56	1,053	3,00	1,0	4,0	5,0	19	0,27	0,949	0,20	-1,4	2,6	5,0
	Pre-cycle 13 (n=17)	2,85	0,838	3,00	1,6	4,0	15,0	17	0,54	1,039	0,20	-1,2	2,8	15,0
	Pre-cycle 25 (n=15)	2,59	1,041	2,80	1,0	4,0	25,0	15	0,31	1,282	0,40	-1,8	3,4	25,0
	Pre-cycle 37 (n=1)	NC	NC	NC	2,0	2,0	95,0	1	NC	NC	NC	0,6	0,6	95,0

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.2 PedsQL parent-report scores over time and change from baseline over time - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=20) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
School functioning score	Baseline (n=18)	58,89	25,699	62,50	15,0	95,0	10,0							
	Pre-cycle 3 (n=13)	59,23	20,088	50,00	30,0	90,0	35,0	11	0,00	27,203	0,00	-40,0	60,0	45,0
	Pre-cycle 5 (n=13)	62,69	16,785	60,00	45,0	95,0	35,0	11	0,45	21,267	10,00	-40,0	25,0	45,0
	Pre-cycle 9 (n=18)	61,94	23,772	60,00	15,0	100,0	10,0	16	5,00	15,492	10,00	-20,0	25,0	20,0
	Pre-cycle 13 (n=16)	66,56	18,140	67,50	35,0	95,0	20,0	15	8,00	24,553	5,00	-45,0	45,0	25,0
	Pre-cycle 25 (n=13)	61,92	19,742	60,00	20,0	85,0	35,0	12	0,42	30,336	0,00	-40,0	60,0	40,0
	Pre-cycle 37 (n=1)	NC	NC	NC	60,0	60,0	95,0	0	NC	NC	NC	NC	NC	100,0
Raw School functioning score	Baseline (n=18)	2,36	1,028	2,50	0,6	3,8	10,0							
	Pre-cycle 3 (n=13)	2,37	0,804	2,00	1,2	3,6	35,0	11	0,00	1,088	0,00	-1,6	2,4	45,0
	Pre-cycle 5 (n=13)	2,51	0,671	2,40	1,8	3,8	35,0	11	0,02	0,851	0,40	-1,6	1,0	45,0
	Pre-cycle 9 (n=18)	2,48	0,951	2,40	0,6	4,0	10,0	16	0,20	0,620	0,40	-0,8	1,0	20,0
	Pre-cycle 13 (n=16)	2,66	0,726	2,70	1,4	3,8	20,0	15	0,32	0,982	0,20	-1,8	1,8	25,0
	Pre-cycle 25 (n=13)	2,48	0,790	2,40	0,8	3,4	35,0	12	0,02	1,213	0,00	-1,6	2,4	40,0
	Pre-cycle 37 (n=1)	NC	NC	NC	2,4	2,4	95,0	0	NC	NC	NC	NC	NC	100,0

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.3 PedsQL parent-report scores over time and change from baseline over time - PN status at enrollment = Progressive
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=21)	60,42	18,908	58,70	27,2	98,9	0,0							
	Pre-cycle 3 (n=21)	71,79	12,774	70,65	52,2	95,7	0,0	21	11,37	15,863	10,87	-17,4	43,7	0,0
	Pre-cycle 5 (n=20)	70,83	13,925	72,13	45,7	94,4	4,8	20	10,97	15,137	11,93	-15,6	45,9	4,8
	Pre-cycle 9 (n=21)	70,11	16,537	70,65	39,1	95,7	0,0	21	9,69	17,052	11,96	-20,7	37,5	0,0
	Pre-cycle 13 (n=20)	73,37	15,232	71,20	52,2	98,9	4,8	20	13,73	15,621	15,22	-14,1	43,2	4,8
	Pre-cycle 25 (n=13)	74,00	18,137	77,78	34,8	100,0	38,1	13	13,26	20,186	18,48	-16,3	43,2	38,1
	Pre-cycle 37 (n=4)	70,09	12,063	69,57	56,5	84,7	81,0	4	22,21	9,254	25,45	8,6	29,3	81,0
Raw Total Score	Baseline (n=21)	2,42	0,756	2,35	1,1	4,0	0,0							
	Pre-cycle 3 (n=21)	2,87	0,511	2,83	2,1	3,8	0,0	21	0,45	0,635	0,43	-0,7	1,7	0,0
	Pre-cycle 5 (n=20)	2,83	0,557	2,89	1,8	3,8	4,8	20	0,44	0,605	0,48	-0,6	1,8	4,8
	Pre-cycle 9 (n=21)	2,80	0,661	2,83	1,6	3,8	0,0	21	0,39	0,682	0,48	-0,8	1,5	0,0
	Pre-cycle 13 (n=20)	2,93	0,609	2,85	2,1	4,0	4,8	20	0,55	0,625	0,61	-0,6	1,7	4,8
	Pre-cycle 25 (n=13)	2,96	0,725	3,11	1,4	4,0	38,1	13	0,53	0,807	0,74	-0,7	1,7	38,1
	Pre-cycle 37 (n=4)	2,80	0,483	2,78	2,3	3,4	81,0	4	0,89	0,370	1,02	0,3	1,2	81,0

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.3 PedsQL parent-report scores over time and change from baseline over time - PN status at enrollment = Progressive
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Physical functioning	Baseline (n=21)	62,20	24,365	68,75	21,9	100,0	0,0							
	Pre-cycle 3 (n=21)	78,27	11,460	78,13	56,3	100,0	0,0	21	16,07	19,169	12,50	-25,0	43,8	0,0
	Pre-cycle 5 (n=20)	71,56	18,020	73,44	43,8	100,0	4,8	20	8,91	18,145	12,50	-28,1	43,8	4,8
	Pre-cycle 9 (n=21)	73,51	19,481	75,00	28,1	100,0	0,0	21	11,31	17,910	12,50	-15,6	43,8	0,0
	Pre-cycle 13 (n=20)	74,84	16,705	78,13	40,6	100,0	4,8	20	13,75	22,475	10,94	-25,0	56,3	4,8
	Pre-cycle 25 (n=13)	78,85	21,992	87,50	25,0	100,0	38,1	13	15,87	22,370	18,75	-28,1	56,3	38,1
	Pre-cycle 37 (n=4)	68,75	15,309	68,75	50,0	87,5	81,0	4	17,97	12,853	17,19	3,1	34,4	81,0
Raw Physical functioning	Baseline (n=21)	2,49	0,975	2,75	0,9	4,0	0,0							
	Pre-cycle 3 (n=21)	3,13	0,458	3,13	2,3	4,0	0,0	21	0,64	0,767	0,50	-1,0	1,8	0,0
	Pre-cycle 5 (n=20)	2,86	0,721	2,94	1,8	4,0	4,8	20	0,36	0,726	0,50	-1,1	1,8	4,8
	Pre-cycle 9 (n=21)	2,94	0,779	3,00	1,1	4,0	0,0	21	0,45	0,716	0,50	-0,6	1,8	0,0
	Pre-cycle 13 (n=20)	2,99	0,668	3,13	1,6	4,0	4,8	20	0,55	0,899	0,44	-1,0	2,3	4,8
	Pre-cycle 25 (n=13)	3,15	0,880	3,50	1,0	4,0	38,1	13	0,63	0,895	0,75	-1,1	2,3	38,1
	Pre-cycle 37 (n=4)	2,75	0,612	2,75	2,0	3,5	81,0	4	0,72	0,514	0,69	0,1	1,4	81,0

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.3 PedsQL parent-report scores over time and change from baseline over time - PN status at enrollment = Progressive
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Emotional functioning	Baseline (n=21)	62,38	22,507	65,00	25,0	100,0	0,0							
	Pre-cycle 3 (n=21)	74,29	17,050	75,00	50,0	100,0	0,0	21	11,90	22,939	15,00	-35,0	50,0	0,0
	Pre-cycle 5 (n=20)	73,75	19,526	70,00	35,0	100,0	4,8	20	12,00	21,300	15,00	-35,0	50,0	4,8
	Pre-cycle 9 (n=21)	78,57	19,567	80,00	35,0	100,0	0,0	21	16,19	24,794	15,00	-40,0	50,0	0,0
	Pre-cycle 13 (n=20)	79,75	15,768	82,50	45,0	100,0	4,8	20	18,25	21,292	15,00	-10,0	70,0	4,8
	Pre-cycle 25 (n=13)	76,54	19,299	80,00	40,0	100,0	38,1	13	20,77	25,646	20,00	-20,0	55,0	38,1
	Pre-cycle 37 (n=4)	77,50	13,229	75,00	65,0	95,0	81,0	4	27,50	28,723	30,00	-10,0	60,0	81,0
Raw Emotional functioning	Baseline (n=21)	2,50	0,900	2,60	1,0	4,0	0,0							
	Pre-cycle 3 (n=21)	2,97	0,682	3,00	2,0	4,0	0,0	21	0,48	0,918	0,60	-1,4	2,0	0,0
	Pre-cycle 5 (n=20)	2,95	0,781	2,80	1,4	4,0	4,8	20	0,48	0,852	0,60	-1,4	2,0	4,8
	Pre-cycle 9 (n=21)	3,14	0,783	3,20	1,4	4,0	0,0	21	0,65	0,992	0,60	-1,6	2,0	0,0
	Pre-cycle 13 (n=20)	3,19	0,631	3,30	1,8	4,0	4,8	20	0,73	0,852	0,60	-0,4	2,8	4,8
	Pre-cycle 25 (n=13)	3,06	0,772	3,20	1,6	4,0	38,1	13	0,83	1,026	0,80	-0,8	2,2	38,1
	Pre-cycle 37 (n=4)	3,10	0,529	3,00	2,6	3,8	81,0	4	1,10	1,149	1,20	-0,4	2,4	81,0

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.3 PedsQL parent-report scores over time and change from baseline over time - PN status at enrollment = Progressive
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Social functioning	Baseline (n=21)	55,48	22,908	55,00	20,0	100,0	0,0							
	Pre-cycle 3 (n=21)	66,67	20,083	65,00	35,0	100,0	0,0	21	11,19	16,651	15,00	-30,0	35,0	0,0
	Pre-cycle 5 (n=20)	68,25	16,163	67,50	25,0	95,0	4,8	20	14,00	19,304	15,00	-15,0	45,0	4,8
	Pre-cycle 9 (n=21)	59,76	23,584	65,00	20,0	90,0	0,0	21	4,29	21,289	0,00	-35,0	50,0	0,0
	Pre-cycle 13 (n=20)	67,25	24,787	67,50	30,0	100,0	4,8	20	12,50	18,743	10,00	-20,0	45,0	4,8
	Pre-cycle 25 (n=13)	65,00	22,546	65,00	35,0	100,0	38,1	13	6,92	26,104	5,00	-40,0	60,0	38,1
	Pre-cycle 37 (n=4)	65,00	26,458	60,00	40,0	100,0	81,0	4	23,75	11,087	20,00	15,0	40,0	81,0
Raw Social functioning	Baseline (n=21)	2,22	0,916	2,20	0,8	4,0	0,0							
	Pre-cycle 3 (n=21)	2,67	0,803	2,60	1,4	4,0	0,0	21	0,45	0,666	0,60	-1,2	1,4	0,0
	Pre-cycle 5 (n=20)	2,73	0,647	2,70	1,0	3,8	4,8	20	0,56	0,772	0,60	-0,6	1,8	4,8
	Pre-cycle 9 (n=21)	2,39	0,943	2,60	0,8	3,6	0,0	21	0,17	0,852	0,00	-1,4	2,0	0,0
	Pre-cycle 13 (n=20)	2,69	0,991	2,70	1,2	4,0	4,8	20	0,50	0,750	0,40	-0,8	1,8	4,8
	Pre-cycle 25 (n=13)	2,60	0,902	2,60	1,4	4,0	38,1	13	0,28	1,044	0,20	-1,6	2,4	38,1
	Pre-cycle 37 (n=4)	2,60	1,058	2,40	1,6	4,0	81,0	4	0,95	0,443	0,80	0,6	1,6	81,0

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.3 PedsQL parent-report scores over time and change from baseline over time - PN status at enrollment = Progressive
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=21) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
School functioning score	Baseline (n=17)	63,73	25,931	70,00	8,3	95,0	19,0							
	Pre-cycle 3 (n=19)	62,89	19,026	60,00	25,0	100,0	9,5	15	-6,00	19,291	-5,00	-30,0	25,0	28,6
	Pre-cycle 5 (n=16)	65,31	18,927	65,00	40,0	100,0	23,8	12	4,31	23,382	0,00	-40,0	41,7	42,9
	Pre-cycle 9 (n=18)	65,19	21,112	60,00	33,3	100,0	14,3	15	3,67	21,084	10,00	-45,0	30,0	28,6
	Pre-cycle 13 (n=17)	69,02	23,489	75,00	20,0	100,0	19,0	14	5,00	13,156	5,00	-25,0	25,0	33,3
	Pre-cycle 25 (n=8)	72,50	20,178	70,00	45,0	100,0	61,9	7	-5,00	19,579	-5,00	-40,0	20,0	66,7
	Pre-cycle 37 (n=3)	65,00	5,000	65,00	60,0	70,0	85,7	0	NC	NC	NC	NC	NC	100,0
Raw School functioning score	Baseline (n=17)	2,55	1,037	2,80	0,3	3,8	19,0							
	Pre-cycle 3 (n=19)	2,52	0,761	2,40	1,0	4,0	9,5	15	-0,24	0,772	-0,20	-1,2	1,0	28,6
	Pre-cycle 5 (n=16)	2,61	0,757	2,60	1,6	4,0	23,8	12	0,17	0,935	0,00	-1,6	1,7	42,9
	Pre-cycle 9 (n=18)	2,61	0,844	2,40	1,3	4,0	14,3	15	0,15	0,843	0,40	-1,8	1,2	28,6
	Pre-cycle 13 (n=17)	2,76	0,940	3,00	0,8	4,0	19,0	14	0,20	0,526	0,20	-1,0	1,0	33,3
	Pre-cycle 25 (n=8)	2,90	0,807	2,80	1,8	4,0	61,9	7	-0,20	0,783	-0,20	-1,6	0,8	66,7
	Pre-cycle 37 (n=3)	2,60	0,200	2,60	2,4	2,8	85,7	0	NC	NC	NC	NC	NC	100,0

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.4 PedsQL parent-report scores over time and change from baseline over time
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=15)	65,34	16,940	69,57	43,5	93,5	0,0							
	Pre-cycle 3 (n=14)	69,38	17,305	65,76	39,1	100,0	6,7	14	4,34	11,130	4,89	-17,4	20,7	6,7
	Pre-cycle 5 (n=14)	70,89	20,733	76,09	25,0	94,6	6,7	14	5,85	11,128	8,03	-19,6	21,7	6,7
	Pre-cycle 9 (n=14)	73,51	15,883	72,83	34,8	94,6	6,7	14	8,48	12,907	9,01	-12,0	26,1	6,7
	Pre-cycle 13 (n=12)	78,09	15,603	80,43	51,1	97,8	20,0	12	9,64	15,484	5,15	-9,8	40,2	20,0
	Pre-cycle 25 (n=12)	76,93	16,560	79,89	54,3	100,0	20,0	12	8,48	22,977	7,07	-29,0	53,3	20,0
	Pre-cycle 37 (n=1)	NC	NC	NC	90,2	90,2	93,3	1	NC	NC	NC	16,3	16,3	93,3
Raw Total Score	Baseline (n=15)	2,61	0,678	2,78	1,7	3,7	0,0							
	Pre-cycle 3 (n=14)	2,78	0,692	2,63	1,6	4,0	6,7	14	0,17	0,445	0,20	-0,7	0,8	6,7
	Pre-cycle 5 (n=14)	2,84	0,829	3,04	1,0	3,8	6,7	14	0,23	0,445	0,32	-0,8	0,9	6,7
	Pre-cycle 9 (n=14)	2,94	0,635	2,91	1,4	3,8	6,7	14	0,34	0,516	0,36	-0,5	1,0	6,7
	Pre-cycle 13 (n=12)	3,12	0,624	3,22	2,0	3,9	20,0	12	0,39	0,619	0,21	-0,4	1,6	20,0
	Pre-cycle 25 (n=12)	3,08	0,662	3,20	2,2	4,0	20,0	12	0,34	0,919	0,28	-1,2	2,1	20,0
	Pre-cycle 37 (n=1)	NC	NC	NC	3,6	3,6	93,3	1	NC	NC	NC	0,7	0,7	93,3

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.4 PedsQL parent-report scores over time and change from baseline over time
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Physical functioning	Baseline (n=15)	64,38	25,078	75,00	25,0	96,9	0,0							
	Pre-cycle 3 (n=14)	65,40	23,336	68,75	18,8	100,0	6,7	14	2,68	15,594	4,69	-31,3	25,0	6,7
	Pre-cycle 5 (n=14)	67,63	24,287	73,44	25,0	100,0	6,7	14	4,91	14,174	7,81	-25,0	28,1	6,7
	Pre-cycle 9 (n=14)	68,97	27,062	78,13	18,8	100,0	6,7	14	6,25	28,850	12,50	-71,9	37,5	6,7
	Pre-cycle 13 (n=12)	79,43	22,865	79,69	18,8	100,0	20,0	12	13,28	16,108	12,50	-6,3	46,9	20,0
	Pre-cycle 25 (n=12)	76,82	27,934	87,50	0,0	100,0	20,0	12	10,68	28,810	7,81	-31,3	71,9	20,0
	Pre-cycle 37 (n=1)	NC	NC	NC	96,9	96,9	93,3	1	NC	NC	NC	15,6	15,6	93,3
Raw Physical functioning	Baseline (n=15)	2,58	1,003	3,00	1,0	3,9	0,0							
	Pre-cycle 3 (n=14)	2,62	0,933	2,75	0,8	4,0	6,7	14	0,11	0,624	0,19	-1,3	1,0	6,7
	Pre-cycle 5 (n=14)	2,71	0,971	2,94	1,0	4,0	6,7	14	0,20	0,567	0,31	-1,0	1,1	6,7
	Pre-cycle 9 (n=14)	2,76	1,082	3,13	0,8	4,0	6,7	14	0,25	1,154	0,50	-2,9	1,5	6,7
	Pre-cycle 13 (n=12)	3,18	0,915	3,19	0,8	4,0	20,0	12	0,53	0,644	0,50	-0,3	1,9	20,0
	Pre-cycle 25 (n=12)	3,07	1,117	3,50	0,0	4,0	20,0	12	0,43	1,152	0,31	-1,3	2,9	20,0
	Pre-cycle 37 (n=1)	NC	NC	NC	3,9	3,9	93,3	1	NC	NC	NC	0,6	0,6	93,3

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.4 PedsQL parent-report scores over time and change from baseline over time
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Emotional functioning	Baseline (n=15)	69,00	19,011	65,00	35,0	100,0	0,0							
	Pre-cycle 3 (n=14)	79,29	21,200	85,00	30,0	100,0	6,7	14	9,64	15,375	5,00	-15,0	35,0	6,7
	Pre-cycle 5 (n=14)	78,21	21,448	85,00	30,0	100,0	6,7	14	8,57	17,478	10,00	-20,0	35,0	6,7
	Pre-cycle 9 (n=14)	77,50	23,018	87,50	25,0	100,0	6,7	14	7,86	19,682	7,50	-40,0	40,0	6,7
	Pre-cycle 13 (n=12)	88,33	16,833	92,50	40,0	100,0	20,0	12	15,00	21,950	15,00	-25,0	45,0	20,0
	Pre-cycle 25 (n=12)	79,58	20,500	80,00	50,0	100,0	20,0	12	6,25	22,272	7,50	-25,0	40,0	20,0
	Pre-cycle 37 (n=1)	NC	NC	NC	100,0	100,0	93,3	1	NC	NC	NC	20,0	20,0	93,3
Raw Emotional functioning	Baseline (n=15)	2,76	0,760	2,60	1,4	4,0	0,0							
	Pre-cycle 3 (n=14)	3,17	0,848	3,40	1,2	4,0	6,7	14	0,39	0,615	0,20	-0,6	1,4	6,7
	Pre-cycle 5 (n=14)	3,13	0,858	3,40	1,2	4,0	6,7	14	0,34	0,699	0,40	-0,8	1,4	6,7
	Pre-cycle 9 (n=14)	3,10	0,921	3,50	1,0	4,0	6,7	14	0,31	0,787	0,30	-1,6	1,6	6,7
	Pre-cycle 13 (n=12)	3,53	0,673	3,70	1,6	4,0	20,0	12	0,60	0,878	0,60	-1,0	1,8	20,0
	Pre-cycle 25 (n=12)	3,18	0,820	3,20	2,0	4,0	20,0	12	0,25	0,891	0,30	-1,0	1,6	20,0
	Pre-cycle 37 (n=1)	NC	NC	NC	4,0	4,0	93,3	1	NC	NC	NC	0,8	0,8	93,3

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.4 PedsQL parent-report scores over time and change from baseline over time
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]											
		Absolute values						Change from baseline					
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Social functioning	Baseline (n=15)	66,33	20,999	65,00	35,0	100,0	0,0							
	Pre-cycle 3 (n=14)	70,00	20,939	70,00	40,0	100,0	6,7	14	3,21	13,673	2,50	-30,0	25,0	6,7
	Pre-cycle 5 (n=14)	69,64	28,384	77,50	15,0	100,0	6,7	14	2,86	15,654	0,00	-25,0	30,0	6,7
	Pre-cycle 9 (n=14)	78,21	20,249	82,50	25,0	100,0	6,7	14	11,43	13,927	15,00	-15,0	30,0	6,7
	Pre-cycle 13 (n=12)	75,83	21,302	77,50	45,0	100,0	20,0	12	4,17	19,637	0,00	-30,0	35,0	20,0
	Pre-cycle 25 (n=12)	79,17	19,287	82,50	45,0	100,0	20,0	12	7,50	28,324	5,00	-45,0	45,0	20,0
	Pre-cycle 37 (n=1)	NC	NC	NC	60,0	60,0	93,3	1	NC	NC	NC	5,0	5,0	93,3
Raw Social functioning	Baseline (n=15)	2,65	0,840	2,60	1,4	4,0	0,0							
	Pre-cycle 3 (n=14)	2,80	0,838	2,80	1,6	4,0	6,7	14	0,13	0,547	0,10	-1,2	1,0	6,7
	Pre-cycle 5 (n=14)	2,79	1,135	3,10	0,6	4,0	6,7	14	0,11	0,626	0,00	-1,0	1,2	6,7
	Pre-cycle 9 (n=14)	3,13	0,810	3,30	1,0	4,0	6,7	14	0,46	0,557	0,60	-0,6	1,2	6,7
	Pre-cycle 13 (n=12)	3,03	0,852	3,10	1,8	4,0	20,0	12	0,17	0,785	0,00	-1,2	1,4	20,0
	Pre-cycle 25 (n=12)	3,17	0,771	3,30	1,8	4,0	20,0	12	0,30	1,133	0,20	-1,8	1,8	20,0
	Pre-cycle 37 (n=1)	NC	NC	NC	2,4	2,4	93,3	1	NC	NC	NC	0,2	0,2	93,3

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.4 PedsQL parent-report scores over time and change from baseline over time
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=15) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
School functioning score	Baseline (n=15)	61,78	17,722	60,00	35,0	95,0	0,0							
	Pre-cycle 3 (n=12)	64,17	21,088	62,50	30,0	100,0	20,0	12	2,78	19,699	0,00	-40,0	33,3	20,0
	Pre-cycle 5 (n=9)	73,70	20,629	80,00	30,0	100,0	40,0	9	11,85	17,901	15,00	-25,0	35,0	40,0
	Pre-cycle 9 (n=12)	71,39	16,343	73,33	40,0	95,0	20,0	12	10,00	11,078	10,00	-10,0	30,0	20,0
	Pre-cycle 13 (n=12)	67,50	20,944	75,00	25,0	100,0	20,0	12	4,03	23,011	2,50	-45,0	40,0	20,0
	Pre-cycle 25 (n=11)	70,45	24,945	75,00	25,0	100,0	26,7	11	4,85	28,465	5,00	-41,7	50,0	26,7
	Pre-cycle 37 (n=1)	NC	NC	NC	100,0	100,0	93,3	1	NC	NC	NC	25,0	25,0	93,3
Raw School functioning score	Baseline (n=15)	2,47	0,709	2,40	1,4	3,8	0,0							
	Pre-cycle 3 (n=12)	2,57	0,844	2,50	1,2	4,0	20,0	12	0,11	0,788	0,00	-1,6	1,3	20,0
	Pre-cycle 5 (n=9)	2,95	0,825	3,20	1,2	4,0	40,0	9	0,47	0,716	0,60	-1,0	1,4	40,0
	Pre-cycle 9 (n=12)	2,86	0,654	2,93	1,6	3,8	20,0	12	0,40	0,443	0,40	-0,4	1,2	20,0
	Pre-cycle 13 (n=12)	2,70	0,838	3,00	1,0	4,0	20,0	12	0,16	0,920	0,10	-1,8	1,6	20,0
	Pre-cycle 25 (n=11)	2,82	0,998	3,00	1,0	4,0	26,7	11	0,19	1,139	0,20	-1,7	2,0	26,7
	Pre-cycle 37 (n=1)	NC	NC	NC	4,0	4,0	93,3	1	NC	NC	NC	1,0	1,0	93,3

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.5 PedsQL parent-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Total Score	Baseline (n=14)	56,47	20,930	58,70	20,7	88,0	0,0							
	Pre-cycle 3 (n=12)	62,32	17,583	53,80	42,4	97,2	14,3	12	8,49	14,366	10,39	-21,7	29,3	14,3
	Pre-cycle 5 (n=13)	63,23	18,002	63,04	30,6	87,0	7,1	13	9,19	14,066	9,78	-11,4	45,7	7,1
	Pre-cycle 9 (n=13)	65,61	20,898	58,70	39,1	98,9	7,1	13	11,57	18,675	10,03	-23,9	58,7	7,1
	Pre-cycle 13 (n=13)	68,89	15,230	75,00	39,1	91,7	7,1	13	14,85	18,500	18,48	-8,7	57,6	7,1
	Pre-cycle 25 (n=10)	73,15	16,365	71,74	38,0	91,3	28,6	10	18,66	21,244	17,39	-8,7	68,5	28,6
Raw Total Score	Baseline (n=14)	2,26	0,837	2,35	0,8	3,5	0,0							
	Pre-cycle 3 (n=12)	2,49	0,703	2,15	1,7	3,9	14,3	12	0,34	0,575	0,42	-0,9	1,2	14,3
	Pre-cycle 5 (n=13)	2,53	0,720	2,52	1,2	3,5	7,1	13	0,37	0,563	0,39	-0,5	1,8	7,1
	Pre-cycle 9 (n=13)	2,62	0,836	2,35	1,6	4,0	7,1	13	0,46	0,747	0,40	-1,0	2,3	7,1
	Pre-cycle 13 (n=13)	2,76	0,609	3,00	1,6	3,7	7,1	13	0,59	0,740	0,74	-0,3	2,3	7,1
	Pre-cycle 25 (n=10)	2,93	0,655	2,87	1,5	3,7	28,6	10	0,75	0,850	0,70	-0,3	2,7	28,6

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.5 PedsQL parent-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Physical functioning	Baseline (n=14)	54,02	27,935	53,13	9,4	100,0	0,0							
	Pre-cycle 3 (n=12)	56,77	27,140	53,13	18,8	100,0	14,3	12	7,03	14,359	9,38	-18,8	28,1	14,3
	Pre-cycle 5 (n=13)	58,65	27,633	56,25	21,9	100,0	7,1	13	8,17	23,334	6,25	-25,0	75,0	7,1
	Pre-cycle 9 (n=13)	64,77	27,545	65,63	12,5	100,0	7,1	13	14,29	24,179	9,38	-21,9	71,9	7,1
	Pre-cycle 13 (n=13)	64,90	24,211	65,63	18,8	96,9	7,1	13	14,42	20,711	9,38	-9,4	65,6	7,1
	Pre-cycle 25 (n=10)	78,44	17,949	84,38	50,0	96,9	28,6	10	24,06	21,753	25,00	-6,3	71,9	28,6
Raw Physical functioning	Baseline (n=14)	2,16	1,117	2,13	0,4	4,0	0,0							
	Pre-cycle 3 (n=12)	2,27	1,086	2,13	0,8	4,0	14,3	12	0,28	0,574	0,38	-0,8	1,1	14,3
	Pre-cycle 5 (n=13)	2,35	1,105	2,25	0,9	4,0	7,1	13	0,33	0,933	0,25	-1,0	3,0	7,1
	Pre-cycle 9 (n=13)	2,59	1,102	2,63	0,5	4,0	7,1	13	0,57	0,967	0,38	-0,9	2,9	7,1
	Pre-cycle 13 (n=13)	2,60	0,968	2,63	0,8	3,9	7,1	13	0,58	0,828	0,38	-0,4	2,6	7,1
	Pre-cycle 25 (n=10)	3,14	0,718	3,38	2,0	3,9	28,6	10	0,96	0,870	1,00	-0,3	2,9	28,6

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.5 PedsQL parent-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Emotional functioning	Baseline (n=14)	64,29	22,690	67,50	15,0	95,0	0,0							
	Pre-cycle 3 (n=13)	73,85	17,097	65,00	50,0	100,0	7,1	13	11,92	15,212	10,00	-5,0	50,0	7,1
	Pre-cycle 5 (n=13)	73,85	19,595	75,00	35,0	100,0	7,1	13	11,92	14,221	15,00	-15,0	35,0	7,1
	Pre-cycle 9 (n=13)	77,31	17,983	80,00	45,0	100,0	7,1	13	15,38	21,743	10,00	-15,0	75,0	7,1
	Pre-cycle 13 (n=13)	80,38	13,144	80,00	65,0	100,0	7,1	13	18,46	21,736	15,00	-20,0	60,0	7,1
	Pre-cycle 25 (n=10)	85,00	19,437	92,50	45,0	100,0	28,6	10	22,50	23,363	12,50	0,0	70,0	28,6
Raw Emotional functioning	Baseline (n=14)	2,57	0,908	2,70	0,6	3,8	0,0							
	Pre-cycle 3 (n=13)	2,95	0,684	2,60	2,0	4,0	7,1	13	0,48	0,608	0,40	-0,2	2,0	7,1
	Pre-cycle 5 (n=13)	2,95	0,784	3,00	1,4	4,0	7,1	13	0,48	0,569	0,60	-0,6	1,4	7,1
	Pre-cycle 9 (n=13)	3,09	0,719	3,20	1,8	4,0	7,1	13	0,62	0,870	0,40	-0,6	3,0	7,1
	Pre-cycle 13 (n=13)	3,22	0,526	3,20	2,6	4,0	7,1	13	0,74	0,869	0,60	-0,8	2,4	7,1
	Pre-cycle 25 (n=10)	3,40	0,777	3,70	1,8	4,0	28,6	10	0,90	0,935	0,50	0,0	2,8	28,6

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 2.12.3.2.5 PedsQL parent-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]												
		Absolute values						Change from baseline						
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
Social functioning	Baseline (n=14)	52,32	28,831	45,00	10,0	100,0	0,0							
	Pre-cycle 3 (n=12)	60,42	24,996	62,50	15,0	100,0	14,3	12	8,13	24,147	10,00	-40,0	35,0	14,3
	Pre-cycle 5 (n=13)	66,54	23,397	70,00	25,0	100,0	7,1	13	16,35	25,873	12,50	-10,0	80,0	7,1
	Pre-cycle 9 (n=13)	63,08	26,024	55,00	30,0	100,0	7,1	13	12,88	28,171	5,00	-40,0	65,0	7,1
	Pre-cycle 13 (n=13)	67,69	24,884	65,00	20,0	100,0	7,1	13	17,50	29,226	5,00	-20,0	70,0	7,1
	Pre-cycle 25 (n=10)	64,00	25,798	70,00	25,0	100,0	28,6	10	15,25	30,651	10,00	-15,0	85,0	28,6
Raw Social functioning	Baseline (n=14)	2,09	1,153	1,80	0,4	4,0	0,0							
	Pre-cycle 3 (n=12)	2,42	1,000	2,50	0,6	4,0	14,3	12	0,33	0,966	0,40	-1,6	1,4	14,3
	Pre-cycle 5 (n=13)	2,66	0,936	2,80	1,0	4,0	7,1	13	0,65	1,035	0,50	-0,4	3,2	7,1
	Pre-cycle 9 (n=13)	2,52	1,041	2,20	1,2	4,0	7,1	13	0,52	1,127	0,20	-1,6	2,6	7,1
	Pre-cycle 13 (n=13)	2,71	0,995	2,60	0,8	4,0	7,1	13	0,70	1,169	0,20	-0,8	2,8	7,1
	Pre-cycle 25 (n=10)	2,56	1,032	2,80	1,0	4,0	28,6	10	0,61	1,226	0,40	-0,6	3,4	28,6

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

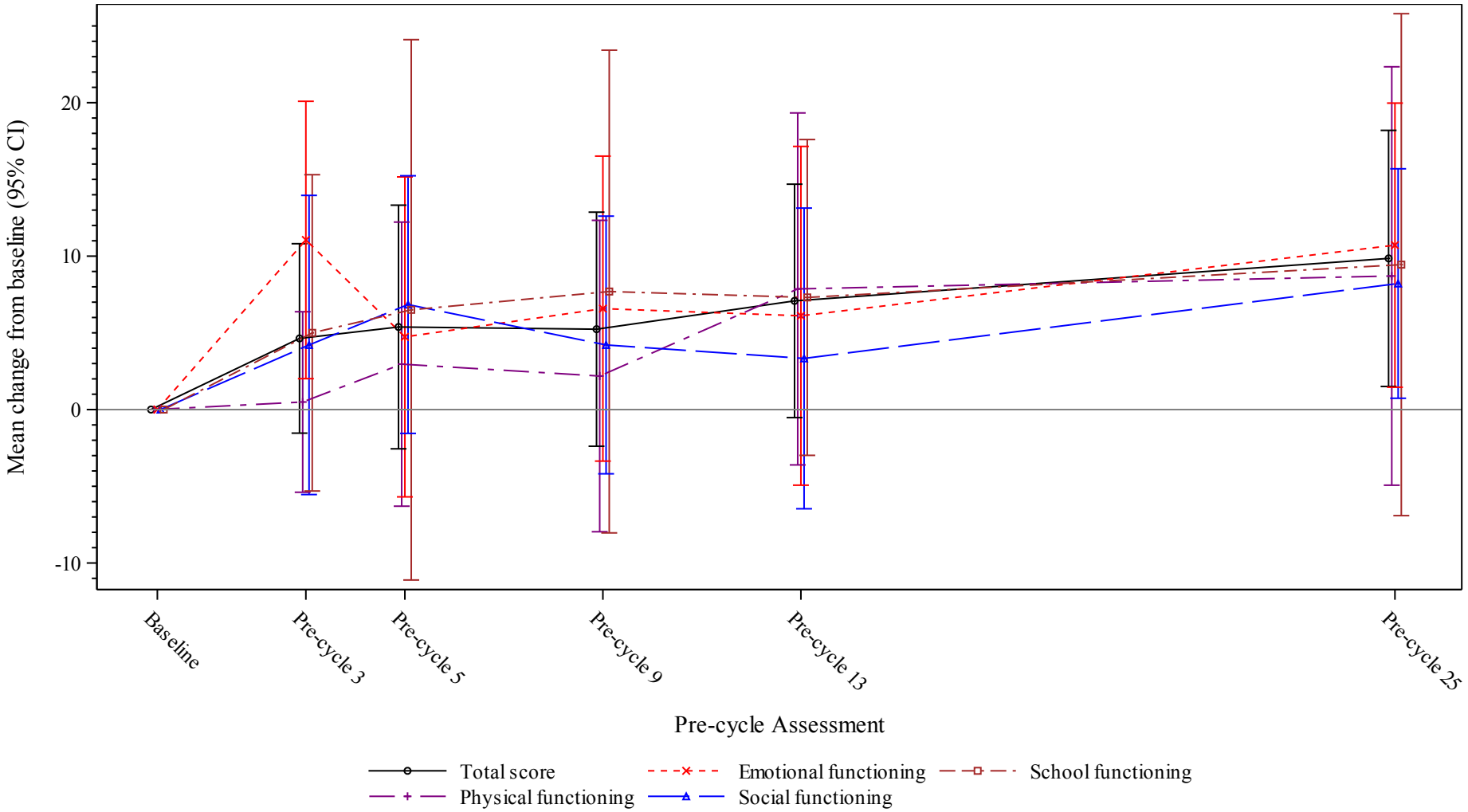
Table 2.12.3.2.5 PedsQL parent-report scores over time and change from baseline over time - PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

		Selumetinib 25 mg/m² BID (N=14) [a]											
		Absolute values						Change from baseline					
PedsQL parent report score	Time point	Mean	SD	Median	Min	Max	%missing [b]	n	Mean	SD	Median	Min	Max	%missing [b]
School functioning score	Baseline (n=12)	55,42	22,101	65,00	15,0	80,0	14,3							
	Pre-cycle 3 (n=9)	60,00	18,875	55,00	40,0	95,0	35,7	7	11,43	30,375	5,00	-30,0	60,0	50,0
	Pre-cycle 5 (n=8)	56,88	8,839	55,00	45,0	70,0	42,9	6	-3,33	17,224	-5,00	-30,0	15,0	57,1
	Pre-cycle 9 (n=12)	56,25	23,561	55,00	15,0	100,0	14,3	10	1,50	18,864	5,00	-40,0	20,0	28,6
	Pre-cycle 13 (n=11)	63,64	15,015	65,00	35,0	80,0	21,4	11	9,55	23,394	5,00	-25,0	45,0	21,4
	Pre-cycle 25 (n=10)	62,00	19,748	65,00	20,0	85,0	28,6	8	11,88	28,276	7,50	-25,0	60,0	42,9
Raw School functioning score	Baseline (n=12)	2,22	0,884	2,60	0,6	3,2	14,3							
	Pre-cycle 3 (n=9)	2,40	0,755	2,20	1,6	3,8	35,7	7	0,46	1,215	0,20	-1,2	2,4	50,0
	Pre-cycle 5 (n=8)	2,28	0,354	2,20	1,8	2,8	42,9	6	-0,13	0,689	-0,20	-1,2	0,6	57,1
	Pre-cycle 9 (n=12)	2,25	0,942	2,20	0,6	4,0	14,3	10	0,06	0,755	0,20	-1,6	0,8	28,6
	Pre-cycle 13 (n=11)	2,55	0,601	2,60	1,4	3,2	21,4	11	0,38	0,936	0,20	-1,0	1,8	21,4
	Pre-cycle 25 (n=10)	2,48	0,790	2,60	0,8	3,4	28,6	8	0,48	1,131	0,30	-1,0	2,4	42,9

[a] Parents/legal guardians of children 2 to 18 years of age at enrolment completed the parent proxy measures of the PedsQL.
[b] Calculated from the number of participants who completed each item at each time point (n) and the number of expected completed forms from the FAS (N) [N-n]/N x 100.
NC = Not Calculated. Max = Maximum. Min = Minimum. SD = Standard deviation.

Figure 2.12.3.3.1 Mean change from baseline of PedsQL self-report transformed scores - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

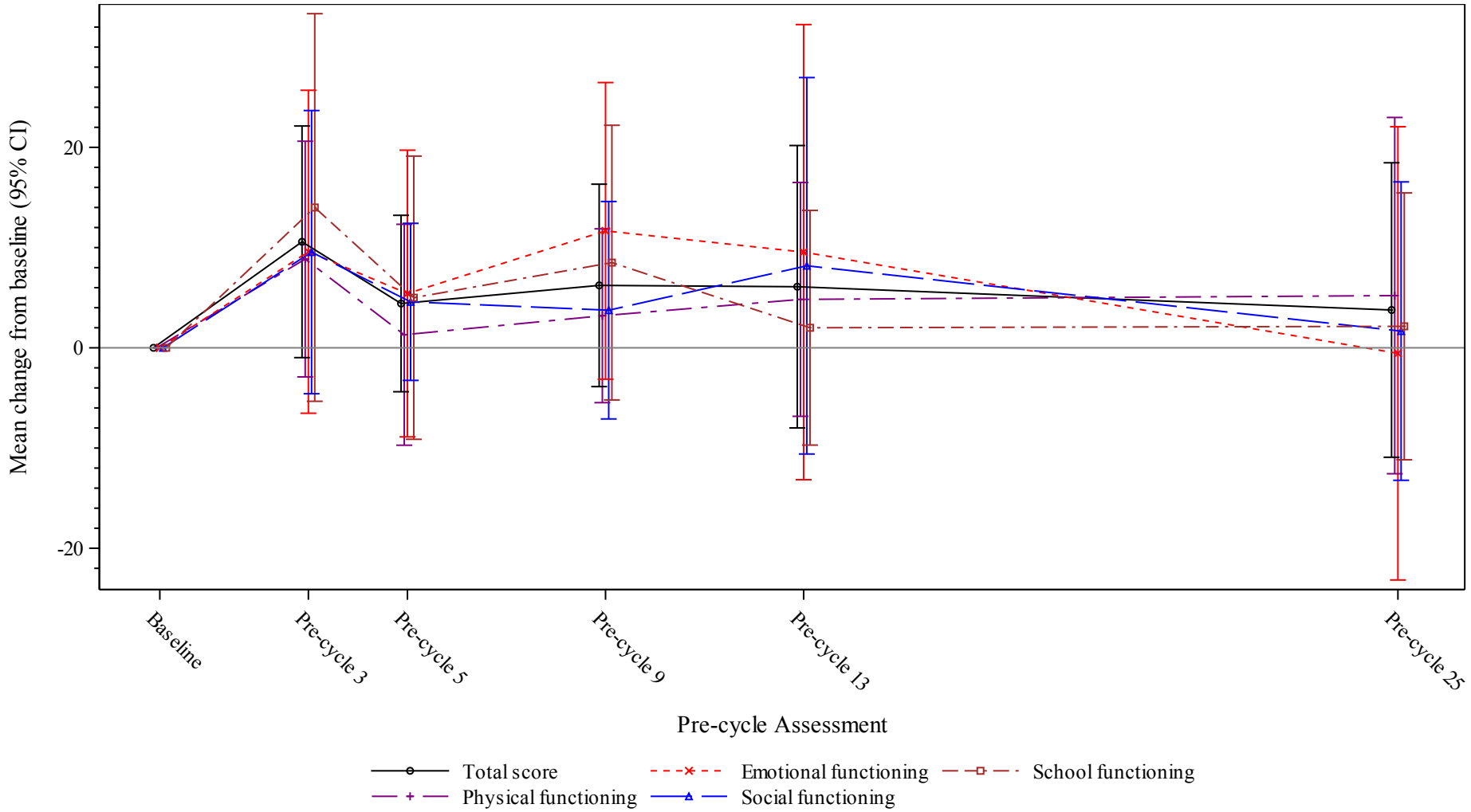
N = 21



Note: Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.3.2 Mean change from baseline of PedsQL self-report transformed scores - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

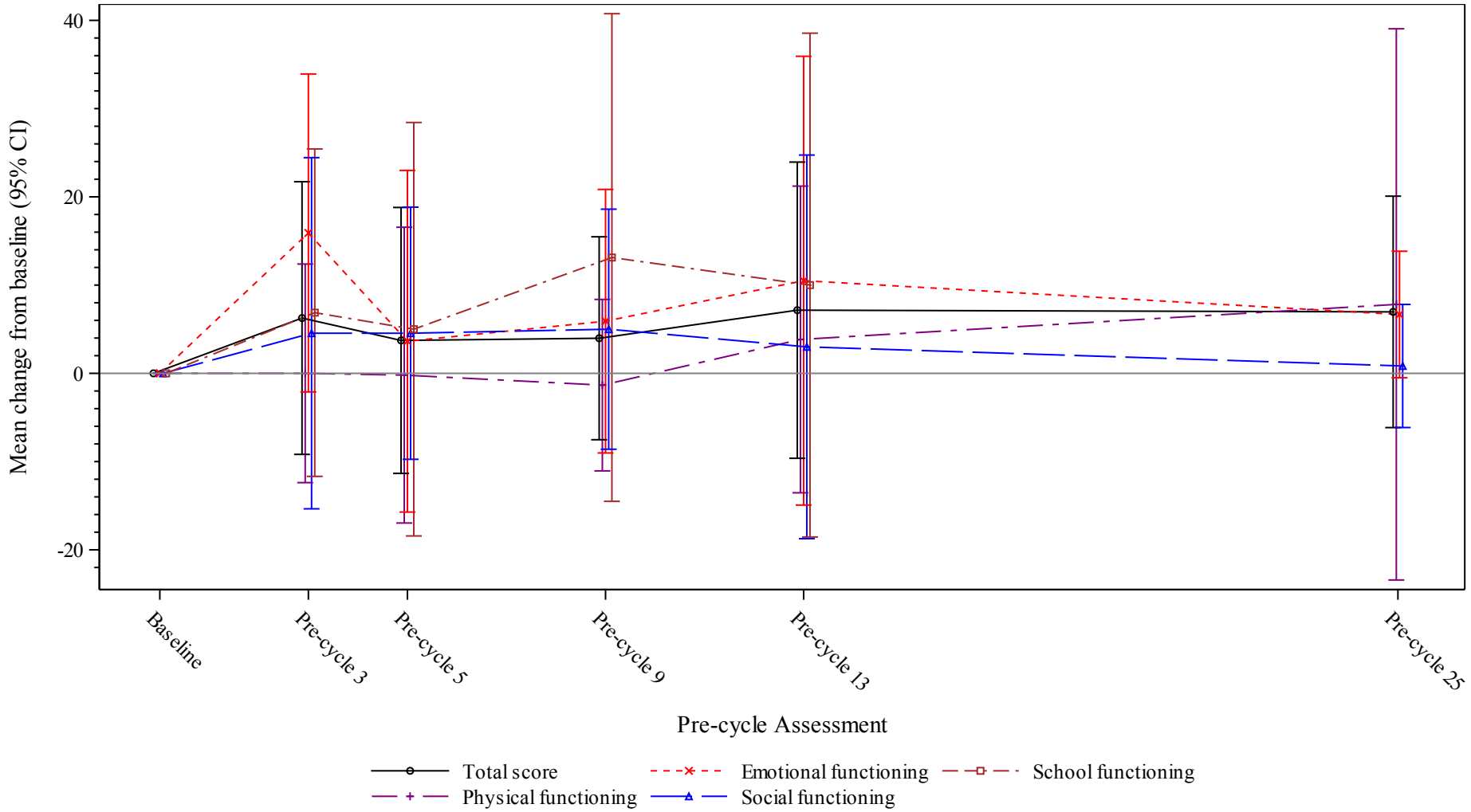
N = 13



Note: Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.3.3 Mean change from baseline of PedsQL self-report transformed scores - PN status at enrol. = Progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

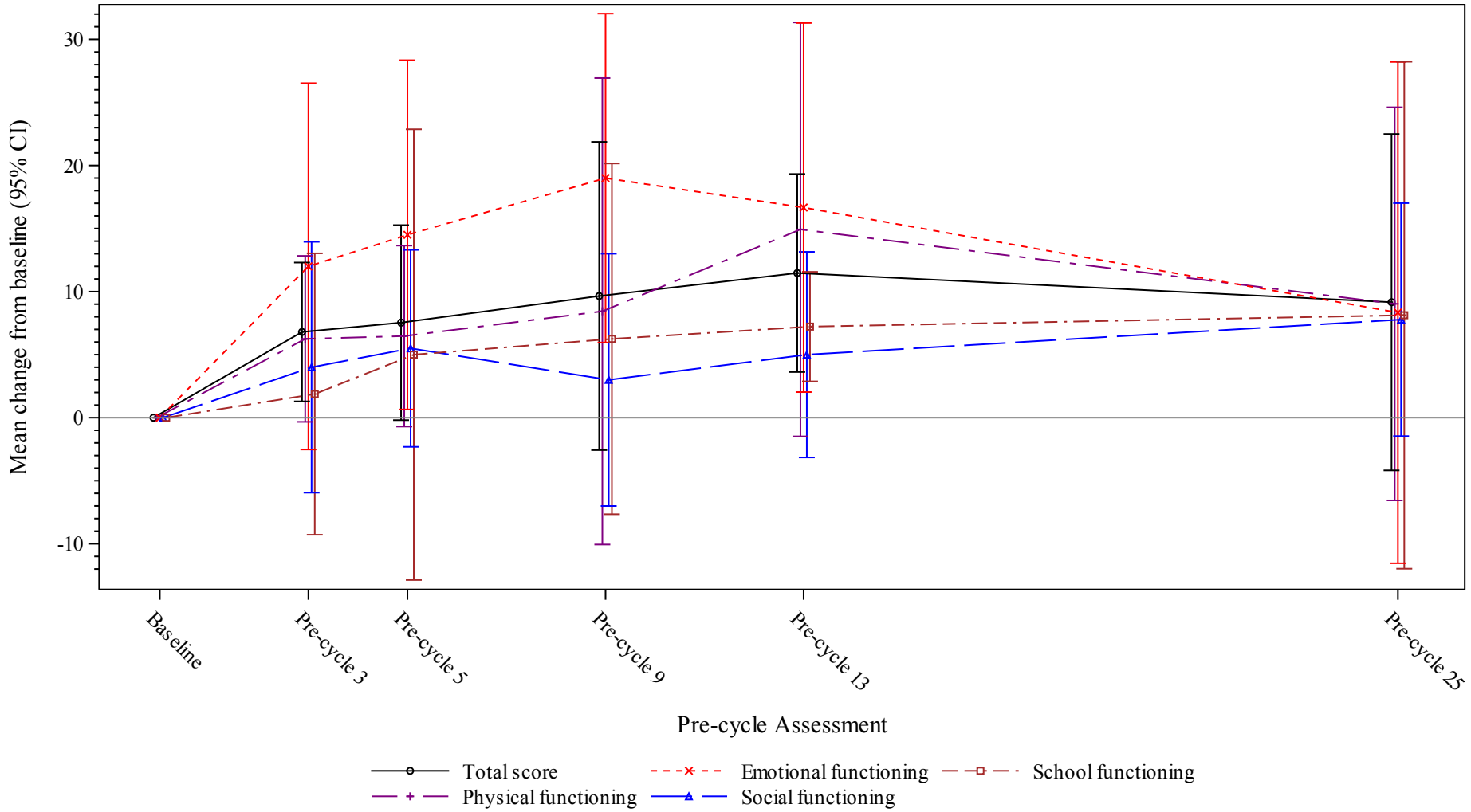
N = 11



Note: Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.3.4 Mean change from baseline of PedsQL self-report transformed scores - PN status at enrol. = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

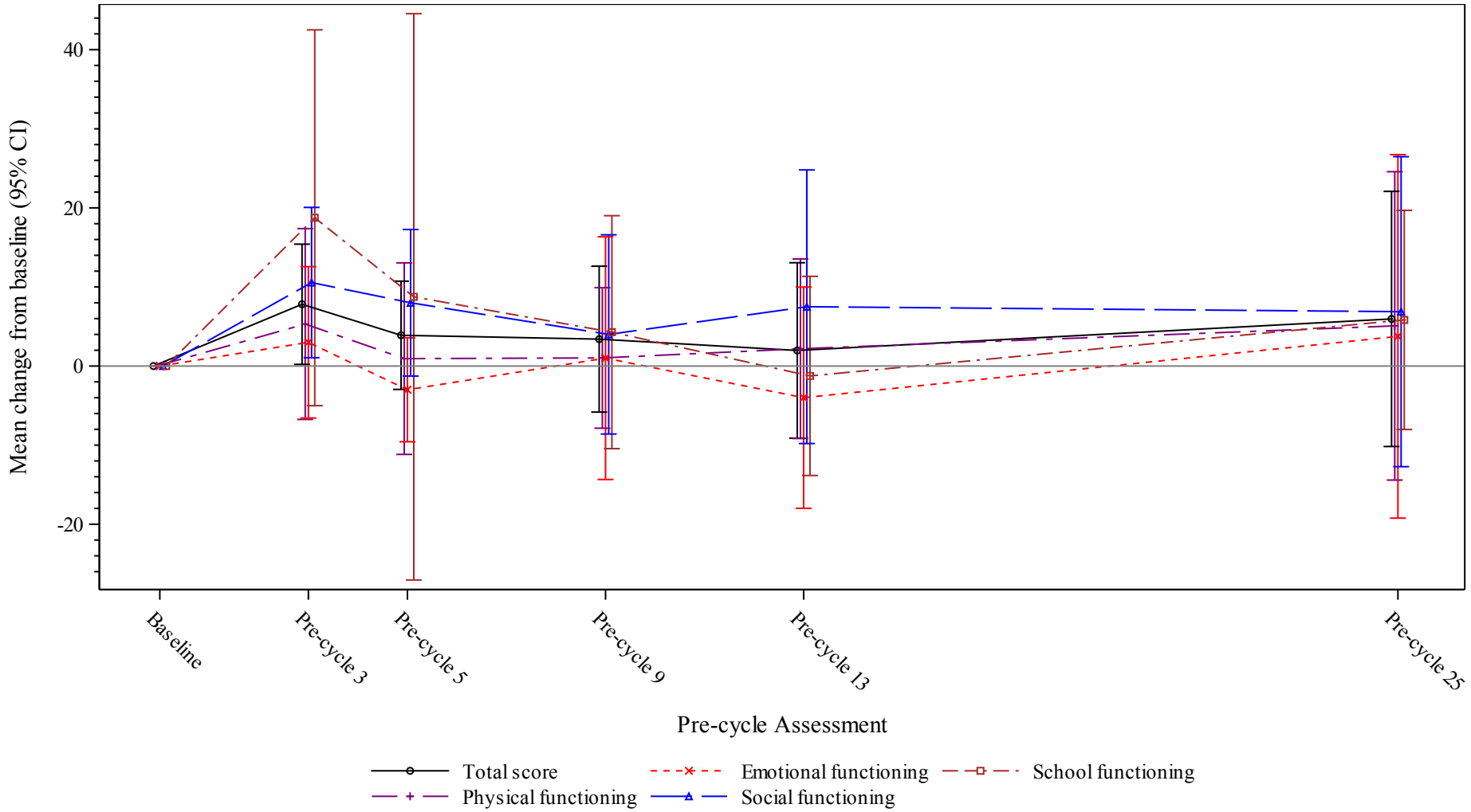
N = 11



Note: Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.3.5 Mean change from baseline of PedsQL self-report transformed scores - PN status at enrol. = Unknown (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

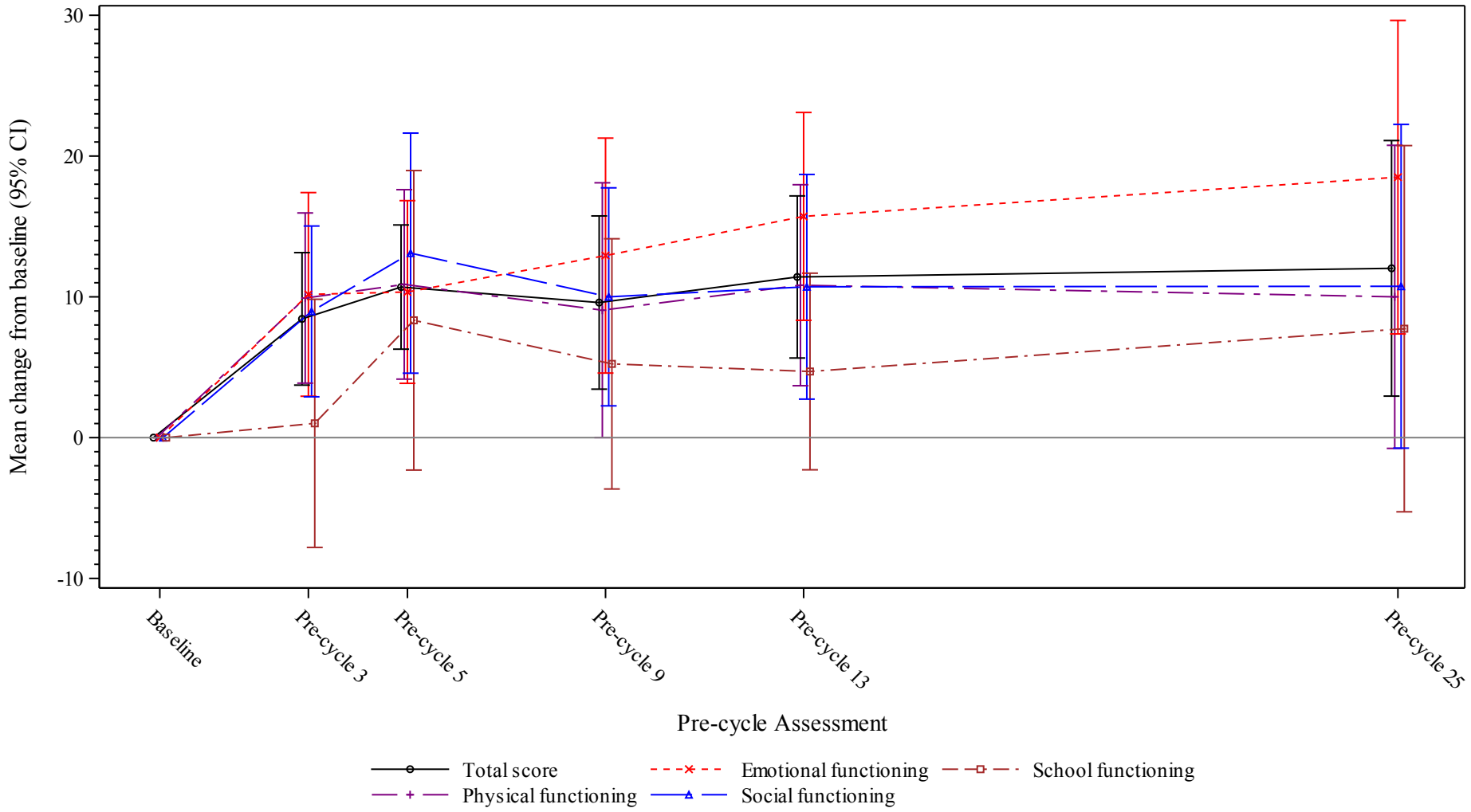
N = 12



Note: Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.4.1 Mean change from baseline of PedsQL parent-report transformed scores - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

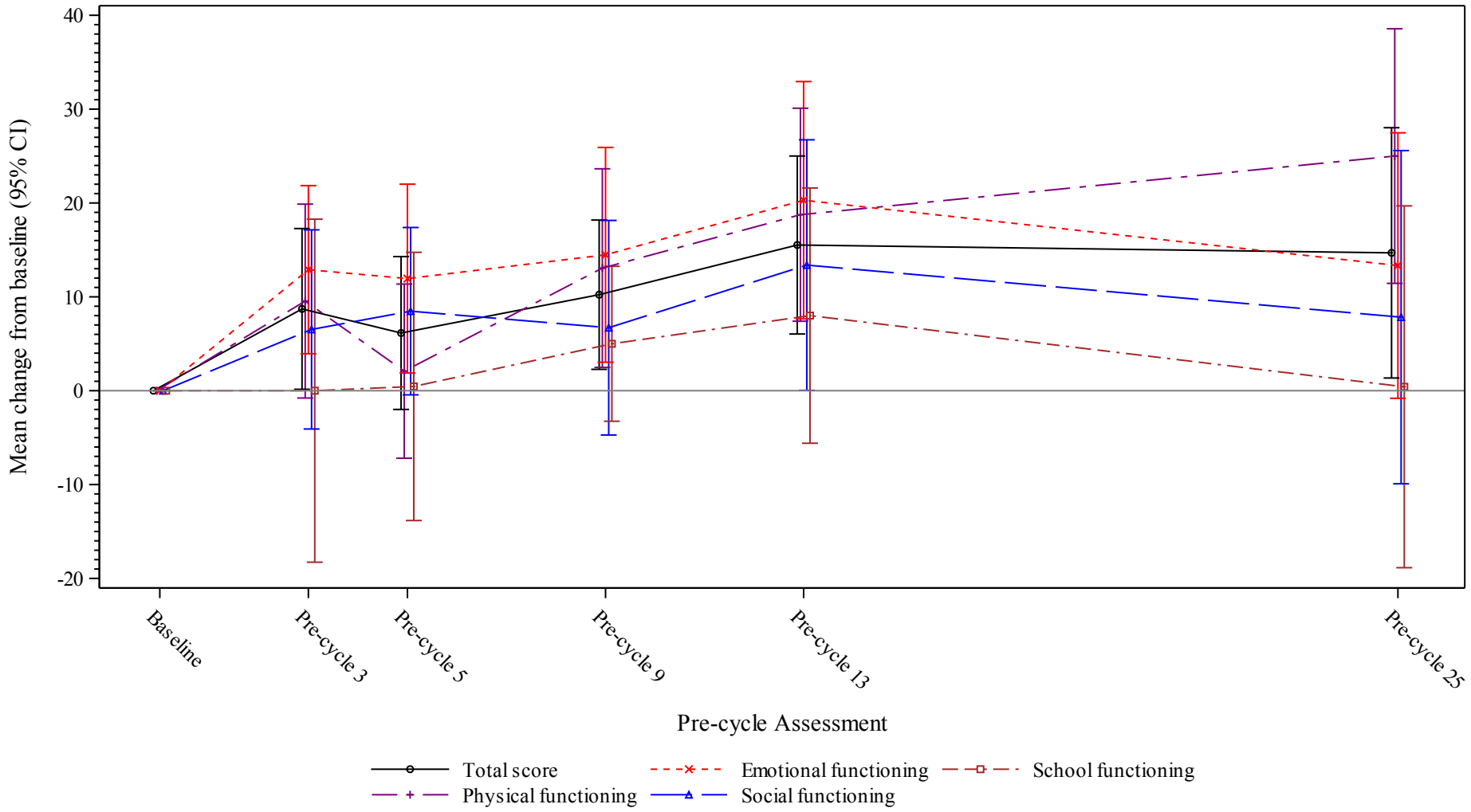
N = 30



Note: Parents or legal guardians of children from 2 to 18 years of age at enrol. completed the parent proxy measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.4.2 Mean change from baseline of PedsQL parent-report transformed scores - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

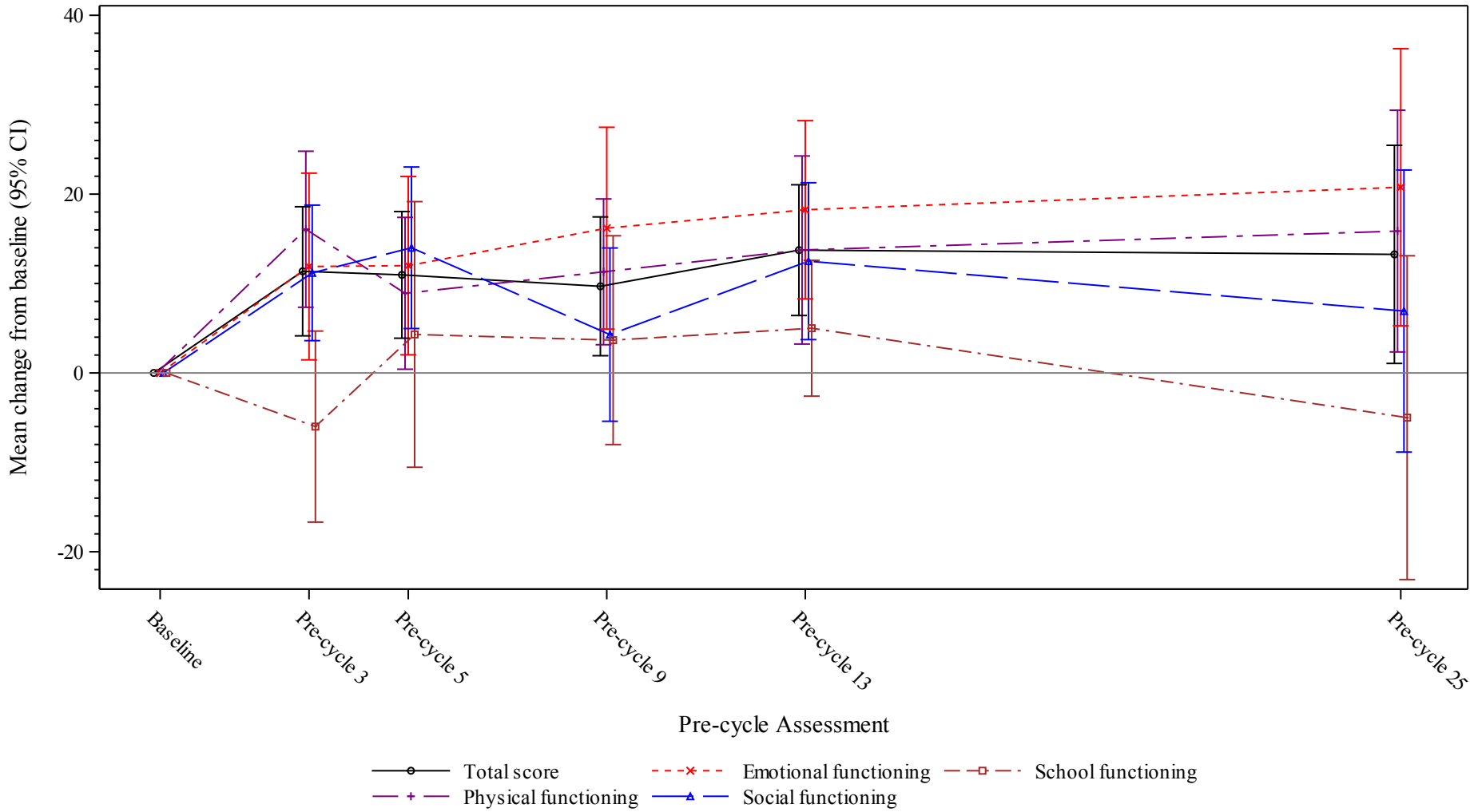
N = 20



Note: Parents or legal guardians of children from 2 to 18 years of age at enrol. completed the parent proxy measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.4.3 Mean change from baseline of PedsQL parent-report transformed scores - PN status at enrol. = Progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

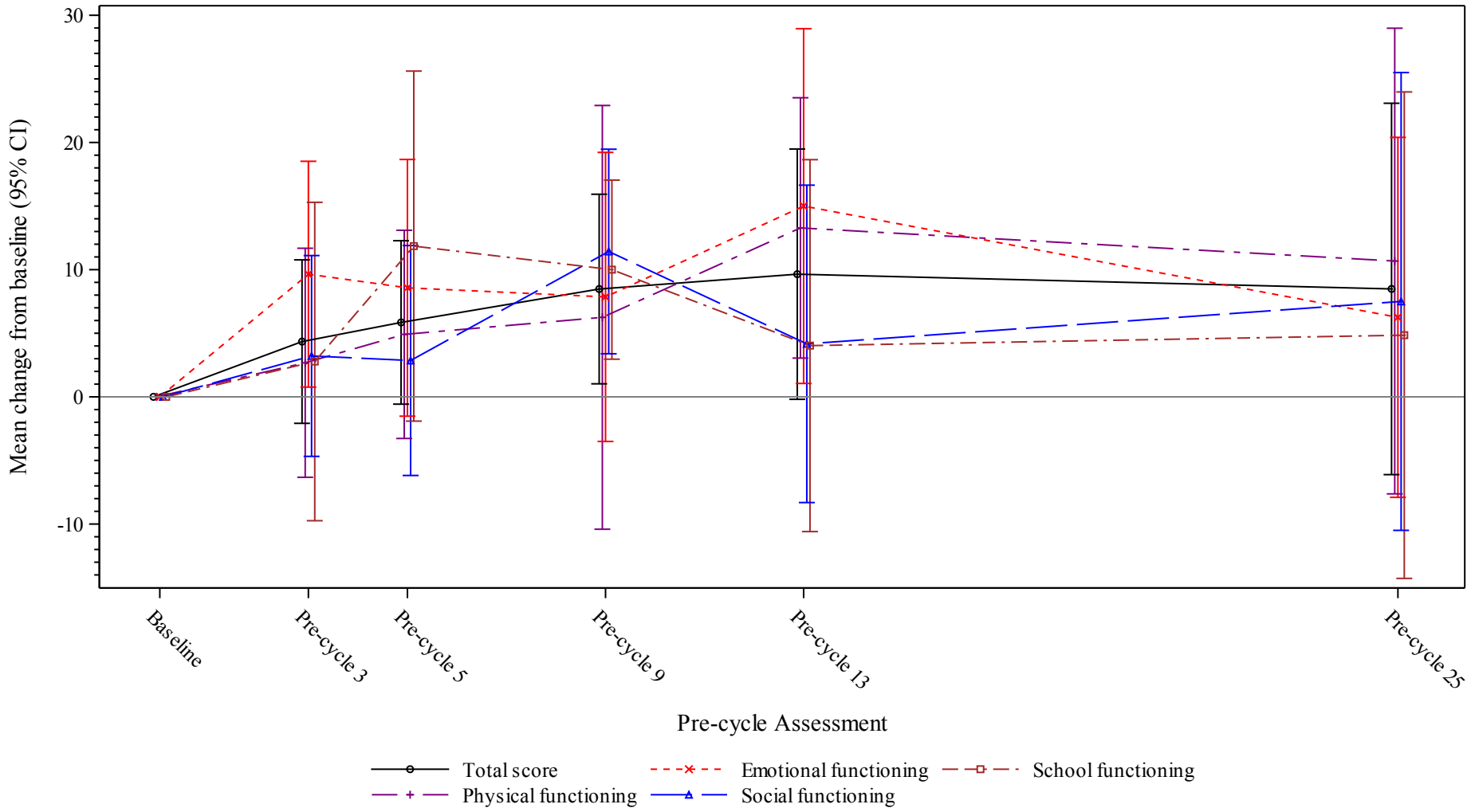
N = 21



Note: Parents or legal guardians of children from 2 to 18 years of age at enrol. completed the parent proxy measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.4.4 Mean change from baseline of PedsQL parent-report transformed scores - PN status at enrol. = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

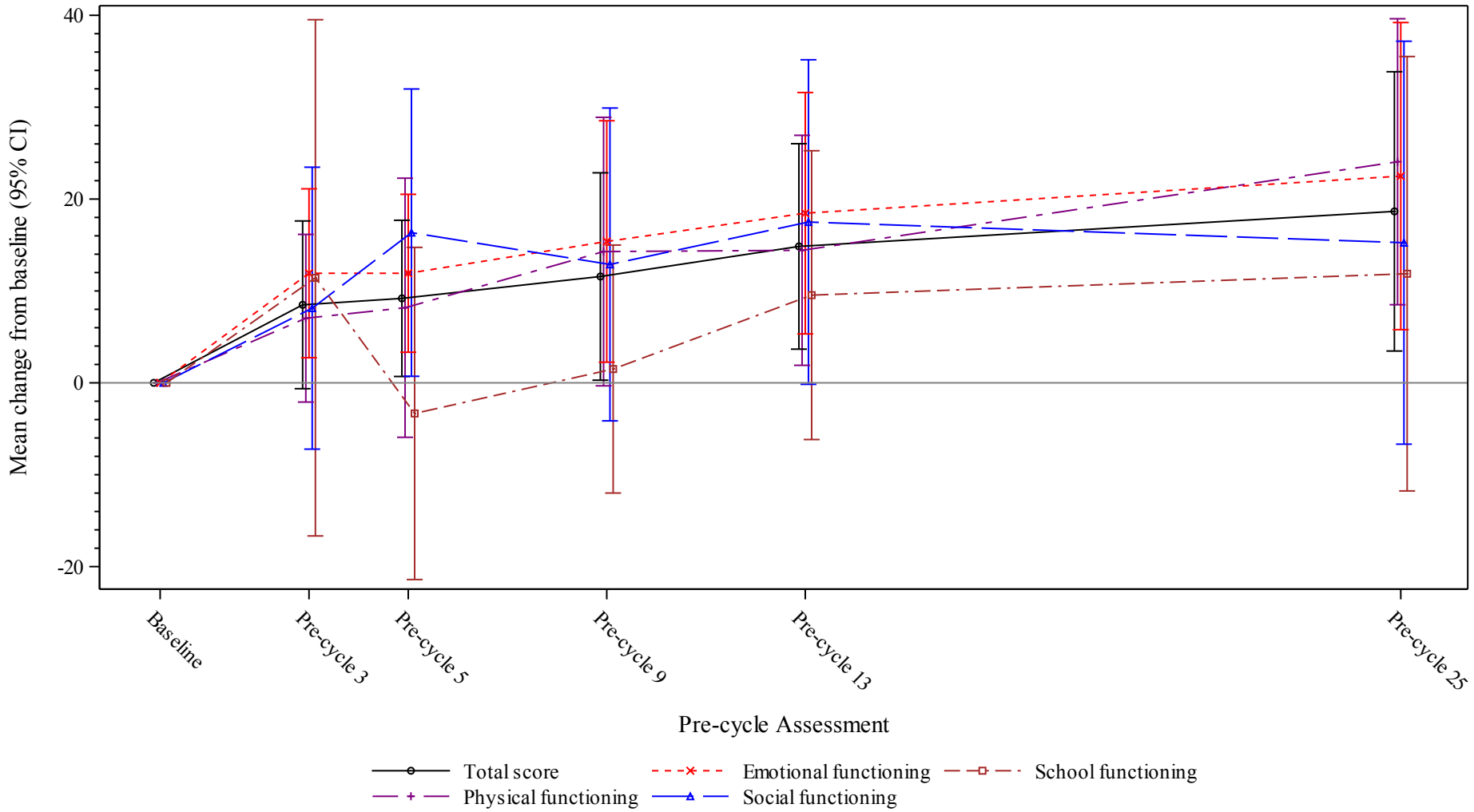
N = 15



Note: Parents or legal guardians of children from 2 to 18 years of age at enrol. completed the parent proxy measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.4.5 Mean change from baseline of PedsQL parent-report transformed scores - PN status at enrol. = Unknown
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

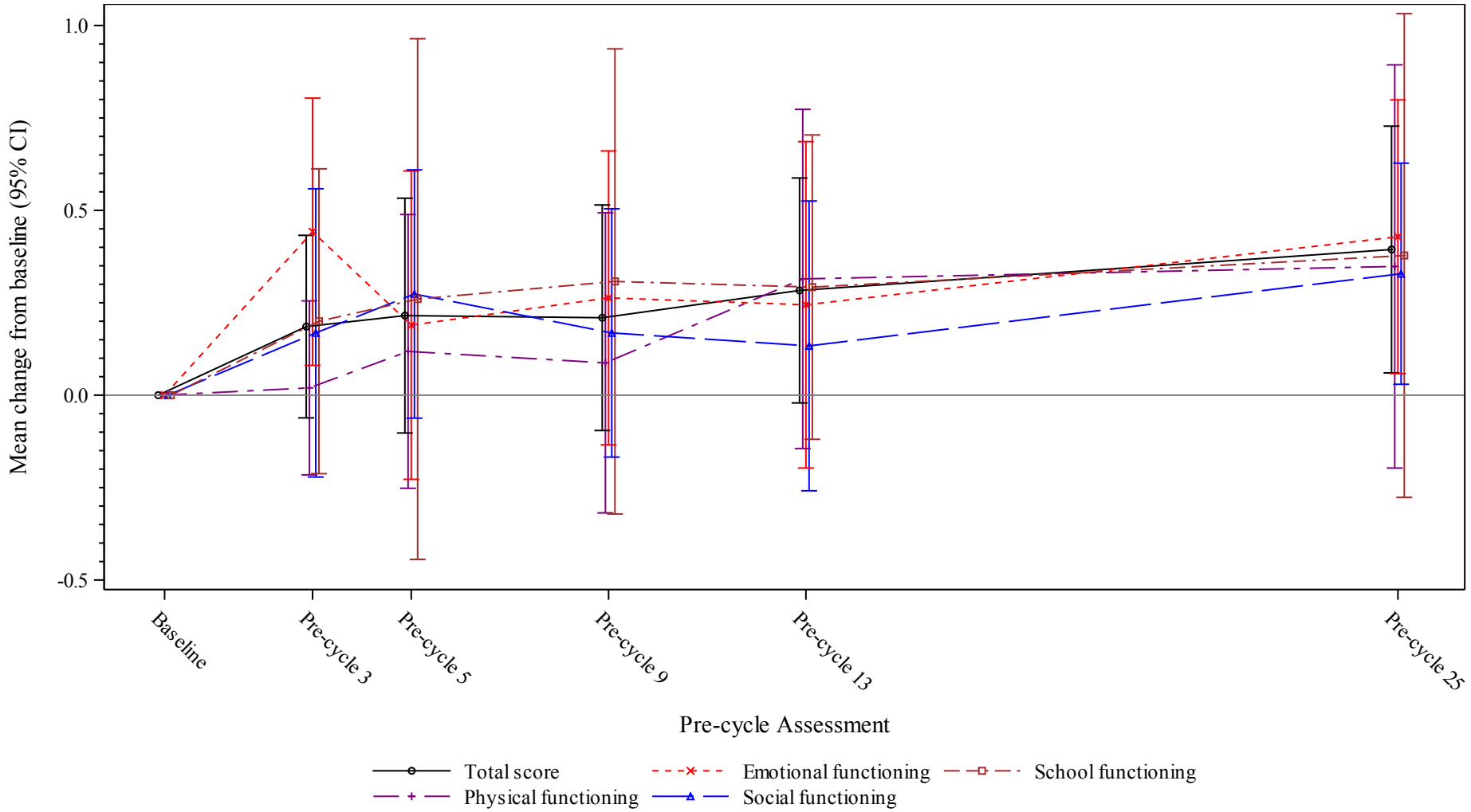
N = 14



Note: Parents or legal guardians of children from 2 to 18 years of age at enrol. completed the parent proxy measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.5.1 Mean change from baseline of PedsQL self-report raw scores over time - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

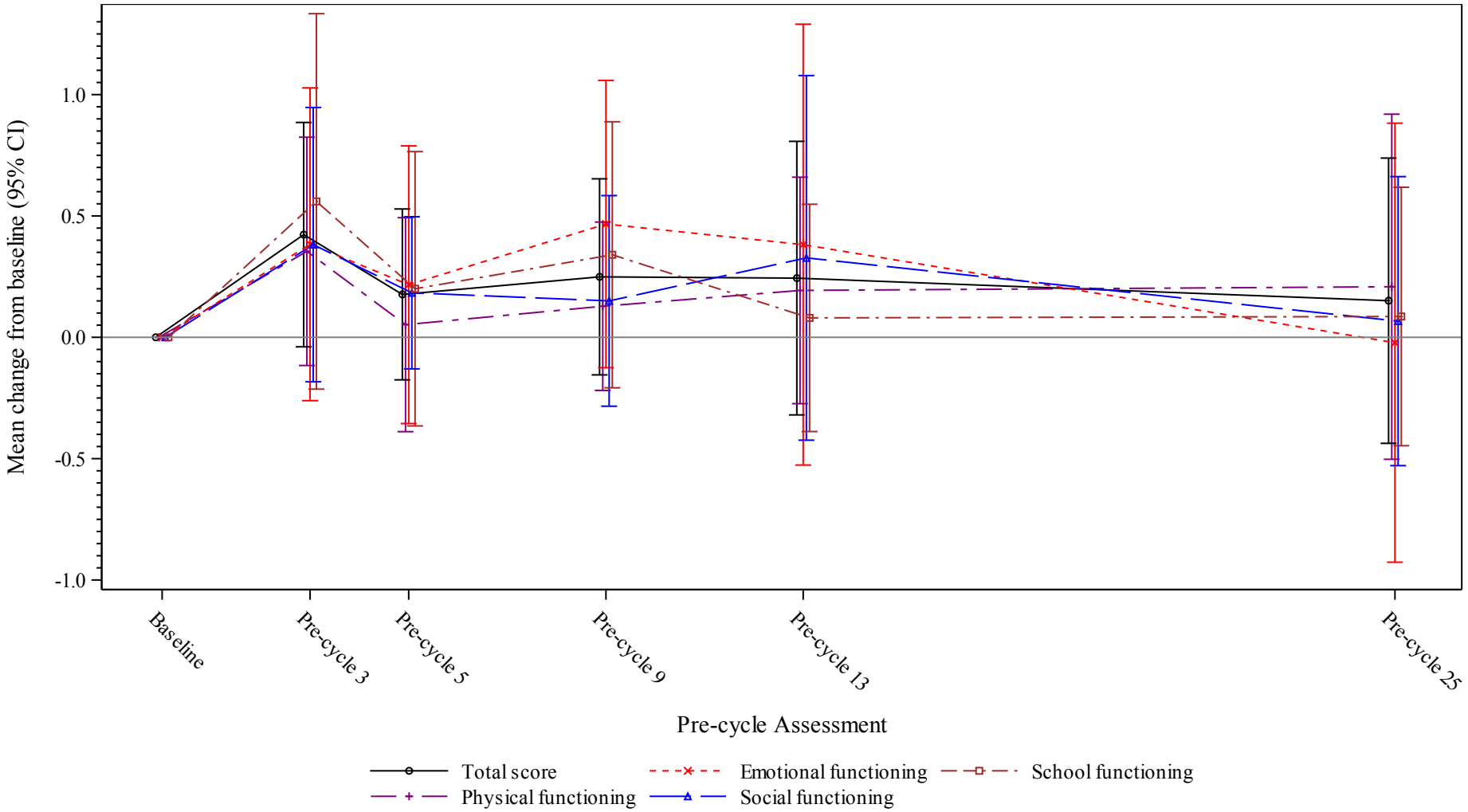
N = 21



Note: Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.5.2 Mean change from baseline of PedsQL self-report raw scores - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

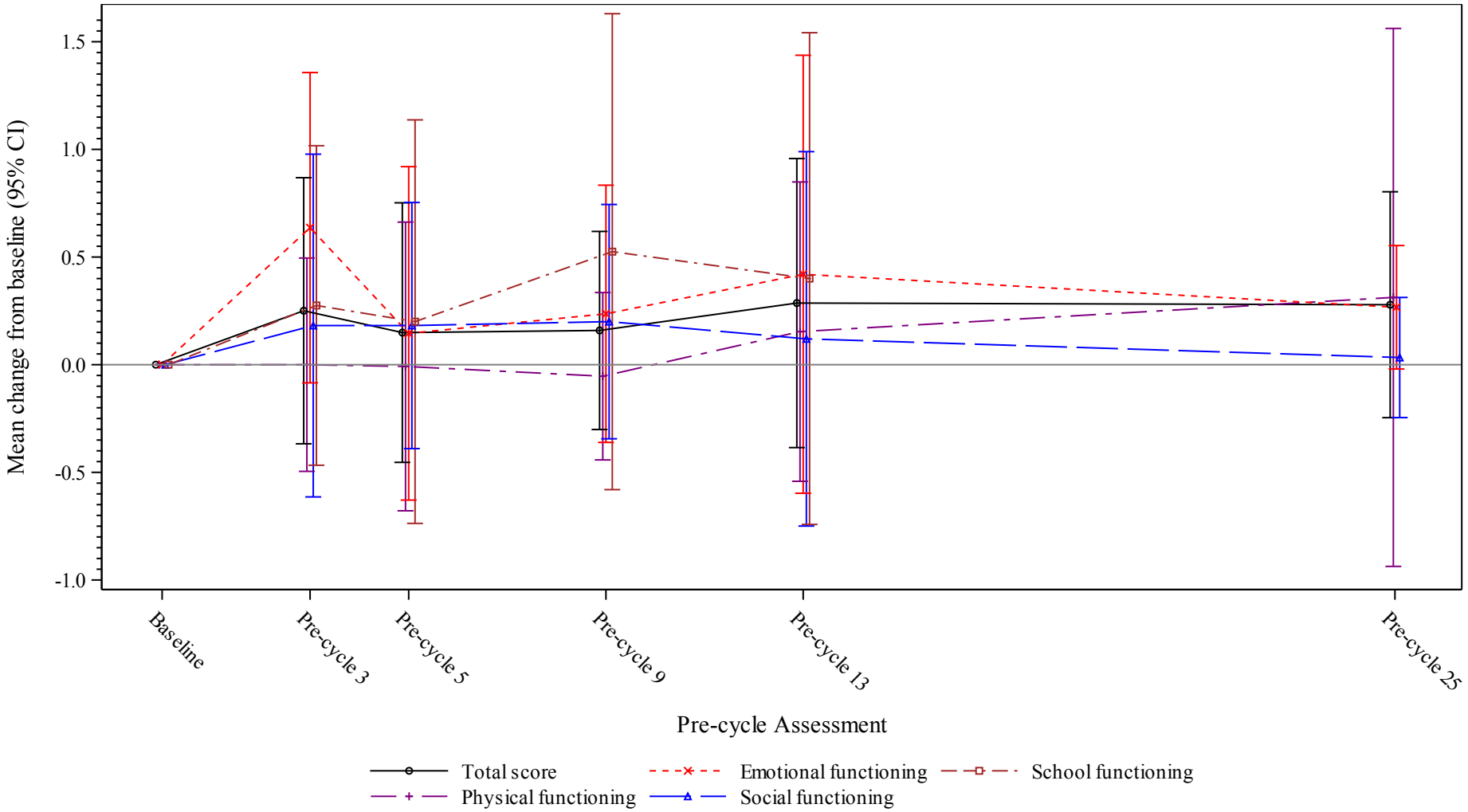
N = 13



Note: Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.5.3 Mean change from baseline of PedsQL self-report raw scores - PN status at enrol. = Progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

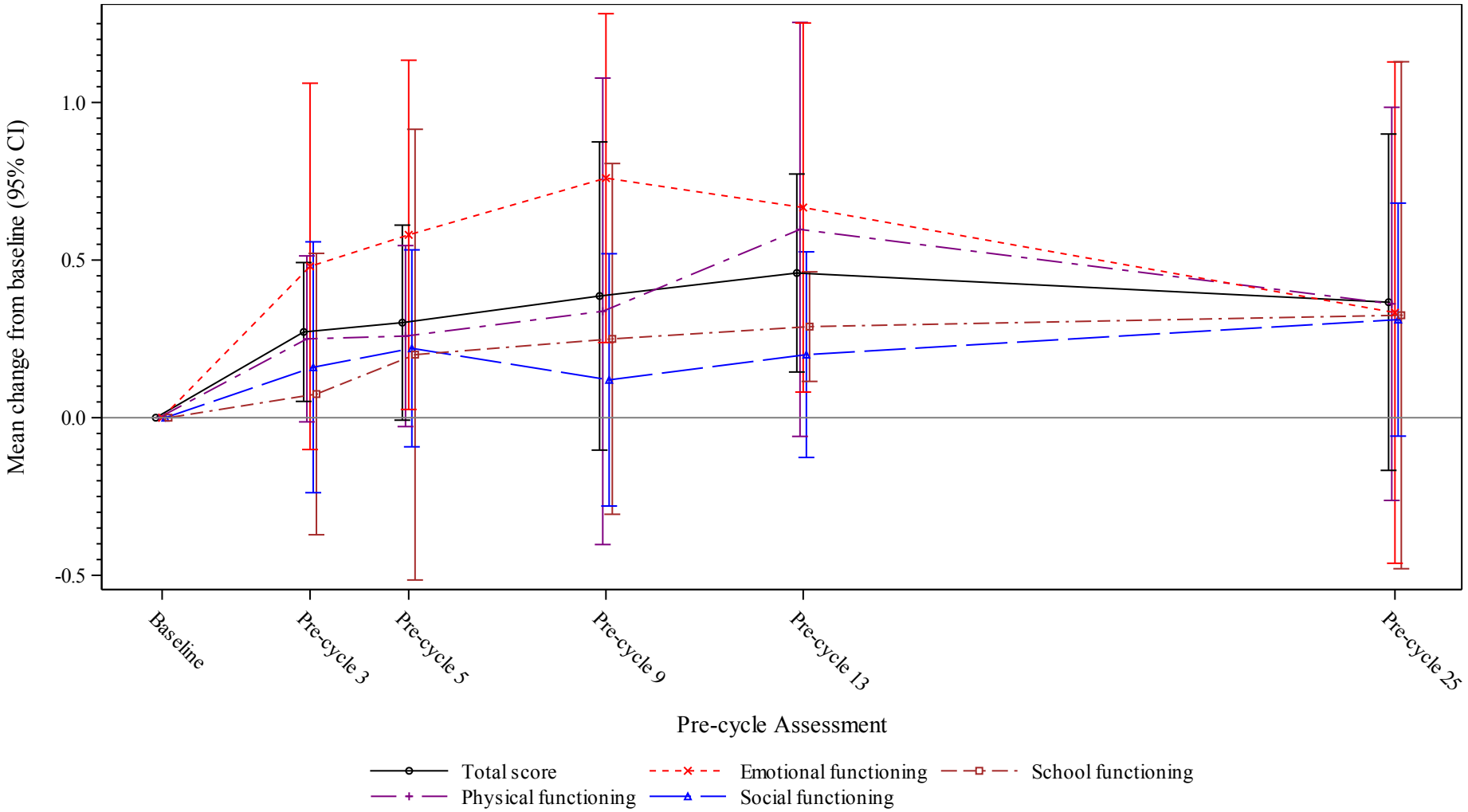
N = 11



Note: Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.5.4 Mean change from baseline of PedsQL self-report raw cores - PN status at enrol. = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

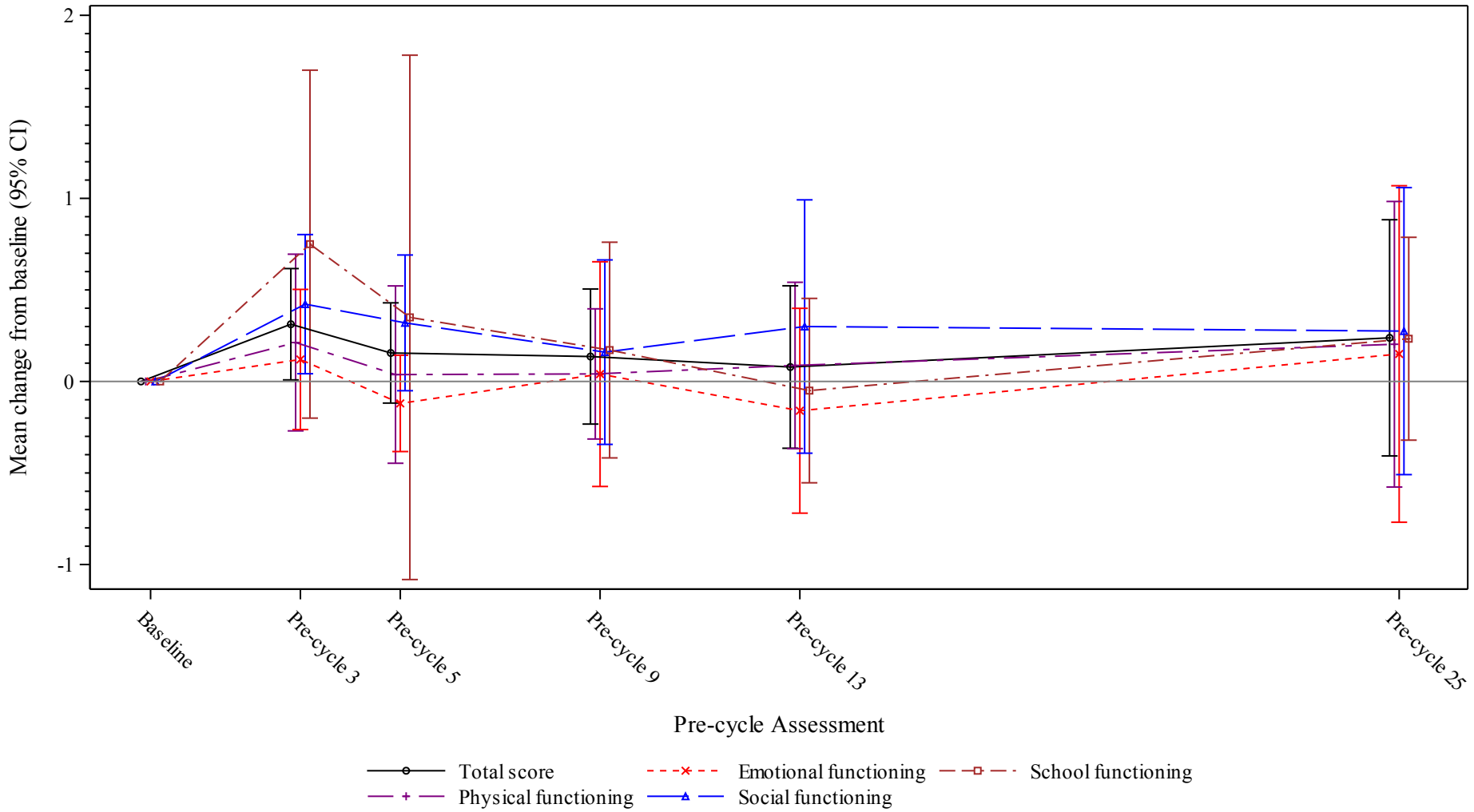
N = 11



Note: Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.5.5 Mean change from baseline of PedsQL self-report raw scores - PN status at enrol. = Unknown (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

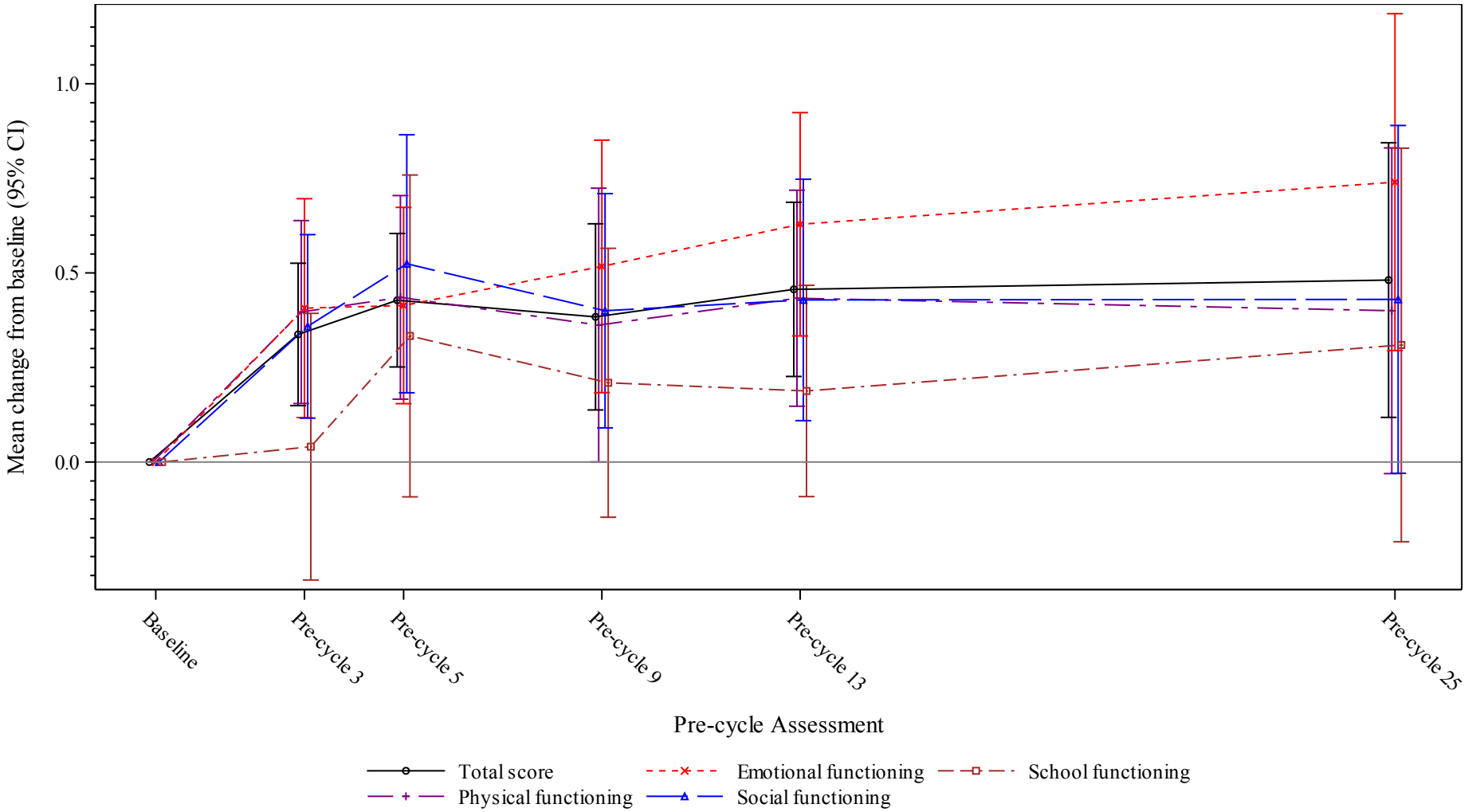
N = 12



Note: Children, ages 8 to 18 years of age at enrolment, completed self-report measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.6.1 Mean change from baseline of PedsQL parent-report raw scores - Gender = Male
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

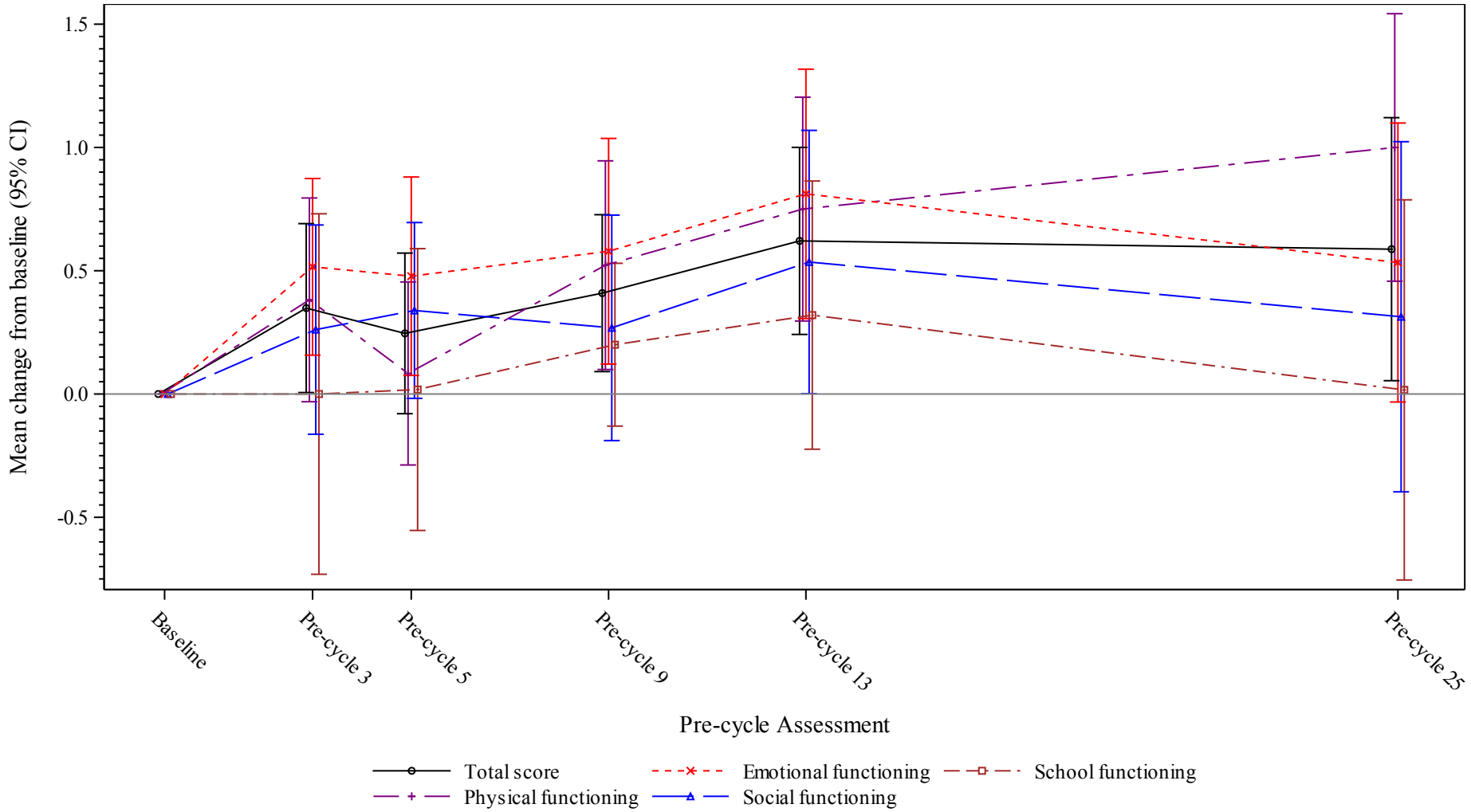
N = 30



Note: Parents or legal guardians of children from 2 to 18 years of age at enrol. completed the parent proxy measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.6.2 Mean change from baseline of PedsQL parent-report raw scores - Gender = Female
(Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

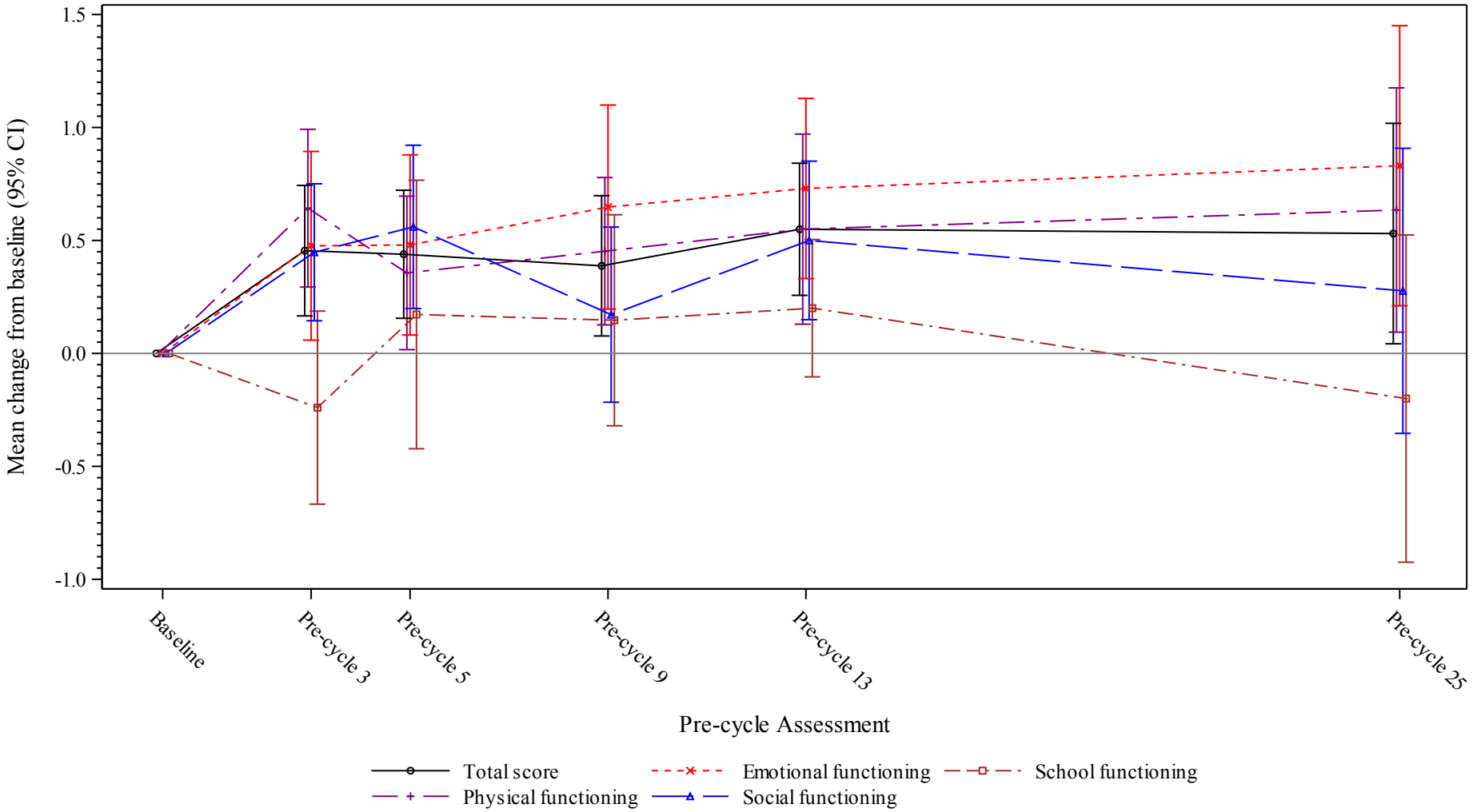
N = 20



Note: Parents or legal guardians of children from 2 to 18 years of age at enrol. completed the parent proxy measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.6.3 Mean change from baseline of PedsQL parent-report raw scores - PN status at enrol. = Progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

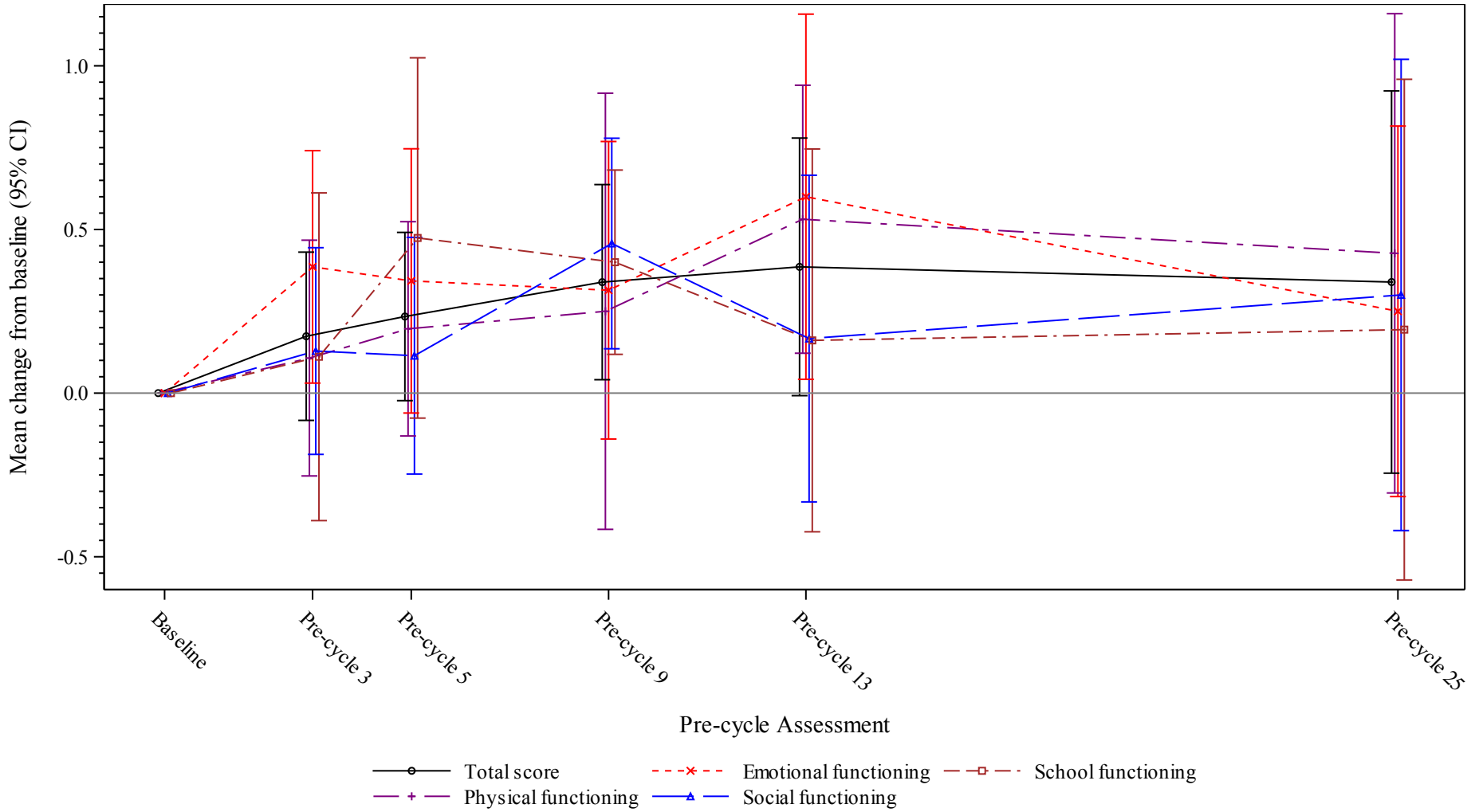
N = 21



Note: Parents or legal guardians of children from 2 to 18 years of age at enrol. completed the parent proxy measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.6.4 Mean change from baseline of PedsQL parent-report raw scores - PN status at enrol. = Non-progressive (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

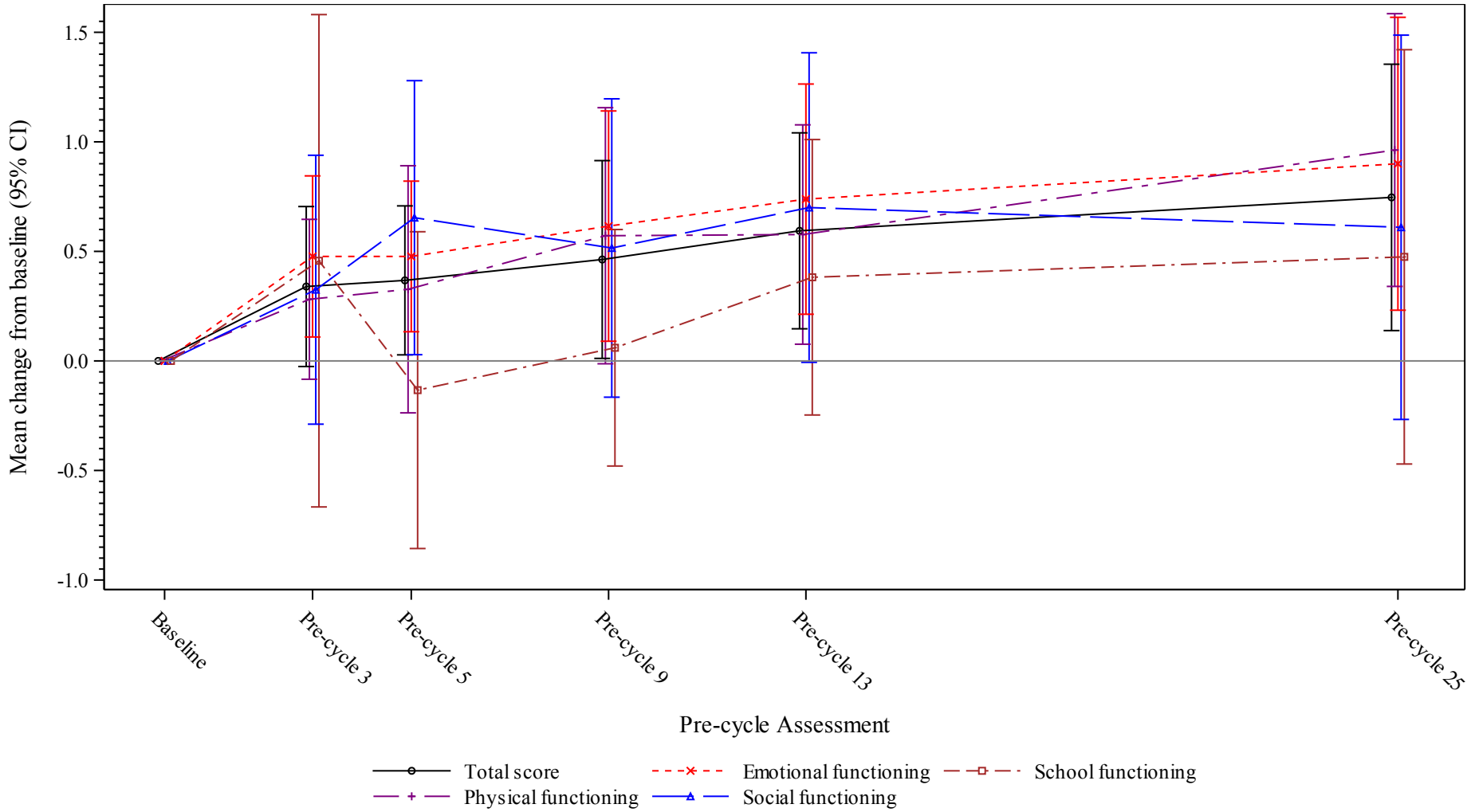
N = 15



Note: Parents or legal guardians of children from 2 to 18 years of age at enrol. completed the parent proxy measures of the PedsQL.
CI = Confidence interval.

Figure 2.12.3.6.5 Mean change from baseline of PedsQL parent-report raw scores - PN status at enrol. = Unknown (Full analysis set) Phase II Stratum 1, Data cut-off: 29th June 2018

N = 14



Note: Parents or legal guardians of children from 2 to 18 years of age at enrol. completed the parent proxy measures of the PedsQL.
CI = Confidence interval.

Table 3.1.1 Adverse Events in any category - patient level (Safety analysis set)

Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

AE category	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=50)
Any non-severe AE (CTCAE <=2)	49 (98,0)
Any AESI	49 (98,0)
Any serious AESI (including events with outcome of death)	3 (6,0)
Any non-severe AESI (CTCAE <=2)	49 (98,0)
Any severe AESI (CTCAE >=3)	11 (22,0)
Any AE excluding disease-related AEs [b]	49 (98,0)
Any serious adverse event (SAE including outcome of death) excluding disease-related SAEs [b]	10 (20,0)
Any severe AE (CTCAE >=3) excluding disease-related AEs [b]	30 (60,0)

[a] Patients with multiple events in the same category are counted only once in that category. Patients with events in more than one category are counted once in each of those categories.
[b] Desease-related SAE are those marked as: 'Definite', 'Possible', 'Probable'.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication. Percentages are based on the total numbers of patients in the treatment group (N).
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.1.1 Adverse Events in any category - patient level - Gender = Male (Safety analysis set)

Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

AE category	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Any AE	30 (100)
Any adverse event (SAE) (including events with outcome of death)	12 (40,0)
Any non-severe AE (CTCAE <=2)	30 (100)
Any severe AE (CTCAE >=3)	21 (70,0)
Any AE leading to death	0
Any AE leading to permanent discontinuation of study drug	5 (16,7)
Any AE leading to dose reduction	8 (26,7)
Any AE leading to interruption of study drug	27 (90,0)
Any AESI	30 (100)
Any serious AESI (including events with outcome of death)	3 (10,0)
Any non-severe AESI (CTCAE <=2)	30 (100)
Any severe AESI (CTCAE >=3)	9 (30,0)
Any AE excluding disease-related AEs [b]	30 (100)
Any serious adverse event (SAE including outcome of death) excluding disease-related SAEs [b]	10 (33,3)
Any severe AE (CTCAE >=3) excluding disease-related AEs [b]	21 (70,0)

[a] Patients with multiple events in the same category are counted only once in that category. Patients with events in more than one category are counted once in each of those categories.
[b] Desease-related SAE are those marked as: 'Definite', 'Possible', 'Probable'.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication. Percentages are based on the total numbers of patients in the treatment group (N).
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.1.2 Adverse Events in any category - patient level - Gender = Female (Safety analysis set)

Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

AE category	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Any AE	19 (95,0)
Any adverse event (SAE) (including events with outcome of death)	0
Any non-severe AE (CTCAE <=2)	19 (95,0)
Any severe AE (CTCAE >=3)	10 (50,0)
Any AE leading to death	0
Any AE leading to permanent discontinuation of study drug	1 (5,0)
Any AE leading to dose reduction	5 (25,0)
Any AE leading to interruption of study drug	15 (75,0)
Any AESI	19 (95,0)
Any serious AESI (including events with outcome of death)	0
Any non-severe AESI (CTCAE <=2)	19 (95,0)
Any severe AESI (CTCAE >=3)	2 (10,0)
Any AE excluding disease-related AEs [b]	19 (95,0)
Any serious adverse event (SAE including outcome of death) excluding disease-related SAEs [b]	0
Any severe AE (CTCAE >=3) excluding disease-related AEs [b]	9 (45,0)

[a] Patients with multiple events in the same category are counted only once in that category. Patients with events in more than one category are counted once in each of those categories.
[b] Desease-related SAE are those marked as: 'Definite', 'Possible', 'Probable'.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication. Percentages are based on the total numbers of patients in the treatment group (N).
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.1.3 Adverse Events in any category - patient level - PN status at enrollment = Progressive (Safety analysis set)

Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

AE category	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Any AE	21 (100)
Any adverse event (SAE) (including events with outcome of death)	3 (14,3)
Any non-severe AE (CTCAE <=2)	21 (100)
Any severe AE (CTCAE >=3)	13 (61,9)
Any AE leading to death	0
Any AE leading to permanent discontinuation of study drug	1 (4,8)
Any AE leading to dose reduction	7 (33,3)
Any AE leading to interruption of study drug	19 (90,5)
Any AESI	21 (100)
Any serious AESI (including events with outcome of death)	1 (4,8)
Any non-severe AESI (CTCAE <=2)	21 (100)
Any severe AESI (CTCAE >=3)	6 (28,6)
Any AE excluding disease-related AEs [b]	21 (100)
Any serious adverse event (SAE including outcome of death) excluding disease-related SAEs [b]	3 (14,3)
Any severe AE (CTCAE >=3) excluding disease-related AEs [b]	13 (61,9)

[a] Patients with multiple events in the same category are counted only once in that category. Patients with events in more than one category are counted once in each of those categories.
[b] Desease-related SAE are those marked as: 'Definite', 'Possible', 'Probable'.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication. Percentages are based on the total numbers of patients in the treatment group (N).
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.1.4 Adverse Events in any category - patient level - PN status at enrollment = Non-progressive (Safety analysis set)

Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

AE category	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Any AE	14 (93,3)
Any adverse event (SAE) (including events with outcome of death)	5 (33,3)
Any non-severe AE (CTCAE <=2)	14 (93,3)
Any severe AE (CTCAE >=3)	10 (66,7)
Any AE leading to death	0
Any AE leading to permanent discontinuation of study drug	2 (13,3)
Any AE leading to dose reduction	2 (13,3)
Any AE leading to interruption of study drug	12 (80,0)
Any AESI	14 (93,3)
Any serious AESI (including events with outcome of death)	1 (6,7)
Any non-severe AESI (CTCAE <=2)	14 (93,3)
Any severe AESI (CTCAE >=3)	3 (20,0)
Any AE excluding disease-related AEs [b]	14 (93,3)
Any serious adverse event (SAE including outcome of death) excluding disease-related SAEs [b]	4 (26,7)
Any severe AE (CTCAE >=3) excluding disease-related AEs [b]	9 (60,0)

[a] Patients with multiple events in the same category are counted only once in that category. Patients with events in more than one category are counted once in each of those categories.
[b] Desease-related SAE are those marked as: 'Definite', 'Possible', 'Probable'.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication. Percentages are based on the total numbers of patients in the treatment group (N).
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.1.5 Adverse Events in any category - patient level - PN status at enrollment = Unknown (Safety analysis set)

Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

AE category	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Any AE	14 (100)
Any adverse event (SAE) (including events with outcome of death)	4 (28,6)
Any non-severe AE (CTCAE <=2)	14 (100)
Any severe AE (CTCAE >=3)	8 (57,1)
Any AE leading to death	0
Any AE leading to permanent discontinuation of study drug	3 (21,4)
Any AE leading to dose reduction	4 (28,6)
Any AE leading to interruption of study drug	11 (78,6)
Any AESI	14 (100)
Any serious AESI (including events with outcome of death)	1 (7,1)
Any non-severe AESI (CTCAE <=2)	14 (100)
Any severe AESI (CTCAE >=3)	2 (14,3)
Any AE excluding disease-related AEs [b]	14 (100)
Any serious adverse event (SAE including outcome of death) excluding disease-related SAEs [b]	3 (21,4)
Any severe AE (CTCAE >=3) excluding disease-related AEs [b]	8 (57,1)

[a] Patients with multiple events in the same category are counted only once in that category. Patients with events in more than one category are counted once in each of those categories.
[b] Desease-related SAE are those marked as: 'Definite', 'Possible', 'Probable'.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication. Percentages are based on the total numbers of patients in the treatment group (N).
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2 Adverse events by system organ class and preferred term (Safety analysis set)

Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=50)
Patients with Any AE	49 (98,0)
INFECTIONS AND INFESTATIONS	41 (82,0)
Cellulitis	5 (10,0)
Conjunctivitis	5 (10,0)
Otitis media	14 (28,0)
Paronychia	23 (46,0)
Pharyngitis	9 (18,0)
Pharyngitis streptococcal	7 (14,0)
Sinusitis	6 (12,0)
Skin infection	8 (16,0)
Upper respiratory tract infection	11 (22,0)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	25 (50,0)
Anaemia	23 (46,0)
IMMUNE SYSTEM DISORDERS	6 (12,0)
Hypersensitivity	6 (12,0)
METABOLISM AND NUTRITION DISORDERS	48 (96,0)
Decreased appetite	13 (26,0)
Dehydration	7 (14,0)
Hyperglycaemia	12 (24,0)
Hyperkalaemia	11 (22,0)
Hypermagnesaemia	5 (10,0)
Hypernatraemia	9 (18,0)
Hypoalbuminaemia	26 (52,0)
Hypocalcaemia	13 (26,0)
Hypoglycaemia	16 (32,0)
Hypokalaemia	13 (26,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
Only SOC and PT with frequency n>=5 are presented.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2 Adverse events by system organ class and preferred term (Safety analysis set)

Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=50)
Hypomagnesaemia	5 (10,0)
Hyponatraemia	8 (16,0)
Hypophosphataemia	8 (16,0)
PSYCHIATRIC DISORDERS	23 (46,0)
Anxiety	6 (12,0)
Insomnia	10 (20,0)
NERVOUS SYSTEM DISORDERS	35 (70,0)
Dizziness	14 (28,0)
Headache	25 (50,0)
EYE DISORDERS	17 (34,0)
Lacrimation increased	8 (16,0)
EAR AND LABYRINTH DISORDERS	12 (24,0)
Ear pain	6 (12,0)
CARDIAC DISORDERS	12 (24,0)
Sinus tachycardia	10 (20,0)
VASCULAR DISORDERS	15 (30,0)
Hypertension	9 (18,0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	41 (82,0)
Cough	21 (42,0)
Epistaxis	14 (28,0)
Nasal congestion	18 (36,0)
Oropharyngeal pain	25 (50,0)
Rhinitis allergic	15 (30,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
Only SOC and PT with frequency n>=5 are presented.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2 Adverse events by system organ class and preferred term (Safety analysis set)

Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=50)
Rhinorrhoea	6 (12,0)
GASTROINTESTINAL DISORDERS	49 (98,0)
Abdominal distension	5 (10,0)
Abdominal pain	23 (46,0)
Abdominal pain upper	21 (42,0)
Constipation	18 (36,0)
Diarrhoea	37 (74,0)
Nausea	35 (70,0)
Stomatitis	25 (50,0)
Vomiting	42 (84,0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	49 (98,0)
Alopecia	12 (24,0)
Dermatitis acneiform	26 (52,0)
Dry skin	32 (64,0)
Eczema	13 (26,0)
Hair colour changes	12 (24,0)
Pruritus	24 (48,0)
Rash maculo-papular	19 (38,0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	36 (72,0)
Arthralgia	5 (10,0)
Back pain	9 (18,0)
Neck pain	8 (16,0)
Pain in extremity	18 (36,0)
RENAL AND URINARY DISORDERS	27 (54,0)
Haematuria	14 (28,0)
Proteinuria	12 (24,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
Only SOC and PT with frequency n>=5 are presented.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2 Adverse events by system organ class and preferred term (Safety analysis set)

Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=50)
Urinary incontinence	7 (14,0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	42 (84,0)
Fatigue	28 (56,0)
Influenza like illness	15 (30,0)
Localised oedema	5 (10,0)
Oedema peripheral	6 (12,0)
Pain	15 (30,0)
Pyrexia	30 (60,0)
INVESTIGATIONS	49 (98,0)
Alanine aminotransferase increased	17 (34,0)
Amylase increased	10 (20,0)
Aspartate aminotransferase increased	22 (44,0)
Blood alkaline phosphatase increased	11 (22,0)
Blood creatine phosphokinase increased	38 (76,0)
Blood creatinine increased	14 (28,0)
Ejection fraction decreased	12 (24,0)
Haemoglobin increased	10 (20,0)
Lipase increased	15 (30,0)
Lymphocyte count decreased	11 (22,0)
Lymphocyte count increased	13 (26,0)
Neutrophil count decreased	17 (34,0)
Platelet count decreased	6 (12,0)
Weight increased	5 (10,0)
White blood cell count decreased	10 (20,0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	23 (46,0)
Fall	14 (28,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
Only SOC and PT with frequency n>=5 are presented.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Patients with Any AE	30 (100)
INFECTIONS AND INFESTATIONS	25 (83,3)
Abscess	1 (3,3)
Bacterial tracheitis	1 (3,3)
Body tinea	1 (3,3)
Bronchitis	1 (3,3)
Bronchitis viral	1 (3,3)
Cellulitis	4 (13,3)
Clostridium difficile colitis	1 (3,3)
Conjunctivitis	2 (6,7)
Conjunctivitis viral	1 (3,3)
Ear infection	1 (3,3)
Eye infection	2 (6,7)
Folliculitis	3 (10,0)
Fungal skin infection	2 (6,7)
Furuncle	1 (3,3)
Gastroenteritis	2 (6,7)
Gastroenteritis viral	1 (3,3)
Impetigo	1 (3,3)
Infected bite	1 (3,3)
Influenza	2 (6,7)
Injection site infection	1 (3,3)
Lung infection	1 (3,3)
Metapneumovirus infection	1 (3,3)
Mucosal infection	2 (6,7)
Nail infection	1 (3,3)
Osteomyelitis	1 (3,3)
Otitis externa	3 (10,0)
Otitis media	11 (36,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
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Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Paronychia	16 (53,3)
Pharyngitis	6 (20,0)
Pharyngitis streptococcal	6 (20,0)
Pilonidal cyst	1 (3,3)
Rash pustular	4 (13,3)
Sinusitis	4 (13,3)
Skin infection	6 (20,0)
Staphylococcal infection	1 (3,3)
Staphylococcal skin infection	1 (3,3)
Tinea infection	2 (6,7)
Tinea pedis	1 (3,3)
Upper respiratory tract infection	9 (30,0)
Urinary tract infection	1 (3,3)
Viral diarrhoea	3 (10,0)
Viral upper respiratory tract infection	1 (3,3)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	4 (13,3)
Peripheral nerve sheath tumour malignant	1 (3,3)
Skin papilloma	2 (6,7)
Tumour pain	1 (3,3)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	19 (63,3)
Anaemia	18 (60,0)
Lymph node pain	1 (3,3)
Lymphadenopathy	2 (6,7)
IMMUNE SYSTEM DISORDERS	5 (16,7)
Contrast media allergy	1 (3,3)
Hypersensitivity	5 (16,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
METABOLISM AND NUTRITION DISORDERS	29 (96,7)
Decreased appetite	5 (16,7)
Dehydration	5 (16,7)
Hypercalcaemia	2 (6,7)
Hyperglycaemia	7 (23,3)
Hyperkalaemia	6 (20,0)
Hypermagnesaemia	4 (13,3)
Hypernatraemia	7 (23,3)
Hyperuricaemia	1 (3,3)
Hypoalbuminaemia	17 (56,7)
Hypocalcaemia	7 (23,3)
Hypoglycaemia	10 (33,3)
Hypokalaemia	8 (26,7)
Hypomagnesaemia	2 (6,7)
Hyponatraemia	8 (26,7)
Hypophosphataemia	7 (23,3)
Lactose intolerance	1 (3,3)
PSYCHIATRIC DISORDERS	14 (46,7)
Agitation	1 (3,3)
Anxiety	4 (13,3)
Attention deficit/hyperactivity disorder	1 (3,3)
Depression	2 (6,7)
Insomnia	6 (20,0)
Irritability	3 (10,0)
Personality change	1 (3,3)
Suicidal ideation	1 (3,3)
Tic	1 (3,3)
NERVOUS SYSTEM DISORDERS	23 (76,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Cognitive disorder	1 (3,3)
Depressed level of consciousness	1 (3,3)
Disturbance in attention	3 (10,0)
Dizziness	7 (23,3)
Drooling	1 (3,3)
Headache	17 (56,7)
Neuralgia	1 (3,3)
Paraesthesia	1 (3,3)
Presyncope	3 (10,0)
EYE DISORDERS	10 (33,3)
Chorioretinal scar	1 (3,3)
Dry eye	2 (6,7)
Eye discharge	1 (3,3)
Eye pain	1 (3,3)
Keratitis	1 (3,3)
Lacrimation increased	4 (13,3)
Ocular hypertension	1 (3,3)
Periorbital oedema	1 (3,3)
Photophobia	2 (6,7)
Vision blurred	3 (10,0)
EAR AND LABYRINTH DISORDERS	8 (26,7)
Ear pain	4 (13,3)
External ear inflammation	1 (3,3)
Middle ear effusion	1 (3,3)
Motion sickness	1 (3,3)
Tinnitus	2 (6,7)
CARDIAC DISORDERS	10 (33,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Nodal arrhythmia	1 (3,3)
Palpitations	1 (3,3)
Sinus bradycardia	2 (6,7)
Sinus tachycardia	8 (26,7)
Supraventricular tachycardia	1 (3,3)
VASCULAR DISORDERS	12 (40,0)
Flushing	2 (6,7)
Haematoma	1 (3,3)
Hypertension	7 (23,3)
Hypotension	1 (3,3)
Phlebitis	1 (3,3)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	24 (80,0)
Allergic cough	1 (3,3)
Asthma	1 (3,3)
Atelectasis	2 (6,7)
Cough	13 (43,3)
Dysphonia	1 (3,3)
Dyspnoea	2 (6,7)
Epistaxis	9 (30,0)
Hypoxia	3 (10,0)
Increased bronchial secretion	2 (6,7)
Nasal congestion	9 (30,0)
Oropharyngeal pain	15 (50,0)
Rhinitis allergic	10 (33,3)
Rhinorrhoea	3 (10,0)
Sleep apnoea syndrome	1 (3,3)
Sneezing	3 (10,0)
Tracheal inflammation	1 (3,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Upper-airway cough syndrome	2 (6,7)
Wheezing	1 (3,3)
GASTROINTESTINAL DISORDERS	30 (100)
Abdominal distension	3 (10,0)
Abdominal pain	14 (46,7)
Abdominal pain upper	12 (40,0)
Anal incontinence	2 (6,7)
Constipation	14 (46,7)
Diarrhoea	26 (86,7)
Dry mouth	1 (3,3)
Dyspepsia	1 (3,3)
Faeces discoloured	1 (3,3)
Flatulence	3 (10,0)
Haematochezia	2 (6,7)
Lower gastrointestinal haemorrhage	1 (3,3)
Mouth haemorrhage	1 (3,3)
Mouth ulceration	1 (3,3)
Nausea	21 (70,0)
Oral pain	2 (6,7)
Post-tussive vomiting	1 (3,3)
Proctalgia	1 (3,3)
Stomatitis	14 (46,7)
Vomiting	26 (86,7)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	30 (100)
Alopecia	4 (13,3)
Dermatitis acneiform	14 (46,7)
Dermatitis atopic	2 (6,7)
Dermatitis diaper	1 (3,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Dry skin	19 (63,3)
Eczema	8 (26,7)
Erythema	3 (10,0)
Exfoliative rash	1 (3,3)
Hair colour changes	5 (16,7)
Miliaria	1 (3,3)
Pain of skin	4 (13,3)
Pruritus	12 (40,0)
Rash	3 (10,0)
Rash erythematous	1 (3,3)
Rash maculo-papular	13 (43,3)
Rash pruritic	1 (3,3)
Seborrhoeic dermatitis	1 (3,3)
Skin fissures	2 (6,7)
Skin hypopigmentation	1 (3,3)
Skin irritation	1 (3,3)
Skin lesion	1 (3,3)
Skin ulcer	2 (6,7)
Urticaria	2 (6,7)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	21 (70,0)
Arthralgia	2 (6,7)
Arthritis	1 (3,3)
Back pain	6 (20,0)
Joint effusion	1 (3,3)
Joint lock	1 (3,3)
Joint swelling	1 (3,3)
Muscular weakness	1 (3,3)
Musculoskeletal pain	2 (6,7)
Myalgia	2 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Neck pain	4 (13,3)
Osteoporosis	1 (3,3)
Pain in extremity	10 (33,3)
Sever's disease	1 (3,3)
Synovial cyst	1 (3,3)
RENAL AND URINARY DISORDERS	13 (43,3)
Acute kidney injury	1 (3,3)
Haematuria	5 (16,7)
Haemoglobinuria	2 (6,7)
Proteinuria	8 (26,7)
Urinary incontinence	4 (13,3)
Urinary tract pain	1 (3,3)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	28 (93,3)
Axillary pain	1 (3,3)
Chills	2 (6,7)
Fatigue	17 (56,7)
Hypothermia	1 (3,3)
Influenza like illness	12 (40,0)
Injection site reaction	1 (3,3)
Localised oedema	2 (6,7)
Malaise	4 (13,3)
Medical device site bruise	1 (3,3)
Medical device site erythema	2 (6,7)
Medical device site haemorrhage	1 (3,3)
Medical device site rash	1 (3,3)
Non-cardiac chest pain	1 (3,3)
Oedema peripheral	4 (13,3)
Pain	9 (30,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Pyrexia	22 (73,3)
Vessel puncture site bruise	1 (3,3)
INVESTIGATIONS	30 (100)
Activated partial thromboplastin time prolonged	1 (3,3)
Alanine aminotransferase increased	9 (30,0)
Amylase increased	6 (20,0)
Aspartate aminotransferase increased	11 (36,7)
Blood alkaline phosphatase increased	4 (13,3)
Blood bilirubin increased	1 (3,3)
Blood creatine phosphokinase increased	24 (80,0)
Blood creatinine increased	9 (30,0)
Breath sounds abnormal	1 (3,3)
Ejection fraction decreased	7 (23,3)
Haemoglobin increased	7 (23,3)
Haptoglobin decreased	1 (3,3)
Lipase increased	9 (30,0)
Lymphocyte count decreased	8 (26,7)
Lymphocyte count increased	8 (26,7)
Neutrophil count decreased	11 (36,7)
Platelet count decreased	5 (16,7)
Serum ferritin decreased	1 (3,3)
Weight decreased	3 (10,0)
Weight increased	3 (10,0)
White blood cell count decreased	6 (20,0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	16 (53,3)
Arthropod bite	2 (6,7)
Conjunctival abrasion	1 (3,3)
Contusion	2 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Fall	11 (36,7)
Foot fracture	1 (3,3)
Fracture	2 (6,7)
Humerus fracture	1 (3,3)
Joint dislocation	1 (3,3)
Laceration	2 (6,7)
Limb injury	1 (3,3)
Procedural hypotension	1 (3,3)
Skin abrasion	2 (6,7)
Stoma site irritation	1 (3,3)
Sunburn	1 (3,3)
Tracheal haemorrhage	1 (3,3)
Upper limb fracture	1 (3,3)
Wrist fracture	2 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Patients with Any AE	19 (95,0)
INFECTIONS AND INFESTATIONS	16 (80,0)
Body tinea	2 (10,0)
Cellulitis	1 (5,0)
Conjunctivitis	3 (15,0)
Eczema infected	1 (5,0)
Eye infection	1 (5,0)
Folliculitis	1 (5,0)
Gastroenteritis	1 (5,0)
Gastroenteritis viral	1 (5,0)
Hordeolum	2 (10,0)
Influenza	1 (5,0)
Lung infection	2 (10,0)
Otitis media	3 (15,0)
Paronychia	7 (35,0)
Pharyngitis	3 (15,0)
Pharyngitis streptococcal	1 (5,0)
Pneumonia	1 (5,0)
Respiratory syncytial virus infection	1 (5,0)
Sinusitis	2 (10,0)
Skin infection	2 (10,0)
Tracheitis	1 (5,0)
Upper respiratory tract infection	2 (10,0)
Urinary tract infection	3 (15,0)
Vaginal infection	1 (5,0)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	6 (30,0)
Anaemia	5 (25,0)
Lymph node pain	1 (5,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
IMMUNE SYSTEM DISORDERS	1 (5,0)
Hypersensitivity	1 (5,0)
METABOLISM AND NUTRITION DISORDERS	19 (95,0)
Decreased appetite	8 (40,0)
Dehydration	2 (10,0)
Hyperglycaemia	5 (25,0)
Hyperkalaemia	5 (25,0)
Hypermagnesaemia	1 (5,0)
Hypernatraemia	2 (10,0)
Hypoalbuminaemia	9 (45,0)
Hypocalcaemia	6 (30,0)
Hypoglycaemia	6 (30,0)
Hypokalaemia	5 (25,0)
Hypomagnesaemia	3 (15,0)
Hypophosphataemia	1 (5,0)
PSYCHIATRIC DISORDERS	9 (45,0)
Anxiety	2 (10,0)
Autoscopy	1 (5,0)
Depression	1 (5,0)
Hallucination, auditory	1 (5,0)
Insomnia	4 (20,0)
Irritability	1 (5,0)
Personality change	1 (5,0)
Social anxiety disorder	1 (5,0)
NERVOUS SYSTEM DISORDERS	12 (60,0)
Aphasia	1 (5,0)
Dizziness	7 (35,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Dysaesthesia	1 (5,0)
Dyspraxia	1 (5,0)
Headache	8 (40,0)
Lethargy	1 (5,0)
Paraesthesia	2 (10,0)
Presyncope	1 (5,0)
Seizure	1 (5,0)
Syncope	2 (10,0)
EYE DISORDERS	7 (35,0)
Amblyopia strabismic	1 (5,0)
Cataract	1 (5,0)
Dry eye	1 (5,0)
Eye oedema	1 (5,0)
Eye pain	3 (15,0)
Eye pruritus	1 (5,0)
Eyelid oedema	1 (5,0)
Lacrimation increased	4 (20,0)
Vision blurred	1 (5,0)
Vitreous disorder	1 (5,0)
EAR AND LABYRINTH DISORDERS	4 (20,0)
Ear pain	2 (10,0)
External ear inflammation	1 (5,0)
Tinnitus	1 (5,0)
CARDIAC DISORDERS	2 (10,0)
Sinus tachycardia	2 (10,0)
VASCULAR DISORDERS	3 (15,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Flushing	1 (5,0)
Hypertension	2 (10,0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	17 (85,0)
Aspiration	1 (5,0)
Atelectasis	2 (10,0)
Cough	8 (40,0)
Dyspnoea	2 (10,0)
Epistaxis	5 (25,0)
Hiccups	1 (5,0)
Hypoxia	1 (5,0)
Nasal congestion	9 (45,0)
Nasal dryness	1 (5,0)
Oropharyngeal pain	10 (50,0)
Rhinitis allergic	5 (25,0)
Rhinorrhoea	3 (15,0)
Tachypnoea	1 (5,0)
Wheezing	1 (5,0)
GASTROINTESTINAL DISORDERS	19 (95,0)
Abdominal distension	2 (10,0)
Abdominal pain	9 (45,0)
Abdominal pain upper	9 (45,0)
Anal haemorrhage	1 (5,0)
Constipation	4 (20,0)
Dental caries	4 (20,0)
Diarrhoea	11 (55,0)
Dry mouth	1 (5,0)
Dysphagia	1 (5,0)
Faeces discoloured	1 (5,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Flatulence	1 (5,0)
Gastrooesophageal reflux disease	2 (10,0)
Impaired gastric emptying	1 (5,0)
Lip dry	1 (5,0)
Nausea	14 (70,0)
Oesophageal stenosis	1 (5,0)
Oesophagitis	1 (5,0)
Oral pain	1 (5,0)
Proctalgia	1 (5,0)
Stomatitis	11 (55,0)
Tongue discolouration	1 (5,0)
Vomiting	16 (80,0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	19 (95,0)
Alopecia	8 (40,0)
Dermatitis	1 (5,0)
Dermatitis acneiform	12 (60,0)
Dermatitis atopic	1 (5,0)
Dry skin	13 (65,0)
Ecchymosis	1 (5,0)
Eczema	5 (25,0)
Erythema	1 (5,0)
Hair colour changes	7 (35,0)
Photosensitivity reaction	1 (5,0)
Pruritus	12 (60,0)
Rash maculo-papular	6 (30,0)
Skin exfoliation	2 (10,0)
Skin hypopigmentation	2 (10,0)
Urticaria	1 (5,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	15 (75,0)
Arthralgia	3 (15,0)
Axillary mass	1 (5,0)
Back pain	3 (15,0)
Bone pain	1 (5,0)
Limb asymmetry	1 (5,0)
Muscle twitching	1 (5,0)
Musculoskeletal pain	1 (5,0)
Neck pain	4 (20,0)
Pain in extremity	8 (40,0)
Tendonitis	1 (5,0)
RENAL AND URINARY DISORDERS	14 (70,0)
Dysuria	1 (5,0)
Haematuria	9 (45,0)
Haemoglobinuria	1 (5,0)
Pollakiuria	2 (10,0)
Proteinuria	4 (20,0)
Urinary incontinence	3 (15,0)
Urinary retention	1 (5,0)
Urinary tract pain	2 (10,0)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	4 (20,0)
Dysmenorrhoea	1 (5,0)
Menorrhagia	1 (5,0)
Menstruation irregular	2 (10,0)
Oligomenorrhoea	1 (5,0)
Ovarian cyst	1 (5,0)
Vulvovaginal dryness	1 (5,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	14 (70,0)
Face oedema	1 (5,0)
Facial pain	1 (5,0)
Fatigue	11 (55,0)
Gait disturbance	1 (5,0)
Influenza like illness	3 (15,0)
Localised oedema	3 (15,0)
Non-cardiac chest pain	2 (10,0)
Oedema peripheral	2 (10,0)
Pain	6 (30,0)
Peripheral swelling	1 (5,0)
Pyrexia	8 (40,0)
Swelling	1 (5,0)
INVESTIGATIONS	19 (95,0)
Alanine aminotransferase increased	8 (40,0)
Amylase increased	4 (20,0)
Aspartate aminotransferase increased	11 (55,0)
Blood alkaline phosphatase increased	7 (35,0)
Blood creatine phosphokinase increased	14 (70,0)
Blood creatinine increased	5 (25,0)
Ejection fraction decreased	5 (25,0)
Haemoglobin increased	3 (15,0)
Lipase increased	6 (30,0)
Lymphocyte count decreased	3 (15,0)
Lymphocyte count increased	5 (25,0)
Neutrophil count decreased	6 (30,0)
Oxygen saturation decreased	1 (5,0)
Platelet count decreased	1 (5,0)
Right ventricular ejection fraction decreased	1 (5,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Weight increased	2 (10,0)
White blood cell count decreased	4 (20,0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	7 (35,0)
Arthropod bite	1 (5,0)
Arthropod sting	1 (5,0)
Conjunctival abrasion	1 (5,0)
Contusion	1 (5,0)
Fall	3 (15,0)
Fracture	1 (5,0)
Head injury	1 (5,0)
Joint injury	1 (5,0)
Poisoning	1 (5,0)
Skin abrasion	2 (10,0)
Stress fracture	1 (5,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.3 Adverse events by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Patients with Any AE	21 (100)
INFECTIONS AND INFESTATIONS	18 (85,7)
Body tinea	3 (14,3)
Bronchitis viral	1 (4,8)
Cellulitis	1 (4,8)
Clostridium difficile colitis	1 (4,8)
Conjunctivitis	3 (14,3)
Ear infection	1 (4,8)
Eye infection	1 (4,8)
Folliculitis	2 (9,5)
Fungal skin infection	1 (4,8)
Gastroenteritis	1 (4,8)
Gastroenteritis viral	1 (4,8)
Hordeolum	1 (4,8)
Impetigo	1 (4,8)
Infected bite	1 (4,8)
Influenza	1 (4,8)
Injection site infection	1 (4,8)
Lung infection	1 (4,8)
Mucosal infection	1 (4,8)
Nail infection	1 (4,8)
Otitis externa	2 (9,5)
Otitis media	10 (47,6)
Paronychia	13 (61,9)
Pharyngitis	5 (23,8)
Pharyngitis streptococcal	6 (28,6)
Rash pustular	2 (9,5)
Sinusitis	4 (19,0)
Skin infection	4 (19,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
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Table 3.1.2.3 Adverse events by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Staphylococcal skin infection	1 (4,8)
Tinea infection	1 (4,8)
Upper respiratory tract infection	8 (38,1)
Urinary tract infection	1 (4,8)
Viral diarrhoea	3 (14,3)
Viral upper respiratory tract infection	1 (4,8)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	3 (14,3)
Skin papilloma	2 (9,5)
Tumour pain	1 (4,8)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	13 (61,9)
Anaemia	11 (52,4)
Lymph node pain	2 (9,5)
Lymphadenopathy	2 (9,5)
IMMUNE SYSTEM DISORDERS	5 (23,8)
Contrast media allergy	1 (4,8)
Hypersensitivity	5 (23,8)
METABOLISM AND NUTRITION DISORDERS	21 (100)
Decreased appetite	7 (33,3)
Dehydration	2 (9,5)
Hyperglycaemia	4 (19,0)
Hyperkalaemia	6 (28,6)
Hypermagnesaemia	4 (19,0)
Hypernatraemia	4 (19,0)
Hypoalbuminaemia	13 (61,9)
Hypocalcaemia	6 (28,6)
Hypoglycaemia	7 (33,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.3 Adverse events by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Hypokalaemia	6 (28,6)
Hypomagnesaemia	3 (14,3)
Hyponatraemia	2 (9,5)
Hypophosphataemia	4 (19,0)
PSYCHIATRIC DISORDERS	12 (57,1)
Agitation	1 (4,8)
Anxiety	3 (14,3)
Attention deficit/hyperactivity disorder	1 (4,8)
Autoscopy	1 (4,8)
Depression	1 (4,8)
Hallucination, auditory	1 (4,8)
Insomnia	4 (19,0)
Irritability	2 (9,5)
Personality change	2 (9,5)
Tic	1 (4,8)
NERVOUS SYSTEM DISORDERS	16 (76,2)
Disturbance in attention	2 (9,5)
Dizziness	6 (28,6)
Dysaesthesia	1 (4,8)
Headache	12 (57,1)
Paraesthesia	2 (9,5)
Presyncope	2 (9,5)
EYE DISORDERS	11 (52,4)
Amblyopia strabismic	1 (4,8)
Dry eye	3 (14,3)
Eye discharge	1 (4,8)
Eye pain	2 (9,5)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.3 Adverse events by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Eyelid oedema	1 (4,8)
Keratitis	1 (4,8)
Lacrimation increased	6 (28,6)
Ocular hypertension	1 (4,8)
Periorbital oedema	1 (4,8)
Photophobia	2 (9,5)
Vision blurred	2 (9,5)
EAR AND LABYRINTH DISORDERS	6 (28,6)
Ear pain	3 (14,3)
External ear inflammation	1 (4,8)
Tinnitus	2 (9,5)
CARDIAC DISORDERS	6 (28,6)
Sinus tachycardia	6 (28,6)
VASCULAR DISORDERS	5 (23,8)
Flushing	1 (4,8)
Hypertension	2 (9,5)
Hypotension	1 (4,8)
Phlebitis	1 (4,8)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	18 (85,7)
Allergic cough	1 (4,8)
Asthma	1 (4,8)
Atelectasis	1 (4,8)
Cough	14 (66,7)
Dyspnoea	1 (4,8)
Epistaxis	8 (38,1)
Hiccups	1 (4,8)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
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Table 3.1.2.3 Adverse events by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Nasal congestion	11 (52,4)
Oropharyngeal pain	11 (52,4)
Rhinitis allergic	7 (33,3)
Rhinorrhoea	4 (19,0)
Sneezing	1 (4,8)
Upper-airway cough syndrome	1 (4,8)
Wheezing	2 (9,5)
GASTROINTESTINAL DISORDERS	21 (100)
Abdominal distension	2 (9,5)
Abdominal pain	11 (52,4)
Abdominal pain upper	11 (52,4)
Anal incontinence	2 (9,5)
Constipation	9 (42,9)
Dental caries	1 (4,8)
Diarrhoea	18 (85,7)
Dyspepsia	1 (4,8)
Dysphagia	1 (4,8)
Faeces discoloured	1 (4,8)
Flatulence	3 (14,3)
Haematochezia	2 (9,5)
Lower gastrointestinal haemorrhage	1 (4,8)
Nausea	15 (71,4)
Oral pain	1 (4,8)
Post-tussive vomiting	1 (4,8)
Proctalgia	1 (4,8)
Stomatitis	11 (52,4)
Vomiting	18 (85,7)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	21 (100)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.3 Adverse events by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Alopecia	8 (38,1)
Dermatitis	1 (4,8)
Dermatitis acneiform	7 (33,3)
Dermatitis atopic	2 (9,5)
Dry skin	15 (71,4)
Eczema	10 (47,6)
Erythema	2 (9,5)
Hair colour changes	6 (28,6)
Miliaria	1 (4,8)
Pain of skin	3 (14,3)
Pruritus	13 (61,9)
Rash	2 (9,5)
Rash maculo-papular	8 (38,1)
Seborrhoeic dermatitis	1 (4,8)
Skin fissures	2 (9,5)
Skin hypopigmentation	1 (4,8)
Urticaria	2 (9,5)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	13 (61,9)
Arthralgia	2 (9,5)
Arthritis	1 (4,8)
Back pain	2 (9,5)
Joint effusion	1 (4,8)
Joint swelling	1 (4,8)
Muscle twitching	1 (4,8)
Muscular weakness	1 (4,8)
Musculoskeletal pain	2 (9,5)
Myalgia	1 (4,8)
Neck pain	3 (14,3)
Pain in extremity	8 (38,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.3 Adverse events by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Synovial cyst	1 (4,8)
Tendonitis	1 (4,8)
RENAL AND URINARY DISORDERS	14 (66,7)
Dysuria	1 (4,8)
Haematuria	4 (19,0)
Haemoglobinuria	1 (4,8)
Pollakiuria	2 (9,5)
Proteinuria	6 (28,6)
Urinary incontinence	5 (23,8)
Urinary retention	1 (4,8)
Urinary tract pain	2 (9,5)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	19 (90,5)
Axillary pain	1 (4,8)
Chills	1 (4,8)
Facial pain	1 (4,8)
Fatigue	13 (61,9)
Gait disturbance	1 (4,8)
Influenza like illness	10 (47,6)
Localised oedema	2 (9,5)
Malaise	3 (14,3)
Non-cardiac chest pain	1 (4,8)
Oedema peripheral	1 (4,8)
Pain	5 (23,8)
Pyrexia	14 (66,7)
INVESTIGATIONS	21 (100)
Activated partial thromboplastin time prolonged	1 (4,8)
Alanine aminotransferase increased	6 (28,6)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.3 Adverse events by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Amylase increased	4 (19,0)
Aspartate aminotransferase increased	9 (42,9)
Blood alkaline phosphatase increased	3 (14,3)
Blood bilirubin increased	1 (4,8)
Blood creatine phosphokinase increased	18 (85,7)
Blood creatinine increased	6 (28,6)
Breath sounds abnormal	1 (4,8)
Ejection fraction decreased	4 (19,0)
Haemoglobin increased	9 (42,9)
Haptoglobin decreased	1 (4,8)
Lipase increased	8 (38,1)
Lymphocyte count decreased	4 (19,0)
Lymphocyte count increased	9 (42,9)
Neutrophil count decreased	11 (52,4)
Platelet count decreased	3 (14,3)
Weight decreased	1 (4,8)
Weight increased	3 (14,3)
White blood cell count decreased	4 (19,0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	12 (57,1)
Arthropod bite	1 (4,8)
Conjunctival abrasion	2 (9,5)
Contusion	1 (4,8)
Fall	8 (38,1)
Fracture	1 (4,8)
Head injury	1 (4,8)
Laceration	2 (9,5)
Limb injury	1 (4,8)
Poisoning	1 (4,8)
Skin abrasion	2 (9,5)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.3 Adverse events by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Wrist fracture	1 (4,8)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.4 Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Patients with Any AE	14 (93,3)
INFECTIONS AND INFESTATIONS	11 (73,3)
Abscess	1 (6,7)
Bacterial tracheitis	1 (6,7)
Bronchitis	1 (6,7)
Cellulitis	2 (13,3)
Conjunctivitis	1 (6,7)
Eye infection	1 (6,7)
Folliculitis	2 (13,3)
Fungal skin infection	1 (6,7)
Furuncle	1 (6,7)
Gastroenteritis	1 (6,7)
Gastroenteritis viral	1 (6,7)
Influenza	1 (6,7)
Metapneumovirus infection	1 (6,7)
Mucosal infection	1 (6,7)
Otitis externa	1 (6,7)
Otitis media	1 (6,7)
Paronychia	5 (33,3)
Pharyngitis	1 (6,7)
Rash pustular	1 (6,7)
Skin infection	2 (13,3)
Staphylococcal infection	1 (6,7)
Tinea infection	1 (6,7)
Tinea pedis	1 (6,7)
Upper respiratory tract infection	2 (13,3)
Urinary tract infection	2 (13,3)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	6 (40,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.4 Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Anaemia	6 (40,0)
METABOLISM AND NUTRITION DISORDERS	14 (93,3)
Decreased appetite	1 (6,7)
Dehydration	3 (20,0)
Hypercalcaemia	1 (6,7)
Hyperglycaemia	3 (20,0)
Hyperkalaemia	3 (20,0)
Hypermagnesaemia	1 (6,7)
Hypernatraemia	3 (20,0)
Hyperuricaemia	1 (6,7)
Hypoalbuminaemia	5 (33,3)
Hypocalcaemia	3 (20,0)
Hypoglycaemia	6 (40,0)
Hypokalaemia	3 (20,0)
Hypomagnesaemia	1 (6,7)
Hyponatraemia	3 (20,0)
Hypophosphataemia	2 (13,3)
Lactose intolerance	1 (6,7)
PSYCHIATRIC DISORDERS	6 (40,0)
Anxiety	2 (13,3)
Depression	1 (6,7)
Insomnia	3 (20,0)
Irritability	1 (6,7)
Social anxiety disorder	1 (6,7)
NERVOUS SYSTEM DISORDERS	11 (73,3)
Cognitive disorder	1 (6,7)
Depressed level of consciousness	1 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.4 Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Dizziness	6 (40,0)
Drooling	1 (6,7)
Dyspraxia	1 (6,7)
Headache	7 (46,7)
Presyncope	1 (6,7)
Syncope	1 (6,7)
EYE DISORDERS	3 (20,0)
Chorioretinal scar	1 (6,7)
Vision blurred	1 (6,7)
Vitreous disorder	1 (6,7)
EAR AND LABYRINTH DISORDERS	5 (33,3)
Ear pain	2 (13,3)
External ear inflammation	1 (6,7)
Middle ear effusion	1 (6,7)
Motion sickness	1 (6,7)
Tinnitus	1 (6,7)
CARDIAC DISORDERS	3 (20,0)
Nodal arrhythmia	1 (6,7)
Palpitations	1 (6,7)
Sinus bradycardia	2 (13,3)
Sinus tachycardia	1 (6,7)
Supraventricular tachycardia	1 (6,7)
VASCULAR DISORDERS	8 (53,3)
Flushing	2 (13,3)
Haematoma	1 (6,7)
Hypertension	5 (33,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.4 Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	10 (66,7)
Atelectasis	2 (13,3)
Cough	2 (13,3)
Epistaxis	4 (26,7)
Hypoxia	1 (6,7)
Increased bronchial secretion	1 (6,7)
Nasal congestion	2 (13,3)
Oropharyngeal pain	6 (40,0)
Rhinitis allergic	3 (20,0)
Sleep apnoea syndrome	1 (6,7)
Sneezing	1 (6,7)
GASTROINTESTINAL DISORDERS	14 (93,3)
Abdominal distension	1 (6,7)
Abdominal pain	5 (33,3)
Abdominal pain upper	7 (46,7)
Anal haemorrhage	1 (6,7)
Constipation	4 (26,7)
Dental caries	1 (6,7)
Diarrhoea	11 (73,3)
Dry mouth	1 (6,7)
Faeces discoloured	1 (6,7)
Gastrooesophageal reflux disease	1 (6,7)
Mouth haemorrhage	1 (6,7)
Mouth ulceration	1 (6,7)
Nausea	10 (66,7)
Oral pain	2 (13,3)
Stomatitis	6 (40,0)
Tongue discolouration	1 (6,7)
Vomiting	12 (80,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.4 Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	14 (93,3)
Alopecia	2 (13,3)
Dermatitis acneiform	9 (60,0)
Dermatitis atopic	1 (6,7)
Dermatitis diaper	1 (6,7)
Dry skin	9 (60,0)
Eczema	1 (6,7)
Hair colour changes	4 (26,7)
Pain of skin	1 (6,7)
Pruritus	5 (33,3)
Rash	1 (6,7)
Rash maculo-papular	6 (40,0)
Rash pruritic	1 (6,7)
Skin hypopigmentation	1 (6,7)
Skin ulcer	1 (6,7)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	12 (80,0)
Arthralgia	3 (20,0)
Back pain	3 (20,0)
Bone pain	1 (6,7)
Joint lock	1 (6,7)
Limb asymmetry	1 (6,7)
Myalgia	1 (6,7)
Neck pain	3 (20,0)
Osteoporosis	1 (6,7)
Pain in extremity	4 (26,7)
RENAL AND URINARY DISORDERS	5 (33,3)
Acute kidney injury	1 (6,7)
Haematuria	4 (26,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.4 Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Haemoglobinuria	1 (6,7)
Proteinuria	3 (20,0)
Urinary incontinence	1 (6,7)
Urinary tract pain	1 (6,7)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	3 (20,0)
Menorrhagia	1 (6,7)
Menstruation irregular	2 (13,3)
Oligomenorrhoea	1 (6,7)
Ovarian cyst	1 (6,7)
Vulvovaginal dryness	1 (6,7)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	12 (80,0)
Chills	1 (6,7)
Face oedema	1 (6,7)
Fatigue	9 (60,0)
Hypothermia	1 (6,7)
Influenza like illness	4 (26,7)
Injection site reaction	1 (6,7)
Localised oedema	2 (13,3)
Malaise	1 (6,7)
Medical device site bruise	1 (6,7)
Medical device site erythema	1 (6,7)
Medical device site rash	1 (6,7)
Non-cardiac chest pain	2 (13,3)
Oedema peripheral	3 (20,0)
Pain	7 (46,7)
Pyrexia	8 (53,3)
Vessel puncture site bruise	1 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.4 Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
INVESTIGATIONS	14 (93,3)
Alanine aminotransferase increased	5 (33,3)
Amylase increased	5 (33,3)
Aspartate aminotransferase increased	6 (40,0)
Blood alkaline phosphatase increased	4 (26,7)
Blood creatine phosphokinase increased	12 (80,0)
Blood creatinine increased	3 (20,0)
Ejection fraction decreased	2 (13,3)
Lipase increased	4 (26,7)
Lymphocyte count decreased	5 (33,3)
Lymphocyte count increased	4 (26,7)
Neutrophil count decreased	5 (33,3)
Platelet count decreased	2 (13,3)
Right ventricular ejection fraction decreased	1 (6,7)
Serum ferritin decreased	1 (6,7)
Weight increased	2 (13,3)
White blood cell count decreased	4 (26,7)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	6 (40,0)
Arthropod bite	1 (6,7)
Contusion	1 (6,7)
Fall	3 (20,0)
Foot fracture	1 (6,7)
Fracture	2 (13,3)
Humerus fracture	1 (6,7)
Skin abrasion	1 (6,7)
Stoma site irritation	1 (6,7)
Stress fracture	1 (6,7)
Sunburn	1 (6,7)
Tracheal haemorrhage	1 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.4 Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Upper limb fracture	1 (6,7)
Wrist fracture	1 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.5 Adverse events by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Patients with Any AE	14 (100)
INFECTIONS AND INFESTATIONS	12 (85,7)
Cellulitis	2 (14,3)
Conjunctivitis	1 (7,1)
Conjunctivitis viral	1 (7,1)
Eczema infected	1 (7,1)
Eye infection	1 (7,1)
Gastroenteritis	1 (7,1)
Hordeolum	1 (7,1)
Influenza	1 (7,1)
Lung infection	2 (14,3)
Osteomyelitis	1 (7,1)
Otitis media	3 (21,4)
Paronychia	5 (35,7)
Pharyngitis	3 (21,4)
Pharyngitis streptococcal	1 (7,1)
Pilonidal cyst	1 (7,1)
Pneumonia	1 (7,1)
Rash pustular	1 (7,1)
Respiratory syncytial virus infection	1 (7,1)
Sinusitis	2 (14,3)
Skin infection	2 (14,3)
Tracheitis	1 (7,1)
Upper respiratory tract infection	1 (7,1)
Urinary tract infection	1 (7,1)
Vaginal infection	1 (7,1)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (7,1)
Peripheral nerve sheath tumour malignant	1 (7,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.5 Adverse events by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	6 (42,9)
Anaemia	6 (42,9)
IMMUNE SYSTEM DISORDERS	1 (7,1)
Hypersensitivity	1 (7,1)
METABOLISM AND NUTRITION DISORDERS	13 (92,9)
Decreased appetite	5 (35,7)
Dehydration	2 (14,3)
Hypercalcaemia	1 (7,1)
Hyperglycaemia	5 (35,7)
Hyperkalaemia	2 (14,3)
Hypernatraemia	2 (14,3)
Hypoalbuminaemia	8 (57,1)
Hypocalcaemia	4 (28,6)
Hypoglycaemia	3 (21,4)
Hypokalaemia	4 (28,6)
Hypomagnesaemia	1 (7,1)
Hyponatraemia	3 (21,4)
Hypophosphataemia	2 (14,3)
PSYCHIATRIC DISORDERS	5 (35,7)
Anxiety	1 (7,1)
Depression	1 (7,1)
Insomnia	3 (21,4)
Irritability	1 (7,1)
Suicidal ideation	1 (7,1)
NERVOUS SYSTEM DISORDERS	8 (57,1)
Aphasia	1 (7,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.5 Adverse events by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Disturbance in attention	1 (7,1)
Dizziness	2 (14,3)
Headache	6 (42,9)
Lethargy	1 (7,1)
Neuralgia	1 (7,1)
Paraesthesia	1 (7,1)
Presyncope	1 (7,1)
Seizure	1 (7,1)
Syncope	1 (7,1)
EYE DISORDERS	3 (21,4)
Cataract	1 (7,1)
Eye oedema	1 (7,1)
Eye pain	2 (14,3)
Eye pruritus	1 (7,1)
Lacrimation increased	2 (14,3)
Vision blurred	1 (7,1)
EAR AND LABYRINTH DISORDERS	1 (7,1)
Ear pain	1 (7,1)
CARDIAC DISORDERS	3 (21,4)
Sinus tachycardia	3 (21,4)
VASCULAR DISORDERS	2 (14,3)
Hypertension	2 (14,3)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	13 (92,9)
Aspiration	1 (7,1)
Atelectasis	1 (7,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.5 Adverse events by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Cough	5 (35,7)
Dysphonia	1 (7,1)
Dyspnoea	3 (21,4)
Epistaxis	2 (14,3)
Hypoxia	3 (21,4)
Increased bronchial secretion	1 (7,1)
Nasal congestion	5 (35,7)
Nasal dryness	1 (7,1)
Oropharyngeal pain	8 (57,1)
Rhinitis allergic	5 (35,7)
Rhinorrhoea	2 (14,3)
Sneezing	1 (7,1)
Tachypnoea	1 (7,1)
Tracheal inflammation	1 (7,1)
Upper-airway cough syndrome	1 (7,1)
GASTROINTESTINAL DISORDERS	14 (100)
Abdominal distension	2 (14,3)
Abdominal pain	7 (50,0)
Abdominal pain upper	3 (21,4)
Constipation	5 (35,7)
Dental caries	2 (14,3)
Diarrhoea	8 (57,1)
Dry mouth	1 (7,1)
Flatulence	1 (7,1)
Gastrooesophageal reflux disease	1 (7,1)
Impaired gastric emptying	1 (7,1)
Lip dry	1 (7,1)
Nausea	10 (71,4)
Oesophageal stenosis	1 (7,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.5 Adverse events by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Oesophagitis	1 (7,1)
Proctalgia	1 (7,1)
Stomatitis	8 (57,1)
Vomiting	12 (85,7)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	14 (100)
Alopecia	2 (14,3)
Dermatitis acneiform	10 (71,4)
Dry skin	8 (57,1)
Ecchymosis	1 (7,1)
Eczema	2 (14,3)
Erythema	2 (14,3)
Exfoliative rash	1 (7,1)
Hair colour changes	2 (14,3)
Photosensitivity reaction	1 (7,1)
Pruritus	6 (42,9)
Rash erythematous	1 (7,1)
Rash maculo-papular	5 (35,7)
Skin exfoliation	2 (14,3)
Skin hypopigmentation	1 (7,1)
Skin irritation	1 (7,1)
Skin lesion	1 (7,1)
Skin ulcer	1 (7,1)
Urticaria	1 (7,1)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	11 (78,6)
Axillary mass	1 (7,1)
Back pain	4 (28,6)
Musculoskeletal pain	1 (7,1)
Neck pain	2 (14,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.5 Adverse events by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Pain in extremity	6 (42,9)
Sever's disease	1 (7,1)
RENAL AND URINARY DISORDERS	8 (57,1)
Haematuria	6 (42,9)
Haemoglobinuria	1 (7,1)
Proteinuria	3 (21,4)
Urinary incontinence	1 (7,1)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (7,1)
Dysmenorrhoea	1 (7,1)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	11 (78,6)
Fatigue	6 (42,9)
Influenza like illness	1 (7,1)
Localised oedema	1 (7,1)
Medical device site erythema	1 (7,1)
Medical device site haemorrhage	1 (7,1)
Oedema peripheral	2 (14,3)
Pain	3 (21,4)
Peripheral swelling	1 (7,1)
Pyrexia	8 (57,1)
Swelling	1 (7,1)
INVESTIGATIONS	14 (100)
Alanine aminotransferase increased	6 (42,9)
Amylase increased	1 (7,1)
Aspartate aminotransferase increased	7 (50,0)
Blood alkaline phosphatase increased	4 (28,6)
Blood creatine phosphokinase increased	8 (57,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.2.5 Adverse events by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Blood creatinine increased	5 (35,7)
Ejection fraction decreased	6 (42,9)
Haemoglobin increased	1 (7,1)
Lipase increased	3 (21,4)
Lymphocyte count decreased	2 (14,3)
Neutrophil count decreased	1 (7,1)
Oxygen saturation decreased	1 (7,1)
Platelet count decreased	1 (7,1)
Weight decreased	2 (14,3)
White blood cell count decreased	2 (14,3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	5 (35,7)
Arthropod bite	1 (7,1)
Arthropod sting	1 (7,1)
Contusion	1 (7,1)
Fall	3 (21,4)
Joint dislocation	1 (7,1)
Joint injury	1 (7,1)
Procedural hypotension	1 (7,1)
Skin abrasion	1 (7,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.3.1 Serious Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Patients with Any SAE	12 (40,0)
INFECTIONS AND INFESTATIONS	6 (20,0)
Bacterial tracheitis	1 (3,3)
Clostridium difficile colitis	1 (3,3)
Influenza	1 (3,3)
Osteomyelitis	1 (3,3)
Skin infection	1 (3,3)
Urinary tract infection	1 (3,3)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (3,3)
Peripheral nerve sheath tumour malignant	1 (3,3)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	2 (6,7)
Anaemia	2 (6,7)
METABOLISM AND NUTRITION DISORDERS	1 (3,3)
Hyperkalaemia	1 (3,3)
Hyperuricaemia	1 (3,3)
Hypocalcaemia	1 (3,3)
VASCULAR DISORDERS	1 (3,3)
Haematoma	1 (3,3)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	2 (6,7)
Hypoxia	2 (6,7)
GASTROINTESTINAL DISORDERS	3 (10,0)
Constipation	1 (3,3)
Diarrhoea	2 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.3.1 Serious Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (3,3)
Skin ulcer	1 (3,3)
RENAL AND URINARY DISORDERS	1 (3,3)
Acute kidney injury	1 (3,3)
Proteinuria	1 (3,3)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (3,3)
Pyrexia	1 (3,3)
INVESTIGATIONS	2 (6,7)
Blood creatine phosphokinase increased	1 (3,3)
Blood creatinine increased	1 (3,3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	2 (6,7)
Humerus fracture	1 (3,3)
Procedural hypotension	1 (3,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.3.2 Serious Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Patients with Any SAE	0

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.3.3 Serious Adverse events by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Patients with Any SAE	3 (14,3)
INFECTIONS AND INFESTATIONS	1 (4,8)
Clostridium difficile colitis	1 (4,8)
GASTROINTESTINAL DISORDERS	1 (4,8)
Diarrhoea	1 (4,8)
INVESTIGATIONS	1 (4,8)
Blood creatine phosphokinase increased	1 (4,8)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.3.4 Serious Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Patients with Any SAE	5 (33,3)
INFECTIONS AND INFESTATIONS	4 (26,7)
Bacterial tracheitis	1 (6,7)
Influenza	1 (6,7)
Skin infection	1 (6,7)
Urinary tract infection	1 (6,7)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (6,7)
Anaemia	1 (6,7)
METABOLISM AND NUTRITION DISORDERS	1 (6,7)
Hyperkalaemia	1 (6,7)
Hyperuricaemia	1 (6,7)
Hypocalcaemia	1 (6,7)
VASCULAR DISORDERS	1 (6,7)
Haematoma	1 (6,7)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (6,7)
Hypoxia	1 (6,7)
GASTROINTESTINAL DISORDERS	1 (6,7)
Constipation	1 (6,7)
RENAL AND URINARY DISORDERS	1 (6,7)
Acute kidney injury	1 (6,7)
Proteinuria	1 (6,7)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.3.4 Serious Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Pyrexia	1 (6,7)
INVESTIGATIONS	1 (6,7)
Blood creatinine increased	1 (6,7)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (6,7)
Humerus fracture	1 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.3.5 Serious Adverse events by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Patients with Any SAE	4 (28,6)
INFECTIONS AND INFESTATIONS	1 (7,1)
Osteomyelitis	1 (7,1)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (7,1)
Peripheral nerve sheath tumour malignant	1 (7,1)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (7,1)
Anaemia	1 (7,1)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (7,1)
Hypoxia	1 (7,1)
GASTROINTESTINAL DISORDERS	1 (7,1)
Diarrhoea	1 (7,1)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (7,1)
Skin ulcer	1 (7,1)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (7,1)
Procedural hypotension	1 (7,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.1 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Patients with Any Severe AE (CTCAE >=3)	21 (70,0)
INFECTIONS AND INFESTATIONS	8 (26,7)
Clostridium difficile colitis	1 (3,3)
Influenza	1 (3,3)
Osteomyelitis	1 (3,3)
Paronychia	3 (10,0)
Skin infection	1 (3,3)
Urinary tract infection	1 (3,3)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	2 (6,7)
Peripheral nerve sheath tumour malignant	1 (3,3)
Tumour pain	1 (3,3)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	2 (6,7)
Anaemia	2 (6,7)
IMMUNE SYSTEM DISORDERS	1 (3,3)
Contrast media allergy	1 (3,3)
METABOLISM AND NUTRITION DISORDERS	2 (6,7)
Hyperkalaemia	1 (3,3)
Hyperuricaemia	1 (3,3)
Hypocalcaemia	1 (3,3)
Hypokalaemia	1 (3,3)
PSYCHIATRIC DISORDERS	1 (3,3)
Insomnia	1 (3,3)
NERVOUS SYSTEM DISORDERS	1 (3,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.1 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Headache	1 (3,3)
EAR AND LABYRINTH DISORDERS	1 (3,3)
Motion sickness	1 (3,3)
VASCULAR DISORDERS	1 (3,3)
Haematoma	1 (3,3)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	3 (10,0)
Hypoxia	3 (10,0)
GASTROINTESTINAL DISORDERS	9 (30,0)
Diarrhoea	7 (23,3)
Nausea	1 (3,3)
Vomiting	3 (10,0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	5 (16,7)
Dermatitis acneiform	3 (10,0)
Eczema	1 (3,3)
Skin ulcer	1 (3,3)
RENAL AND URINARY DISORDERS	2 (6,7)
Acute kidney injury	1 (3,3)
Haematuria	1 (3,3)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	3 (10,0)
Influenza like illness	1 (3,3)
Pyrexia	3 (10,0)
INVESTIGATIONS	7 (23,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.1 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Alanine aminotransferase increased	1 (3,3)
Blood creatine phosphokinase increased	2 (6,7)
Blood creatinine increased	1 (3,3)
Lipase increased	1 (3,3)
Lymphocyte count decreased	1 (3,3)
Neutrophil count decreased	1 (3,3)
Weight increased	2 (6,7)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	3 (10,0)
Humerus fracture	1 (3,3)
Procedural hypotension	1 (3,3)
Upper limb fracture	1 (3,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.2 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Patients with Any Severe AE (CTCAE >=3)	10 (50,0)
INFECTIONS AND INFESTATIONS	1 (5,0)
Lung infection	1 (5,0)
Tracheitis	1 (5,0)
NERVOUS SYSTEM DISORDERS	2 (10,0)
Syncope	2 (10,0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (5,0)
Hypoxia	1 (5,0)
GASTROINTESTINAL DISORDERS	4 (20,0)
Dental caries	2 (10,0)
Diarrhoea	1 (5,0)
Nausea	1 (5,0)
Vomiting	1 (5,0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (5,0)
Dry skin	1 (5,0)
Eczema	1 (5,0)
Rash maculo-papular	1 (5,0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (5,0)
Limb asymmetry	1 (5,0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (5,0)
Pyrexia	1 (5,0)
INVESTIGATIONS	4 (20,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.2 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Alanine aminotransferase increased	1 (5,0)
Aspartate aminotransferase increased	1 (5,0)
Blood creatine phosphokinase increased	1 (5,0)
Lipase increased	1 (5,0)
Weight increased	2 (10,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.3 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Patients with Any Severe AE (CTCAE >=3)	13 (61,9)
INFECTIONS AND INFESTATIONS	4 (19,0)
Clostridium difficile colitis	1 (4,8)
Paronychia	3 (14,3)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (4,8)
Tumour pain	1 (4,8)
IMMUNE SYSTEM DISORDERS	1 (4,8)
Contrast media allergy	1 (4,8)
METABOLISM AND NUTRITION DISORDERS	1 (4,8)
Hypokalaemia	1 (4,8)
PSYCHIATRIC DISORDERS	1 (4,8)
Insomnia	1 (4,8)
NERVOUS SYSTEM DISORDERS	1 (4,8)
Headache	1 (4,8)
GASTROINTESTINAL DISORDERS	7 (33,3)
Dental caries	1 (4,8)
Diarrhoea	5 (23,8)
Vomiting	1 (4,8)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	4 (19,0)
Dermatitis acneiform	2 (9,5)
Dry skin	1 (4,8)
Eczema	2 (9,5)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.3 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Rash maculo-papular	1 (4,8)
RENAL AND URINARY DISORDERS	1 (4,8)
Haematuria	1 (4,8)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	3 (14,3)
Influenza like illness	1 (4,8)
Pyrexia	3 (14,3)
INVESTIGATIONS	5 (23,8)
Alanine aminotransferase increased	1 (4,8)
Blood creatine phosphokinase increased	2 (9,5)
Lipase increased	1 (4,8)
Weight increased	2 (9,5)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.4 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Patients with Any Severe AE (CTCAE >=3)	10 (66,7)
INFECTIONS AND INFESTATIONS	3 (20,0)
Influenza	1 (6,7)
Skin infection	1 (6,7)
Urinary tract infection	1 (6,7)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (6,7)
Anaemia	1 (6,7)
METABOLISM AND NUTRITION DISORDERS	1 (6,7)
Hyperkalaemia	1 (6,7)
Hyperuricaemia	1 (6,7)
Hypocalcaemia	1 (6,7)
NERVOUS SYSTEM DISORDERS	1 (6,7)
Syncope	1 (6,7)
EAR AND LABYRINTH DISORDERS	1 (6,7)
Motion sickness	1 (6,7)
VASCULAR DISORDERS	1 (6,7)
Haematoma	1 (6,7)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (6,7)
Hypoxia	1 (6,7)
GASTROINTESTINAL DISORDERS	3 (20,0)
Dental caries	1 (6,7)
Diarrhoea	1 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.4 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Nausea	1 (6,7)
Vomiting	2 (13,3)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (6,7)
Limb asymmetry	1 (6,7)
RENAL AND URINARY DISORDERS	1 (6,7)
Acute kidney injury	1 (6,7)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (6,7)
Pyrexia	1 (6,7)
INVESTIGATIONS	5 (33,3)
Blood creatine phosphokinase increased	1 (6,7)
Blood creatinine increased	1 (6,7)
Lymphocyte count decreased	1 (6,7)
Neutrophil count decreased	1 (6,7)
Weight increased	2 (13,3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	2 (13,3)
Humerus fracture	1 (6,7)
Upper limb fracture	1 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.5 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Patients with Any Severe AE (CTCAE >=3)	8 (57,1)
INFECTIONS AND INFESTATIONS	2 (14,3)
Lung infection	1 (7,1)
Osteomyelitis	1 (7,1)
Tracheitis	1 (7,1)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (7,1)
Peripheral nerve sheath tumour malignant	1 (7,1)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (7,1)
Anaemia	1 (7,1)
NERVOUS SYSTEM DISORDERS	1 (7,1)
Syncope	1 (7,1)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	3 (21,4)
Hypoxia	3 (21,4)
GASTROINTESTINAL DISORDERS	3 (21,4)
Diarrhoea	2 (14,3)
Nausea	1 (7,1)
Vomiting	1 (7,1)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	2 (14,3)
Dermatitis acneiform	1 (7,1)
Skin ulcer	1 (7,1)
INVESTIGATIONS	1 (7,1)
Alanine aminotransferase increased	1 (7,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.4.5 Severe Adverse events (CTCAE >=3) by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Aspartate aminotransferase increased	1 (7,1)
Lipase increased	1 (7,1)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (7,1)
Procedural hypotension	1 (7,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.5.1 Adverse events leading to discontinuation by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Patients with Any AE leading to discontinuation	5 (16,7)
INFECTIONS AND INFESTATIONS	1 (3,3)
Paronychia	1 (3,3)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (3,3)
Peripheral nerve sheath tumour malignant	1 (3,3)
GASTROINTESTINAL DISORDERS	1 (3,3)
Diarrhoea	1 (3,3)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (3,3)
Skin ulcer	1 (3,3)
RENAL AND URINARY DISORDERS	1 (3,3)
Acute kidney injury	1 (3,3)
INVESTIGATIONS	1 (3,3)
Blood creatinine increased	1 (3,3)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.5.2 Adverse events leading to discontinuation by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Patients with Any AE leading to discontinuation	1 (5,0)
INVESTIGATIONS	1 (5,0)
Weight increased	1 (5,0)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.5.3 Adverse events leading to discontinuation by system organ class and preferred term
- PN status at enrollment = Progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Patients with Any AE leading to discontinuation	1 (4,8)
INFECTIONS AND INFESTATIONS	1 (4,8)
Paronychia	1 (4,8)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.5.4 Adverse events leading to discontinuation by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Patients with Any AE leading to discontinuation	2 (13,3)
RENAL AND URINARY DISORDERS	1 (6,7)
Acute kidney injury	1 (6,7)
INVESTIGATIONS	2 (13,3)
Blood creatinine increased	1 (6,7)
Weight increased	1 (6,7)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 3.1.5.5 Adverse events leading to discontinuation by system organ class and preferred term
- PN status at enrollment = Unknown (Safety analysis set)
Phase II Stratum 1, 90 day safety follow-up data cut-off: 29th March 2019

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Patients with Any AE leading to discontinuation	3 (21,4)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (7,1)
Peripheral nerve sheath tumour malignant	1 (7,1)
GASTROINTESTINAL DISORDERS	1 (7,1)
Diarrhoea	1 (7,1)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (7,1)
Skin ulcer	1 (7,1)

[a] Each patient has only been represented with the maximum reported CTCAE grade for each system organ class/preferred term.
Number (%) of patients with AEs, sorted by international SOC order and alphabetical PT.
Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of study medication.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

Table 4.1.1 Demographics (at baseline/screening) and disease characteristic (Full analysis set)
Phase II Stratum 1, Data cut-off: 29th June 2018

Demographic/disease characteristics		Selumetinib 25 mg/m² BID (N=50)
Country n(%)	Canada	1(2,0)
	Hungary	1(2,0)
	Jamaica	1(2,0)
	United States	47(94,0)
Region n(%)	North America	49(98,0)
	Europe	1(2,0)
Any progressive PN present n(%)	Yes	23(46,0)
	No	27(54,0)
All PN Volume at baseline (mL)	n	50
	Mean	970,00
	SD	979,487
	Median	561,00
	Min	5,6
	Max	3931,0

N = Number of patients in treatment group.
n = Number of patients included in analysis. Max = Maximum. Min = Minimum. SD = Standard deviation.

Table 4.1.2 Demographics (at baseline/screening) and disease characteristic - Natural History Study NF1 age-matched

Demographic/disease characteristics		Natural History Study (N=92)
Country n(%)	United States	92(100)
Region n(%)	North America	92(100)
BSA (m²) [b]	n	69
	Mean	1,03
	SD	0,364
	Median	0,93
	Min	0,6
	Max	2,0
PN volume at baseline (mL)	n	92
	Mean	538,09
	SD	700,753
	Median	301,50
	Min	3,7
	Max	4895,0
PN classification - Nodular n(%)	No	92(100)
Any PN-directed medical treatment [a] n(%)	Yes	65(70,7)
	No	27(29,3)

N = Number of patients in treatment group.
n = Number of patients included in analysis. Max = Maximum. Min = Minimum. SD = Standard deviation.
[a] PN-directed medical treatments include treatments on date of imaging or present in interval between date of imaging and most recent prior imaging. Medical treatments directed at other NF1 tumours may also be included. Includes data until the last MRI assessment or last MRI assessment date prior to the first use of a MEK inhibitor including Selumetinib.
[b] BSA calculated using DuBois method (BSA = 0.007184 * Height(cm)0.725 * Weight(kg)0.425).