Dossier zur Nutzenbewertung gemäß § 35a SGB V

Selumetinib (Koselugo®)

Alexion Pharma Germany GmbH

Anhang 4-G1

Studie SPRINT (Phase II, Stratum 1)
3. Datenschnitt vom 31.03.2021 –
weitere Auswertungen

Stand: 14.11.2025

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Anhang 4-G1 Studie SPRINT (Phase II, Stratum 1) 3. Datenschnitt vom 31.03.2021

1 Endpunktkategorie Morbidität

1.1 Endpunkt Volumenänderung

1.1.1 Subgruppenanalysen zur Volumenänderung der Zielläsion

Table 1.15.1.1 Target PN volume, absolute and percentage change from baseline - NCI assessment - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Absolute change (ml)						Percentage change					
Group	Time point	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Selumetinib*n25 mg/m² BID	Pre-cycle 5	29	-168.12	209.434	-678.0	-72.00	-0.4	29	-14.90	7.227	-26.8	-15.03	-1.0
	Pre-cycle 9	27	-206.81	267.764	-936.0	-79.00	25.0	27	-18.60	10.471	-37.5	-20.54	5.2
	Pre-cycle 13	28	-218.79	266.063	-884.0	-109.50	24.0	28	-19.49	12.162	-38.6	-22.25	10.6
	Pre-cycle 17	24	-174.09	249.249	-964.0	-80.00	72.0	24	-20.05	15.571	-45.9	-24.57	18.5
	Pre-cycle 21	22	-139.39	204.134	-592.0	-75.50	90.0	22	-18.22	19.393	-50.0	-23.95	30.4
	Pre-cycle 25	19	-168.00	198.147	-602.0	-93.70	0.0	19	-24.08	13.532	-50.6	-27.44	0.0
	Pre-cycle 31	15	-173.96	197.350	-590.0	-114.00	24.0	15	-24.41	16.055	-53.0	-23.70	14.5
	Pre-cycle 37	17	-179.60	189.500	-606.0	-123.00	-5.7	17	-26.54	11.242	-54.5	-25.20	-8.0
	Pre-cycle 43	17	-194.31	234.503	-711.0	-115.00	-4.5	17	-24.78	13.407	-55.1	-25.78	-2.3
	Pre-cycle 49	16	-175.45	262.845	-800.0	-89.45	93.0	16	-19.82	19.008	-57.2	-23.54	9.7
	Pre-cycle 55	14	-187.19	274.599	-684.0	-112.80	366.0	14	-22.51	22.567	-60.3	-23.59	35.2
	Pre-cycle 61	9	-201.73	256.894	-708.0	-108.00	18.0	9	-25.87	14.349	-42.4	-28.32	8.0
	Pre-cycle 67	4	-154.18	154.766	-354.0	-138.35	14.0	4	-23.47	24.467	-53.4	-23.39	6.3
	Pre-cycle 73	2	NC	NC	NC	NC	NC	2	NC	NC	NC	NC	NC

A negative change denotes a reduction in target PN volume.
SD = Standard deviation.
Patient 2019002 only has partial volumes throughout the study.

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Table 1.15.1.2 Target PN volume, absolute and percentage change from baseline - NCI assessment - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Absolute change (ml)						Percentage change					
Group	Time point	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Selumetinib*n25 mg/m² BID	Pre-cycle 5	19	-87.27	83.170	-255.0	-65.00	14.0	19	-13.31	8.737	-27.0	-13.50	5.2
	Pre-cycle 9	18	-91.33	108.599	-374.0	-62.15	80.0	18	-16.08	11.653	-35.8	-16.24	6.8
	Pre-cycle 13	15	-139.47	145.521	-521.0	-101.00	46.0	15	-21.83	13.040	-38.9	-23.20	17.1
	Pre-cycle 17	17	-155.90	150.078	-525.0	-116.00	49.0	17	-24.95	12.855	-43.1	-28.26	18.2
	Pre-cycle 21	15	-173.18	133.582	-489.0	-156.00	-15.4	15	-27.95	6.972	-37.6	-27.02	-12.4
	Pre-cycle 25	15	-155.07	128.387	-499.0	-154.00	-15.0	15	-25.13	6.419	-36.4	-26.09	-12.5
	Pre-cycle 31	14	-163.01	157.006	-596.0	-135.50	-6.0	14	-24.64	10.785	-36.9	-27.69	-4.7
	Pre-cycle 37	12	-170.39	175.649	-587.0	-152.50	61.0	12	-26.93	12.541	-46.5	-26.50	4.9
	Pre-cycle 43	10	-184.43	171.821	-552.0	-148.00	-13.3	10	-29.60	9.120	-45.6	-28.59	-16.5
	Pre-cycle 49	8	-132.34	126.303	-389.0	-102.50	-12.7	8	-27.62	9.585	-44.7	-25.76	-15.1
	Pre-cycle 55	7	-118.16	92.027	-227.0	-132.00	-15.1	7	-29.61	7.318	-39.5	-28.45	-20.5
	Pre-cycle 61	5	-167.62	170.633	-437.0	-148.00	-14.1	5	-32.17	10.731	-50.2	-30.04	-21.9
	Pre-cycle 67	1	NC	NC	NC	NC	NC	1	NC	NC	NC	NC	NC

A negative change denotes a reduction in target PN volume.
SD = Standard deviation.
Patient 2019002 only has partial volumes throughout the study.

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Table 1.15.1.3 Target PN volume, absolute and percentage change from baseline - NCI assessment -
PN status at enrollment = Progressive
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Absolute change (ml)						Percentage change				
Group	Time point	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Selumetinib*n25 mg/m² BID	Pre-cycle 5	21	-88.05	114.977	-428.0	-38.00	14.0	21	-12.80	9.123	-26.8	-10.89	5.2
	Pre-cycle 9	21	-109.61	142.055	-459.0	-79.00	80.0	21	-15.59	12.468	-37.5	-20.09	6.8
	Pre-cycle 13	19	-118.02	141.909	-435.0	-84.00	46.0	19	-18.20	16.276	-38.6	-23.17	17.1
	Pre-cycle 17	19	-122.71	162.444	-485.0	-85.00	72.0	19	-17.89	18.858	-45.9	-24.59	18.5
	Pre-cycle 21	18	-129.27	182.028	-592.0	-76.50	90.0	18	-18.96	20.794	-50.0	-24.62	30.4
	Pre-cycle 25	14	-156.93	151.064	-548.0	-115.50	-5.2	14	-25.87	11.830	-50.6	-25.44	-7.4
	Pre-cycle 31	12	-130.02	132.389	-467.0	-106.05	-4.1	12	-23.02	15.119	-53.0	-23.44	-4.7
	Pre-cycle 37	12	-147.97	116.821	-378.0	-123.50	-5.7	12	-26.43	12.321	-54.5	-25.03	-8.0
	Pre-cycle 43	10	-105.34	113.873	-396.0	-107.45	-4.5	10	-22.91	15.862	-55.1	-23.15	-2.3
	Pre-cycle 49	10	-70.73	112.814	-317.0	-75.95	93.0	10	-18.40	20.981	-57.2	-19.94	9.1
	Pre-cycle 55	8	-65.08	208.039	-382.0	-108.30	366.0	8	-17.43	28.701	-60.3	-21.60	35.2
	Pre-cycle 61	3	-31.63	67.119	-108.0	-4.90	18.0	3	-18.97	23.748	-36.6	-28.32	8.0
	Pre-cycle 67	3	-146.23	188.549	-354.0	-98.70	14.0	3	-22.45	29.861	-53.4	-20.25	6.3
	Pre-cycle 73	1	NC	NC	NC	NC	NC	1	NC	NC	NC	NC	NC

A negative change denotes a reduction in target PN volume.
SD = Standard deviation.
Patient 2019002 only has partial volumes throughout the study.

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Table 1.15.1.4 Target PN volume, absolute and percentage change from baseline - NCI assessment -
PN status at enrollment = Non-progressive
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Absolute change (ml)						Percentage change					
Group	Time point	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Selumetinib*n25 mg/m² BID	Pre-cycle 5	14	-138.82	180.695	-678.0	-73.00	-3.0	14	-15.27	6.836	-23.1	-18.07	-1.0
	Pre-cycle 9	13	-151.17	211.707	-760.0	-77.00	-12.0	13	-17.87	8.855	-31.5	-16.53	-0.5
	Pre-cycle 13	12	-191.97	223.510	-742.0	-118.50	-6.0	12	-22.10	9.012	-36.2	-23.24	-2.5
	Pre-cycle 17	11	-168.53	166.143	-564.0	-136.00	-21.8	11	-27.29	8.394	-43.1	-28.26	-12.6
	Pre-cycle 21	10	-174.30	154.966	-535.0	-152.00	-21.0	10	-27.04	7.271	-37.1	-27.93	-10.1
	Pre-cycle 25	11	-153.01	158.436	-548.0	-144.00	-9.0	11	-23.95	10.097	-36.4	-26.09	-3.8
	Pre-cycle 31	9	-184.69	182.528	-590.0	-167.00	24.0	9	-25.14	16.124	-39.1	-30.25	14.5
	Pre-cycle 37	9	-189.84	182.150	-592.0	-167.00	-22.0	9	-27.64	8.035	-41.4	-29.50	-13.3
	Pre-cycle 43	9	-192.77	172.246	-552.0	-173.00	-17.0	9	-28.60	9.205	-42.9	-30.82	-10.3
	Pre-cycle 49	8	-189.61	174.307	-487.0	-176.00	16.0	8	-25.15	16.050	-44.7	-26.80	9.7
	Pre-cycle 55	7	-191.44	153.962	-507.0	-170.00	-23.1	7	-29.75	6.280	-39.8	-28.45	-21.3
	Pre-cycle 61	8	-225.59	181.088	-558.0	-178.50	-25.7	8	-32.42	9.548	-50.2	-30.60	-20.2
	Pre-cycle 67	2	NC	NC	NC	NC	NC	2	NC	NC	NC	NC	NC
	Pre-cycle 73	1	NC	NC	NC	NC	NC	1	NC	NC	NC	NC	NC

A negative change denotes a reduction in target PN volume.
SD = Standard deviation.
Patient 2019002 only has partial volumes throughout the study.

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Table 1.15.1.5 Target PN volume, absolute and percentage change from baseline - NCI assessment
PN status at enrollment = Unknown
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Absolute change (ml)						Percentage change					
Group	Time point	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Selumetinib*n25 mg/m² BID	Pre-cycle 5	13	-210.85	226.868	-672.0	-121.00	-3.0	13	-15.56	6.537	-27.0	-15.80	-2.2
	Pre-cycle 9	11	-269.16	328.907	-936.0	-52.30	-14.5	11	-21.08	9.792	-35.8	-20.50	-6.2
	Pre-cycle 13	12	-306.03	315.833	-884.0	-156.50	-17.3	12	-21.85	7.472	-38.9	-21.69	-11.8
	Pre-cycle 17	11	-240.29	307.431	-964.0	-101.00	-16.2	11	-24.11	8.218	-36.4	-25.24	-7.7
	Pre-cycle 21	9	-177.16	204.864	-541.0	-115.00	4.0	9	-23.16	12.067	-37.6	-23.97	1.8
	Pre-cycle 25	9	-182.00	219.761	-602.0	-117.00	0.0	9	-23.20	11.174	-34.7	-26.71	0.0
	Pre-cycle 31	8	-208.64	231.221	-596.0	-129.50	-15.1	8	-26.08	8.257	-33.9	-27.60	-10.9
	Pre-cycle 37	8	-201.71	262.557	-606.0	-86.50	61.0	8	-26.03	14.903	-46.5	-27.65	4.9
	Pre-cycle 43	8	-294.91	300.558	-711.0	-177.50	-13.3	8	-28.84	9.381	-45.6	-27.27	-16.5
	Pre-cycle 49	6	-273.62	365.114	-800.0	-58.00	-12.7	6	-25.48	8.304	-39.3	-24.68	-15.1
	Pre-cycle 55	6	-264.52	304.612	-684.0	-128.50	-15.1	6	-29.11	9.547	-39.5	-27.47	-20.2
	Pre-cycle 61	3	-251.37	395.557	-708.0	-32.00	-14.1	3	-25.80	5.182	-31.7	-23.80	-21.9

A negative change denotes a reduction in target PN volume.
SD = Standard deviation.
Patient 2019002 only has partial volumes throughout the study.

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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: 31 March 2021 (DC02)

Subgroup		Selumetinib 25 mg/m² BID (N=50)
Gender: Male (n=30)	n	29
	Mean	-25.48
	SD	13.447
	Min	-60.3
	Median	-26.53
	Max	-1.0
	Proportion with any reduction	100
	Proportion with reduction >= 20%	72.4
	Proportion with reduction >= 40%	10.3
	Proportion with reduction >= 60%	3.4
	Proportion with reduction >= 80%	0
Gender: Female (n=20)	n	19
	Mean	-28.10
	SD	13.953
	Min	-52.6
	Median	-30.48
	Max	2.2
	Proportion with any reduction	89.5
	Proportion with reduction >= 20%	84.2
	Proportion with reduction >= 40%	10.5
	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.

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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: 31 March 2021 (DC02)

Subgroup		Selumetinib 25 mg/m² BID (N=50)
PN status at enrollment: Progressive (n=21)	n	21
	Mean	-24.35
	SD	16.091
	Min	-60.3
	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%	4.8
	Proportion with reduction >= 80%	0
PN status at enrollment: Non-progressive (n=15)	n	14
	Mean	-26.70
	SD	13.454
	Min	-52.6
	Median	-27.39
	Max	-1.0
	Proportion with any reduction	100
	Proportion with reduction >= 20%	78.6
	Proportion with reduction >= 40%	14.3
	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.

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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: 31 March 2021 (DC02)

Subgroup		Selumetinib 25 mg/m² BID (N=50)
PN status at enrollment: Unknown (n=14)	n	13
	Mean	-29.80
	SD	8.542
	Min	-46.5
	Median	-26.89
	Max	-16.4
	Proportion with any reduction	100
	Proportion with reduction >= 20%	92.3
	Proportion with reduction >= 40%	7.7
	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.

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1.2 Endpunkt Ansprechen

1.2.1 Subgruppenanalysen zur objektiven Ansprechrate (ORR)

Table 1.4.1 Confirmed Objective Response Rate - NCI assessment by subgroups (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Subgroup	N	Number (%) of patients with response [a]	95% CI [b]
Gender: Female	20	15 (75.0)	50.9, 91.3
Gender: Male	30	19 (63.3)	43.9, 80.1
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	11 (78.6)	49.2, 95.3

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.

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1.2.2 Subgruppenanalysen zum besten objektiven Ansprechen (BOR)

Table 1.6.1 Best objective response - NCI assessment by subgroups (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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]	19 (63.3)
	Unconfirmed partial response [b]	2 (6.7)
	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: 31 March 2021 (DC02)

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]	11 (78.6)
	Unconfirmed partial response [b]	1 (7.1)
	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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1.2.3 Subgruppenanalysen zur Zeit bis zum Ansprechen (TTR)

Table 1.5.1.1 Time to response (TTR) - NCI assessment - Gender = Male
(Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=30)
Total events [a], n (%)	19 (63.3)
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]	52.6
95% CI for not in response at cycle 5 [b]	28.7 - 71.9
Not in response at cycle 9 (%) [b]	15.8
95% CI for not in response at cycle 9 [b]	3.9 - 34.9
Not in response at cycle 13 (%) [b]	5.3
95% CI for not in response at cycle 13 [b]	0.4 - 21.4
Not in response at cycle 17 (%) [b]	5.3
95% CI for not in response at cycle 17 [b]	0.4 - 21.4
Not in response at cycle 21 (%) [b]	5.3
95% CI for not in response at cycle 21 [b]	0.4 - 21.4
Not in response at cycle 25 (%) [b]	5.3
95% CI for not in response at cycle 25 [b]	0.4 - 21.4
Not in response at cycle 29 (%) [b]	5.3
95% CI for not in response at cycle 29 [b]	0.4 - 21.4
Not in response at cycle 33 (%) [b]	5.3
95% CI for not in response at cycle 33 [b]	0.4 - 21.4
Not in response at cycle 37 (%) [b]	5.3
95% CI for not in response at cycle 37 [b]	0.4 - 21.4
Not in response at cycle 41 (%) [b]	5.3
95% CI for not in response at cycle 41 [b]	0.4 - 21.4
Not in response at cycle 45 (%) [b]	0.0
95% CI for not in response at cycle 45 [b]	NC - NC
Median follow-up for Time to response (cycles) [c]	8.0 (4.0 - 42.0)

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.

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Table 1.5.1.2 Time to response (TTR) - NCI assessment - Gender = Female
(Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

	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]	NC - NC
Not in response at cycle 25 (%) [b]	0.0
95% CI for not in response at cycle 25 [b]	NC - NC
Not in response at cycle 29 (%) [b]	0.0
95% CI for not in response at cycle 29 [b]	NC - NC
Not in response at cycle 33 (%) [b]	0.0
95% CI for not in response at cycle 33 [b]	NC - NC
Not in response at cycle 37 (%) [b]	0.0
95% CI for not in response at cycle 37 [b]	NC - NC
Not in response at cycle 41 (%) [b]	0.0
95% CI for not in response at cycle 41 [b]	NC - NC
Not in response at cycle 45 (%) [b]	0.0
95% CI for not in response at cycle 45 [b]	NC - NC
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.

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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: 31 March 2021 (DC02)

	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]	NC - NC
Not in response at cycle 17 (%) [b]	0.0
95% CI for not in response at cycle 17 [b]	NC - NC
Not in response at cycle 21 (%) [b]	0.0
95% CI for not in response at cycle 21 [b]	NC - NC
Not in response at cycle 25 (%) [b]	0.0
95% CI for not in response at cycle 25 [b]	NC - NC
Not in response at cycle 29 (%) [b]	0.0
95% CI for not in response at cycle 29 [b]	NC - NC
Not in response at cycle 33 (%) [b]	0.0
95% CI for not in response at cycle 33 [b]	NC - NC
Not in response at cycle 37 (%) [b]	0.0
95% CI for not in response at cycle 37 [b]	NC - NC
Not in response at cycle 41 (%) [b]	0.0
95% CI for not in response at cycle 41 [b]	NC - NC
Not in response at cycle 45 (%) [b]	0.0
95% CI for not in response at cycle 45 [b]	NC - NC
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.

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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: 31 March 2021 (DC02)

	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 - NC
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]	NC - NC
Not in response at cycle 17 (%) [b]	0.0
95% CI for not in response at cycle 17 [b]	NC - NC
Not in response at cycle 21 (%) [b]	0.0
95% CI for not in response at cycle 21 [b]	NC - NC
Not in response at cycle 25 (%) [b]	0.0
95% CI for not in response at cycle 25 [b]	NC - NC
Not in response at cycle 29 (%) [b]	0.0
95% CI for not in response at cycle 29 [b]	NC - NC
Not in response at cycle 33 (%) [b]	0.0
95% CI for not in response at cycle 33 [b]	NC - NC
Not in response at cycle 37 (%) [b]	0.0
95% CI for not in response at cycle 37 [b]	NC - NC
Not in response at cycle 41 (%) [b]	0.0
95% CI for not in response at cycle 41 [b]	NC - NC
Not in response at cycle 45 (%) [b]	0.0
95% CI for not in response at cycle 45 [b]	NC - NC
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.

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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=14)
Total events [a], n (%)	11 (78.6)
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]	63.6
95% CI for not in response at cycle 5 [b]	29.7 - 84.5
Not in response at cycle 9 (%) [b]	27.3
95% CI for not in response at cycle 9 [b]	6.5 - 53.9
Not in response at cycle 13 (%) [b]	18.2
95% CI for not in response at cycle 13 [b]	2.9 - 44.2
Not in response at cycle 17 (%) [b]	18.2
95% CI for not in response at cycle 17 [b]	2.9 - 44.2
Not in response at cycle 21 (%) [b]	9.1
95% CI for not in response at cycle 21 [b]	0.5 - 33.3
Not in response at cycle 25 (%) [b]	9.1
95% CI for not in response at cycle 25 [b]	0.5 - 33.3
Not in response at cycle 29 (%) [b]	9.1
95% CI for not in response at cycle 29 [b]	0.5 - 33.3
Not in response at cycle 33 (%) [b]	9.1
95% CI for not in response at cycle 33 [b]	0.5 - 33.3
Not in response at cycle 37 (%) [b]	9.1
95% CI for not in response at cycle 37 [b]	0.5 - 33.3
Not in response at cycle 41 (%) [b]	9.1
95% CI for not in response at cycle 41 [b]	0.5 - 33.3
Not in response at cycle 45 (%) [b]	0.0
95% CI for not in response at cycle 45 [b]	NC - NC
Median follow-up for Time to response (cycles) [c]	8.0 (4.0 - 42.0)

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.

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1.2.4 Subgruppenanalysen zur Dauer des Ansprechens (DOR)

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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=30)
Number of patients with an objective response	19
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	44.0
- 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)	100 (NE, NE)
- >= 12 cycles (95% CI)	100 (NE, NE)
- >= 16 cycles (95% CI)	93.8 (63.2, 99.1)
- >= 20 cycles (95% CI)	93.8 (63.2, 99.1)
- >= 24 cycles (95% CI)	93.8 (63.2, 99.1)
- >= 28 cycles (95% CI)	93.8 (63.2, 99.1)
- >= 32 cycles (95% CI)	93.8 (63.2, 99.1)
- >= 36 cycles (95% CI)	93.8 (63.2, 99.1)
- >= 40 cycles (95% CI)	86.5 (55.8, 96.5)
- >= 44 cycles (95% CI)	72.1 (41.5, 88.6)
- >= 48 cycles (95% CI)	72.1 (41.5, 88.6)
- >= 52 cycles (95% CI)	72.1 (41.5, 88.6)
- >= 56 cycles (95% CI)	72.1 (41.5, 88.6)
- >= 60 cycles (95% CI)	72.1 (41.5, 88.6)
- >= 64 cycles (95% CI)	72.1 (41.5, 88.6)
- >= 68 cycles (95% CI)	NE
Number of censored patients	
- > 0 cycles to <= 4 cycles	0
- > 4 cycles to <= 8 cycles	3
- > 8 cycles to <= 12 cycles	0
- > 12 cycles to <= 16 cycles	0
- > 16 cycles to <= 20 cycles	1
- > 20 cycles to <= 24 cycles	0
- > 24 cycles to <= 28 cycles	0
- > 28 cycles to <= 32 cycles	1
- > 32 cycles to <= 36 cycles	0
- > 36 cycles to <= 40 cycles	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.

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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=30)
- > 40 cycles to <= 44 cycles	0
- > 44 cycles to <= 48 cycles	2
- > 48 cycles to <= 52 cycles	2
- > 52 cycles to <= 56 cycles	4
- > 56 cycles to <= 60 cycles	1
- > 60 cycles to <= 64 cycles	1
- > 64 cycles to <= 68 cycles	0
Median follow-up for Time to response (cycles) [c]	46.0 (8.0 - 64.0)

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.

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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=30)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	19 (100)
- >= 8 cycles	19 (100)
- >= 12 cycles	16 (84.2)
- >= 16 cycles	16 (84.2)
- >= 20 cycles	14 (73.7)
- >= 24 cycles	14 (73.7)
- >= 28 cycles	14 (73.7)
- >= 32 cycles	14 (73.7)
- >= 36 cycles	13 (68.4)
- >= 40 cycles	13 (68.4)
- >= 44 cycles	12 (63.2)
- >= 48 cycles	8 (42.1)
- >= 52 cycles	8 (42.1)
- >= 56 cycles	5 (26.3)
- >= 60 cycles	2 (10.5)
- >= 64 cycles	1 (5.3)
- >= 68 cycles	0
Minimum duration of response (cycles)	8.0
Maximum duration of response (cycles)	64.0
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	9 (47.4)
- <= 8 cycles	16 (84.2)
- <= 12 cycles	18 (94.7)
- <= 16 cycles	18 (94.7)
- <= 20 cycles	18 (94.7)
- <= 24 cycles	18 (94.7)
- <= 28 cycles	18 (94.7)
- <= 32 cycles	18 (94.7)
- <= 36 cycles	18 (94.7)
- <= 40 cycles	18 (94.7)

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.

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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=30)
- <= 44 cycles	18 (94.7)
- <= 48 cycles	18 (94.7)
- <= 52 cycles	18 (94.7)
- <= 56 cycles	18 (94.7)
- <= 60 cycles	18 (94.7)
- <= 64 cycles	18 (94.7)
- <= 68 cycles	18 (94.7)

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.

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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: 31 March 2021 (DC02)

	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	4
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	40.0
- 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)	100 (NE, NE)
- >= 12 cycles (95% CI)	100 (NE, NE)
- >= 16 cycles (95% CI)	100 (NE, NE)
- >= 20 cycles (95% CI)	86.7 (56.4, 96.5)
- >= 24 cycles (95% CI)	86.7 (56.4, 96.5)
- >= 28 cycles (95% CI)	86.7 (56.4, 96.5)
- >= 32 cycles (95% CI)	78.0 (45.5, 92.5)
- >= 36 cycles (95% CI)	78.0 (45.5, 92.5)
- >= 40 cycles (95% CI)	68.3 (34.8, 87.1)
- >= 44 cycles (95% CI)	68.3 (34.8, 87.1)
- >= 48 cycles (95% CI)	68.3 (34.8, 87.1)
- >= 52 cycles (95% CI)	68.3 (34.8, 87.1)
- >= 56 cycles (95% CI)	68.3 (34.8, 87.1)
- >= 60 cycles (95% CI)	NE
- >= 64 cycles (95% CI)	NE
- >= 68 cycles (95% CI)	NE
Number of censored patients	
- > 0 cycles to <= 4 cycles	0
- > 4 cycles to <= 8 cycles	0
- > 8 cycles to <= 12 cycles	0
- > 12 cycles to <= 16 cycles	0
- > 16 cycles to <= 20 cycles	1
- > 20 cycles to <= 24 cycles	1
- > 24 cycles to <= 28 cycles	1
- > 28 cycles to <= 32 cycles	0
- > 32 cycles to <= 36 cycles	1
- > 36 cycles to <= 40 cycles	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.

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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=20)
- > 40 cycles to <= 44 cycles	1
- > 44 cycles to <= 48 cycles	1
- > 48 cycles to <= 52 cycles	3
- > 52 cycles to <= 56 cycles	2
- > 56 cycles to <= 60 cycles	0
- > 60 cycles to <= 64 cycles	0
- > 64 cycles to <= 68 cycles	0
Median follow-up for Time to response (cycles) [c]	40.0 (18.0 - 56.0)

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.

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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=20)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	15 (100)
- >= 8 cycles	15 (100)
- >= 12 cycles	15 (100)
- >= 16 cycles	15 (100)
- >= 20 cycles	13 (86.7)
- >= 24 cycles	12 (80.0)
- >= 28 cycles	11 (73.3)
- >= 32 cycles	10 (66.7)
- >= 36 cycles	8 (53.3)
- >= 40 cycles	8 (53.3)
- >= 44 cycles	6 (40.0)
- >= 48 cycles	6 (40.0)
- >= 52 cycles	3 (20.0)
- >= 56 cycles	1 (6.7)
- >= 60 cycles	0
- >= 64 cycles	0
- >= 68 cycles	0
Minimum duration of response (cycles)	18.0
Maximum duration of response (cycles)	56.0
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)
- <= 28 cycles	15 (100)
- <= 32 cycles	15 (100)
- <= 36 cycles	15 (100)
- <= 40 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.

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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=20)
- <= 44 cycles	15 (100)
- <= 48 cycles	15 (100)
- <= 52 cycles	15 (100)
- <= 56 cycles	15 (100)
- <= 60 cycles	15 (100)
- <= 64 cycles	15 (100)
- <= 68 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.

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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: 31 March 2021 (DC02)

	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	6
Duration of response from onset of response (cycles) [a] [b]	
- 25th percentile	40.0
- Median	44.0
- 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)	92.3 (56.6, 98.9)
- >= 20 cycles (95% CI)	76.9 (44.2, 91.9)
- >= 24 cycles (95% CI)	76.9 (44.2, 91.9)
- >= 28 cycles (95% CI)	76.9 (44.2, 91.9)
- >= 32 cycles (95% CI)	76.9 (44.2, 91.9)
- >= 36 cycles (95% CI)	76.9 (44.2, 91.9)
- >= 40 cycles (95% CI)	67.3 (34.0, 86.5)
- >= 44 cycles (95% CI)	48.1 (18.4, 72.8)
- >= 48 cycles (95% CI)	48.1 (18.4, 72.8)
- >= 52 cycles (95% CI)	48.1 (18.4, 72.8)
- >= 56 cycles (95% CI)	48.1 (18.4, 72.8)
- >= 60 cycles (95% CI)	48.1 (18.4, 72.8)
- >= 64 cycles (95% CI)	48.1 (18.4, 72.8)
- >= 68 cycles (95% CI)	NE
Number of censored patients	
- > 0 cycles to <= 4 cycles	0
- > 4 cycles to <= 8 cycles	0
- > 8 cycles to <= 12 cycles	0
- > 12 cycles to <= 16 cycles	0
- > 16 cycles to <= 20 cycles	0
- > 20 cycles to <= 24 cycles	1
- > 24 cycles to <= 28 cycles	0
- > 28 cycles to <= 32 cycles	1
- > 32 cycles to <= 36 cycles	0
- > 36 cycles to <= 40 cycles	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.

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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=21)
- > 40 cycles to <= 44 cycles	0
- > 44 cycles to <= 48 cycles	1
- > 48 cycles to <= 52 cycles	2
- > 52 cycles to <= 56 cycles	1
- > 56 cycles to <= 60 cycles	0
- > 60 cycles to <= 64 cycles	1
- > 64 cycles to <= 68 cycles	0
Median follow-up for Time to response (cycles) [c]	44.0 (16.0 - 64.0)

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.
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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: 31 March 2021 (DC02)

	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	13 (100)
- >= 20 cycles	10 (76.9)
- >= 24 cycles	10 (76.9)
- >= 28 cycles	9 (69.2)
- >= 32 cycles	9 (69.2)
- >= 36 cycles	8 (61.5)
- >= 40 cycles	8 (61.5)
- >= 44 cycles	7 (53.8)
- >= 48 cycles	4 (30.8)
- >= 52 cycles	3 (23.1)
- >= 56 cycles	2 (15.4)
- >= 60 cycles	1 (7.7)
- >= 64 cycles	1 (7.7)
- >= 68 cycles	0
Minimum duration of response (cycles)	16.0
Maximum duration of response (cycles)	64.0
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)
- <= 28 cycles	13 (100)
- <= 32 cycles	13 (100)
- <= 36 cycles	13 (100)
- <= 40 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.
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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=21)
- <= 44 cycles	13 (100)
- <= 48 cycles	13 (100)
- <= 52 cycles	13 (100)
- <= 56 cycles	13 (100)
- <= 60 cycles	13 (100)
- <= 64 cycles	13 (100)
- <= 68 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.
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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: 31 March 2021 (DC02)

	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)
- >= 28 cycles (95% CI)	100 (NE, NE)
- >= 32 cycles (95% CI)	100 (NE, NE)
- >= 36 cycles (95% CI)	100 (NE, NE)
- >= 40 cycles (95% CI)	100 (NE, NE)
- >= 44 cycles (95% CI)	100 (NE, NE)
- >= 48 cycles (95% CI)	100 (NE, NE)
- >= 52 cycles (95% CI)	100 (NE, NE)
- >= 56 cycles (95% CI)	100 (NE, NE)
- >= 60 cycles (95% CI)	100 (NE, NE)
- >= 64 cycles (95% CI)	NE
- >= 68 cycles (95% CI)	NE
Number of censored patients	
- > 0 cycles to <= 4 cycles	0
- > 4 cycles to <= 8 cycles	1
- > 8 cycles to <= 12 cycles	0
- > 12 cycles to <= 16 cycles	0
- > 16 cycles to <= 20 cycles	1
- > 20 cycles to <= 24 cycles	0
- > 24 cycles to <= 28 cycles	0
- > 28 cycles to <= 32 cycles	0
- > 32 cycles to <= 36 cycles	0
- > 36 cycles to <= 40 cycles	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.
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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=15)
- > 40 cycles to <= 44 cycles	0
- > 44 cycles to <= 48 cycles	1
- > 48 cycles to <= 52 cycles	2
- > 52 cycles to <= 56 cycles	4
- > 56 cycles to <= 60 cycles	1
- > 60 cycles to <= 64 cycles	0
- > 64 cycles to <= 68 cycles	0
Median follow-up for Time to response (cycles) [c]	53.0 (8.0 - 60.0)

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.
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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: 31 March 2021 (DC02)

	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	9 (90.0)
- >= 20 cycles	9 (90.0)
- >= 24 cycles	8 (80.0)
- >= 28 cycles	8 (80.0)
- >= 32 cycles	8 (80.0)
- >= 36 cycles	8 (80.0)
- >= 40 cycles	8 (80.0)
- >= 44 cycles	8 (80.0)
- >= 48 cycles	8 (80.0)
- >= 52 cycles	7 (70.0)
- >= 56 cycles	3 (30.0)
- >= 60 cycles	1 (10.0)
- >= 64 cycles	0
- >= 68 cycles	0
Minimum duration of response (cycles)	8.0
Maximum duration of response (cycles)	60.0
Time to onset of response from first dose (cycles) [b]	
- 25th percentile	4.0
- Median	8.0
- 95% CI for median	4.0, .
- 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)
- <= 28 cycles	10 (100)
- <= 32 cycles	10 (100)
- <= 36 cycles	10 (100)
- <= 40 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.
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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=15)
- <= 44 cycles	10 (100)
- <= 48 cycles	10 (100)
- <= 52 cycles	10 (100)
- <= 56 cycles	10 (100)
- <= 60 cycles	10 (100)
- <= 64 cycles	10 (100)
- <= 68 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.
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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=14)
Number of patients with an objective response	11
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	40.0
- 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)	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)
- >= 28 cycles (95% CI)	100 (NE, NE)
- >= 32 cycles (95% CI)	85.7 (33.4, 97.9)
- >= 36 cycles (95% CI)	85.7 (33.4, 97.9)
- >= 40 cycles (95% CI)	68.6 (21.3, 91.2)
- >= 44 cycles (95% CI)	68.6 (21.3, 91.2)
- >= 48 cycles (95% CI)	68.6 (21.3, 91.2)
- >= 52 cycles (95% CI)	68.6 (21.3, 91.2)
- >= 56 cycles (95% CI)	68.6 (21.3, 91.2)
- >= 60 cycles (95% CI)	NE
- >= 64 cycles (95% CI)	NE
- >= 68 cycles (95% CI)	NE
Number of censored patients	
- > 0 cycles to <= 4 cycles	0
- > 4 cycles to <= 8 cycles	2
- > 8 cycles to <= 12 cycles	0
- > 12 cycles to <= 16 cycles	0
- > 16 cycles to <= 20 cycles	1
- > 20 cycles to <= 24 cycles	0
- > 24 cycles to <= 28 cycles	1
- > 28 cycles to <= 32 cycles	0
- > 32 cycles to <= 36 cycles	1
- > 36 cycles to <= 40 cycles	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.

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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=14)
- > 40 cycles to <= 44 cycles	1
- > 44 cycles to <= 48 cycles	1
- > 48 cycles to <= 52 cycles	1
- > 52 cycles to <= 56 cycles	1
- > 56 cycles to <= 60 cycles	0
- > 60 cycles to <= 64 cycles	0
- > 64 cycles to <= 68 cycles	0
Median follow-up for Time to response (cycles) [c]	34.0 (8.0 - 56.0)

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.
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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=14)
Number and percentage remaining in response - n (%)	
- >= 4 cycles	11 (100)
- >= 8 cycles	11 (100)
- >= 12 cycles	9 (81.8)
- >= 16 cycles	9 (81.8)
- >= 20 cycles	8 (72.7)
- >= 24 cycles	8 (72.7)
- >= 28 cycles	8 (72.7)
- >= 32 cycles	7 (63.6)
- >= 36 cycles	5 (45.5)
- >= 40 cycles	5 (45.5)
- >= 44 cycles	3 (27.3)
- >= 48 cycles	2 (18.2)
- >= 52 cycles	1 (9.1)
- >= 56 cycles	1 (9.1)
- >= 60 cycles	0
- >= 64 cycles	0
- >= 68 cycles	0
Minimum duration of response (cycles)	8.0
Maximum duration of response (cycles)	56.0
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 (36.4)
- <= 8 cycles	8 (72.7)
- <= 12 cycles	9 (81.8)
- <= 16 cycles	9 (81.8)
- <= 20 cycles	10 (90.9)
- <= 24 cycles	10 (90.9)
- <= 28 cycles	10 (90.9)
- <= 32 cycles	10 (90.9)
- <= 36 cycles	10 (90.9)
- <= 40 cycles	10 (90.9)

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.
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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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=14)
- <= 44 cycles	10 (90.9)
- <= 48 cycles	10 (90.9)
- <= 52 cycles	10 (90.9)
- <= 56 cycles	10 (90.9)
- <= 60 cycles	10 (90.9)
- <= 64 cycles	10 (90.9)
- <= 68 cycles	10 (90.9)

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.
REiNS assessment.

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1.3 Endpunkt Progressionsfreien Überleben (PFS)

1.3.1 Subgruppenanalysen zum PFS

Table 1.2.1.1 Progression-free survival (PFS) - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=30)
Total number of events (progression or death), n (%) [a]	6 (20.0)
Number of progressions, n (%)	6 (20.0)
Number of deaths, n (%)	0
Censored patients, n (%)	24 (80.0)
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]	91.7
95% CI for progression-free at cycle 24 (%) [b]	70.6 - 97.8
Progression-free at cycle 30 (%) [b]	86.6
95% CI for progression-free at cycle 30 (%) [b]	63.7 - 95.5
Progression-free at cycle 36 (%) [b]	86.6
95% CI for progression-free at cycle 36 (%) [b]	63.7 - 95.5
Progression-free at cycle 42 (%) [b]	86.6
95% CI for progression-free at cycle 42 (%) [b]	63.7 - 95.5
Progression-free at cycle 48 (%) [b]	70.3
95% CI for progression-free at cycle 48 (%) [b]	45.1 - 85.6
Progression-free at cycle 54 (%) [b]	70.3
95% CI for progression-free at cycle 54 (%) [b]	45.1 - 85.6
Progression-free at cycle 60 (%) [b]	70.3

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 1.2.1.1 Progression-free survival (PFS) - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=30)
95% CI for progression-free at cycle 60 (%) [b]	45.1 - 85.6
Median follow-up for Progression-free survival (cycles) [c]	39.0 (20.0 - 48.0)
Median follow-up for Progression-free survival (cycles) (censored patients only) [d]	51.0 (0.0 - 72.0)
Median follow-up (cycles) [e]	48.0 (0.0 - 72.0)

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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=20)
Total number of events (progression or death), n (%) [a]	4 (20.0)
Number of progressions, n (%)	4 (20.0)
Number of deaths, n (%)	0
Censored patients, n (%)	16 (80.0)
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]	85.7
95% CI for progression-free at cycle 30 (%) [b]	53.9 - 96.2
Progression-free at cycle 36 (%) [b]	78.6
95% CI for progression-free at cycle 36 (%) [b]	47.2 - 92.5
Progression-free at cycle 42 (%) [b]	78.6
95% CI for progression-free at cycle 42 (%) [b]	47.2 - 92.5
Progression-free at cycle 48 (%) [b]	69.8
95% CI for progression-free at cycle 48 (%) [b]	37.8 - 87.6
Progression-free at cycle 54 (%) [b]	69.8
95% CI for progression-free at cycle 54 (%) [b]	37.8 - 87.6
Progression-free at cycle 60 (%) [b]	69.8

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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=20)
95% CI for progression-free at cycle 60 (%) [b]	37.8 - 87.6
Median follow-up for Progression-free survival (cycles) [c]	33.0 (30.0 - 48.0)
Median follow-up for Progression-free survival (cycles) (censored patients only) [d]	45.0 (0.0 - 66.0)
Median follow-up (cycles) [e]	39.0 (0.0 - 66.0)

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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=21)
Total number of events (progression or death), n (%) [a]	7 (33.3)
Number of progressions, n (%)	7 (33.3)
Number of deaths, n (%)	0
Censored patients, n (%)	14 (66.7)
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]	76.2
95% CI for progression-free at cycle 30 (%) [b]	48.1 - 90.4
Progression-free at cycle 36 (%) [b]	76.2
95% CI for progression-free at cycle 36 (%) [b]	48.1 - 90.4
Progression-free at cycle 42 (%) [b]	76.2
95% CI for progression-free at cycle 42 (%) [b]	48.1 - 90.4
Progression-free at cycle 48 (%) [b]	53.3
95% CI for progression-free at cycle 48 (%) [b]	25.6 - 74.8
Progression-free at cycle 54 (%) [b]	53.3
95% CI for progression-free at cycle 54 (%) [b]	25.6 - 74.8
Progression-free at cycle 60 (%) [b]	53.3

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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=21)
95% CI for progression-free at cycle 60 (%) [b]	25.6 - 74.8
Median follow-up for Progression-free survival (cycles) [c]	30.0 (20.0 - 48.0)
Median follow-up for Progression-free survival (cycles) (censored patients only) [d]	42.0 (8.0 - 72.0)
Median follow-up (cycles) [e]	36.0 (8.0 - 72.0)

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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=15)
Total number of events (progression or death), n (%) [a]	1 (6.7)
Number of progressions, n (%)	1 (6.7)
Number of deaths, n (%)	0
Censored patients, n (%)	14 (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]	100.0
95% CI for progression-free at cycle 24 (%) [b]	NE - NE
Progression-free at cycle 30 (%) [b]	88.9
95% CI for progression-free at cycle 30 (%) [b]	43.3 - 98.4
Progression-free at cycle 36 (%) [b]	88.9
95% CI for progression-free at cycle 36 (%) [b]	43.3 - 98.4
Progression-free at cycle 42 (%) [b]	88.9
95% CI for progression-free at cycle 42 (%) [b]	43.3 - 98.4
Progression-free at cycle 48 (%) [b]	88.9
95% CI for progression-free at cycle 48 (%) [b]	43.3 - 98.4
Progression-free at cycle 54 (%) [b]	88.9
95% CI for progression-free at cycle 54 (%) [b]	43.3 - 98.4
Progression-free at cycle 60 (%) [b]	88.9

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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=15)
95% CI for progression-free at cycle 60 (%) [b]	43.3 - 98.4
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]	60.0 (0.0 - 72.0)
Median follow-up (cycles) [e]	60.0 (0.0 - 72.0)

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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=14)
Total number of events (progression or death), n (%) [a]	2 (14.3)
Number of progressions, n (%)	2 (14.3)
Number of deaths, n (%)	0
Censored patients, n (%)	12 (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]	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]	88.9
95% CI for progression-free at cycle 36 (%) [b]	43.3 - 98.4
Progression-free at cycle 42 (%) [b]	88.9
95% CI for progression-free at cycle 42 (%) [b]	43.3 - 98.4
Progression-free at cycle 48 (%) [b]	76.2
95% CI for progression-free at cycle 48 (%) [b]	33.2 - 93.5
Progression-free at cycle 54 (%) [b]	76.2
95% CI for progression-free at cycle 54 (%) [b]	33.2 - 93.5
Progression-free at cycle 60 (%) [b]	76.2

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: 31 March 2021 (DC02)

	Selumetinib 25 mg/m² BID (N=14)
95% CI for progression-free at cycle 60 (%) [b]	33.2 - 93.5
Median follow-up for Progression-free survival (cycles) [c]	42.0 (36.0 - 48.0)
Median follow-up for Progression-free survival (cycles) (censored patients only) [d]	45.0 (0.0 - 60.0)
Median follow-up (cycles) [e]	45.0 (0.0 - 60.0)

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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1.4 Endpunkt Schmerz: NRS-11-Schmerzskala

1.4.1 Subgruppenanalysen zur NRS-11-Schmerzskala

1.4.1.1 Subgruppenanalyse zur NRS-11-Schmerzskala: Veränderung gegenüber Baseline

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: 31 March 2021 (DC02)

		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=12)	0,25	0,866	0,00	0,0	3,0	42,9	12	-1,58	1,975	-1,00	-5,0	1,0	42,9
	Pre-cycle 49 (n=12)	0,00	0,000	0,00	0,0	0,0	42,9	12	-1,83	1,801	-2,00	-5,0	0,0	42,9
	Pre-cycle 61 (n=3)	1,00	1,732	0,00	0,0	3,0	85,7	3	-1,00	1,732	0,00	-3,0	0,0	85,7
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=9)	0,44	1,333	0,00	0,0	4,0	57,1	9	-1,33	1,658	0,00	-4,0	0,0	57,1
	Pre-cycle 49 (n=9)	0,11	0,333	0,00	0,0	1,0	57,1	9	-1,67	1,658	-2,00	-4,0	0,0	57,1

[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.

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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: 31 March 2021 (DC02)

		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=10)	0,40	1,265	0,00	0,0	4,0	52,4	7	-1,14	2,340	0,00	-5,0	1,0	66,7
	Pre-cycle 49 (n=8)	0,00	0,000	0,00	0,0	0,0	61,9	6	-2,00	2,280	-1,50	-5,0	0,0	71,4
	Pre-cycle 61 (n=3)	0,00	0,000	0,00	0,0	0,0	85,7	3	-1,33	2,309	0,00	-4,0	0,0	85,7
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=6)	2,00	1,897	2,00	0,0	5,0	71,4	6	-1,67	3,386	-2,50	-6,0	4,0	71,4
	Pre-cycle 49 (n=7)	1,14	1,215	1,00	0,0	3,0	66,7	7	-2,00	2,646	-1,00	-6,0	1,0	66,7
	Pre-cycle 61 (n=3)	1,33	2,309	0,00	0,0	4,0	85,7	3	-2,67	3,055	-2,00	-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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=9)	1,78	2,587	0,00	0,0	6,0	30,8	9	-2,00	4,062	-3,00	-6,0	6,0	30,8
	Pre-cycle 49 (n=7)	1,71	2,360	1,00	0,0	6,0	46,2	7	-2,43	4,198	-4,00	-6,0	6,0	46,2
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
	Pre-cycle 37 (n=9)	1,56	2,455	0,00	0,0	6,0	30,8	9	-1,22	4,265	-1,00	-6,0	6,0	30,8
	Pre-cycle 49 (n=7)	1,43	2,507	0,00	0,0	6,0	46,2	7	-1,43	3,952	-1,00	-6,0	6,0	46,2

[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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	1,43	1,902	1,00	0,0	5,0	46,2	7	-3,00	2,887	-4,00	-6,0	0,0	46,2
	Pre-cycle 49 (n=6)	1,67	2,251	0,50	0,0	5,0	53,8	6	-2,67	4,457	-4,00	-7,0	5,0	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
	Pre-cycle 37 (n=5)	3,20	2,387	3,00	0,0	6,0	61,5	5	-1,80	3,194	-1,00	-6,0	2,0	61,5
	Pre-cycle 49 (n=4)	2,00	2,708	1,00	0,0	6,0	69,2	3	-3,33	1,528	-3,00	-5,0	-2,0	76,9

[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.

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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: 31 March 2021 (DC02)

		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=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 49 (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 61 (n=2)	NC	NC	NC	0,0	3,0	81,8	2	NC	NC	NC	-3,0	0,0	81,8
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=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 49 (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

[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.

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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: 31 March 2021 (DC02)

		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=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 49 (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 61 (n=2)	NC	NC	NC	0,0	0,0	81,8	2	NC	NC	NC	-4,0	0,0	81,8
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=3)	1,67	1,528	2,00	0,0	3,0	72,7	3	-4,00	1,732	-3,00	-6,0	-3,0	72,7
	Pre-cycle 49 (n=4)	0,75	0,957	0,50	0,0	2,0	63,6	4	-3,50	2,517	-4,00	-6,0	0,0	63,6
	Pre-cycle 61 (n=2)	NC	NC	NC	0,0	4,0	81,8	2	NC	NC	NC	-6,0	-2,0	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.

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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: 31 March 2021 (DC02)

		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=8)	0,13	0,354	0,00	0,0	1,0	27,3	8	-3,00	2,268	-3,00	-6,0	0,0	27,3
	Pre-cycle 49 (n=8)	0,13	0,354	0,00	0,0	1,0	27,3	8	-3,00	2,268	-3,00	-6,0	0,0	27,3
	Pre-cycle 61 (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
	Pre-cycle 37 (n=7)	0,71	1,890	0,00	0,0	5,0	36,4	7	-1,86	3,132	-3,00	-6,0	4,0	36,4
	Pre-cycle 49 (n=7)	0,00	0,000	0,00	0,0	0,0	36,4	7	-2,57	1,902	-3,00	-6,0	0,0	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.

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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: 31 March 2021 (DC02)

		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=8)	0,13	0,354	0,00	0,0	1,0	27,3	6	-2,83	3,125	-2,50	-6,0	0,0	45,5
	Pre-cycle 49 (n=6)	0,00	0,000	0,00	0,0	0,0	45,5	5	-3,60	3,362	-5,00	-7,0	0,0	54,5
	Pre-cycle 61 (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=3)	1,33	1,155	2,00	0,0	2,0	72,7	3	-2,67	3,055	-2,00	-6,0	0,0	72,7
	Pre-cycle 49 (n=5)	2,00	2,550	1,00	0,0	6,0	54,5	4	-2,00	2,160	-1,50	-5,0	0,0	63,6
	Pre-cycle 61 (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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	2,57	2,699	3,00	0,0	6,0	41,7	7	-0,43	4,036	0,00	-6,0	6,0	41,7
	Pre-cycle 49 (n=5)	2,20	2,683	1,00	0,0	6,0	58,3	5	-1,00	4,359	-2,00	-5,0	6,0	58,3
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
	Pre-cycle 37 (n=7)	1,86	2,478	0,00	0,0	6,0	41,7	7	-0,86	3,934	0,00	-6,0	6,0	41,7
	Pre-cycle 49 (n=5)	2,20	2,683	1,00	0,0	6,0	58,3	5	-0,60	4,159	-1,00	-5,0	6,0	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=5)	2,60	2,074	3,00	0,0	5,0	58,3	5	-1,60	2,702	0,00	-5,0	1,0	58,3
	Pre-cycle 49 (n=4)	2,50	2,380	2,50	0,0	5,0	66,7	4	-1,50	4,359	-3,50	-4,0	5,0	66,7
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
	Pre-cycle 37 (n=5)	3,80	2,387	5,00	0,0	6,0	58,3	5	0,20	3,033	0,00	-4,0	4,0	58,3
	Pre-cycle 49 (n=2)	NC	NC	NC	1,0	2,0	83,3	2	NC	NC	NC	-3,0	1,0	83,3

[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.

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Table 2.2.3.6.1 NRS-11 pain intensity scores over time and change from baseline over time - Patients whose self-selected and target (physician-selected) PN were not the same - Gender = Male
SPRINT Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [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=5)	4,20	2,950	3,00	2,0	9,0	0,0							
	Pre-cycle 3 (n=5)	0,20	0,447	0,00	0,0	1,0	0,0	5	-4,00	3,162	-3,00	-9,0	-1,0	0,0
	Pre-cycle 5 (n=5)	0,40	0,548	0,00	0,0	1,0	0,0	5	-3,80	2,683	-2,00	-8,0	-2,0	0,0
	Pre-cycle 9 (n=5)	0,40	0,548	0,00	0,0	1,0	0,0	5	-3,80	2,683	-2,00	-8,0	-2,0	0,0
	Pre-cycle 13 (n=4)	0,00	0,000	0,00	0,0	0,0	20,0	4	-3,00	1,414	-2,50	-5,0	-2,0	20,0
	Pre-cycle 25 (n=3)	0,00	0,000	0,00	0,0	0,0	40,0	3	-3,00	1,732	-2,00	-5,0	-2,0	40,0
	Pre-cycle 37 (n=2)	NC	NC	NC	0,0	3,0	60,0	2	NC	NC	NC	-5,0	1,0	60,0
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	0,0	60,0	2	NC	NC	NC	-5,0	-2,0	60,0
Physician-selected target tumour pain [c]	Baseline (n=5)	2,60	1,140	3,00	1,0	4,0	0,0							
	Pre-cycle 3 (n=5)	1,20	0,837	1,00	0,0	2,0	0,0	5	-1,40	1,140	-1,00	-3,0	0,0	0,0
	Pre-cycle 5 (n=5)	2,00	2,345	1,00	0,0	5,0	0,0	5	-0,60	1,817	0,00	-3,0	1,0	0,0
	Pre-cycle 9 (n=5)	0,60	0,894	0,00	0,0	2,0	0,0	5	-2,00	0,707	-2,00	-3,0	-1,0	0,0
	Pre-cycle 13 (n=4)	0,50	1,000	0,00	0,0	2,0	20,0	4	-2,00	2,160	-2,50	-4,0	1,0	20,0
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	1,0	60,0	2	NC	NC	NC	-3,0	-3,0	60,0
	Pre-cycle 37 (n=2)	NC	NC	NC	0,0	4,0	60,0	2	NC	NC	NC	-3,0	0,0	60,0
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	1,0	60,0	2	NC	NC	NC	-3,0	-3,0	60,0

[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.

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Table 2.2.3.6.1 NRS-11 pain intensity scores over time and change from baseline over time - Patients whose self-selected and target (physician-selected) PN were not the same - Gender = Male
SPRINT Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [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=5)	3,00	2,550	3,00	0,0	6,0	0,0							
	Pre-cycle 3 (n=5)	1,80	1,643	1,00	0,0	4,0	0,0	5	-1,20	2,683	0,00	-5,0	1,0	0,0
	Pre-cycle 5 (n=5)	1,20	2,168	0,00	0,0	5,0	0,0	5	-1,80	3,493	0,00	-6,0	2,0	0,0
	Pre-cycle 9 (n=5)	1,20	1,095	2,00	0,0	2,0	0,0	5	-1,80	2,588	-1,00	-5,0	1,0	0,0
	Pre-cycle 13 (n=4)	0,25	0,500	0,00	0,0	1,0	20,0	4	-2,00	2,449	-1,50	-5,0	0,0	20,0
	Pre-cycle 25 (n=3)	0,00	0,000	0,00	0,0	0,0	40,0	3	-2,67	2,517	-3,00	-5,0	0,0	40,0
	Pre-cycle 37 (n=2)	NC	NC	NC	0,0	4,0	60,0	2	NC	NC	NC	-5,0	1,0	60,0
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	0,0	60,0	2	NC	NC	NC	-5,0	-3,0	60,0
Other pain	Baseline (n=4)	4,25	3,304	4,00	1,0	8,0	20,0							
	Pre-cycle 3 (n=5)	2,60	1,817	2,00	1,0	5,0	0,0	4	-1,25	4,113	-1,50	-6,0	4,0	20,0
	Pre-cycle 5 (n=4)	2,00	1,633	2,00	0,0	4,0	20,0	3	-1,00	4,583	0,00	-6,0	3,0	40,0
	Pre-cycle 9 (n=4)	3,00	0,816	3,00	2,0	4,0	20,0	3	-1,67	3,215	-3,00	-4,0	2,0	40,0
	Pre-cycle 13 (n=1)	NC	NC	NC	4,0	4,0	80,0	0	NC	NC	NC	NC	NC	100,0
	Pre-cycle 37 (n=1)	NC	NC	NC	5,0	5,0	80,0	1	NC	NC	NC	4,0	4,0	80,0
	Pre-cycle 49 (n=1)	NC	NC	NC	2,0	2,0	80,0	1	NC	NC	NC	1,0	1,0	80,0

[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.

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Table 2.2.3.6.2 NRS-11 pain intensity scores over time and change from baseline over time - Patients whose self-selected and target (physician-selected) PN were not the same - Gender = Female
SPRINT Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=2) [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=2)	NC	NC	NC	5,0	6,0	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	1,0	6,0	0,0	2	NC	NC	NC	-5,0	1,0	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	2,0	3,0	0,0	2	NC	NC	NC	-4,0	-2,0	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	2,0	4,0	0,0	2	NC	NC	NC	-4,0	-1,0	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	1,0	4,0	0,0	2	NC	NC	NC	-5,0	-1,0	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	1,0	5,0	0,0	2	NC	NC	NC	-5,0	0,0	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	1,0	6,0	0,0	2	NC	NC	NC	-5,0	1,0	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	1,0	1,0	0,0	2	NC	NC	NC	-5,0	-4,0	0,0
Physician-selected target tumour pain [c]	Baseline (n=2)	NC	NC	NC	1,0	1,0	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	0,0	1,0	0,0	2	NC	NC	NC	-1,0	0,0	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	0,0	0,0	2	NC	NC	NC	-1,0	-1,0	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	0,0	1,0	0,0	2	NC	NC	NC	-1,0	0,0	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	0,0	0,0	0,0	2	NC	NC	NC	-1,0	-1,0	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	0,0	0,0	2	NC	NC	NC	-1,0	-1,0	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	0,0	5,0	0,0	2	NC	NC	NC	-1,0	4,0	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	0,0	0,0	2	NC	NC	NC	-1,0	-1,0	0,0

[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.

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Table 2.2.3.6.2 NRS-11 pain intensity scores over time and change from baseline over time - Patients whose self-selected and target (physician-selected) PN were not the same - Gender = Female
SPRINT Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=2) [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=2)	NC	NC	NC	5,0	7,0	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	1,0	6,0	0,0	2	NC	NC	NC	-6,0	1,0	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	3,0	0,0	2	NC	NC	NC	-7,0	-2,0	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	2,0	4,0	0,0	2	NC	NC	NC	-5,0	-1,0	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	0,0	2,0	0,0	2	NC	NC	NC	-7,0	-3,0	0,0
	Pre-cycle 25 (n=1)	NC	NC	NC	3,0	3,0	50,0	1	NC	NC	NC	-2,0	-2,0	50,0
	Pre-cycle 37 (n=2)	NC	NC	NC	1,0	5,0	0,0	2	NC	NC	NC	-6,0	0,0	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	1,0	0,0	2	NC	NC	NC	-7,0	-4,0	0,0
Other pain	Baseline (n=2)	NC	NC	NC	4,0	8,0	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	3,0	7,0	0,0	2	NC	NC	NC	-5,0	3,0	0,0
	Pre-cycle 5 (n=1)	NC	NC	NC	4,0	4,0	50,0	1	NC	NC	NC	-4,0	-4,0	50,0
	Pre-cycle 9 (n=1)	NC	NC	NC	4,0	4,0	50,0	1	NC	NC	NC	-4,0	-4,0	50,0
	Pre-cycle 13 (n=2)	NC	NC	NC	3,0	4,0	0,0	2	NC	NC	NC	-5,0	0,0	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	2,0	5,0	0,0	2	NC	NC	NC	-6,0	1,0	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	2,0	6,0	0,0	2	NC	NC	NC	-6,0	2,0	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	1,0	6,0	0,0	2	NC	NC	NC	-3,0	-2,0	0,0

[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.

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Table 2.2.3.6.4 NRS-11 pain intensity scores over time and change from baseline over time - Patients whose self-selected and target (physician-selected) PN were not the same - PN status at enrollment = Non-progressive
SPRINT Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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=4)	5,50	2,887	5,50	2,0	9,0	0,0							
	Pre-cycle 3 (n=4)	0,50	0,577	0,50	0,0	1,0	0,0	4	-5,00	3,266	-5,00	-9,0	-1,0	0,0
	Pre-cycle 5 (n=4)	0,75	0,957	0,50	0,0	2,0	0,0	4	-4,75	2,500	-4,50	-8,0	-2,0	0,0
	Pre-cycle 9 (n=4)	0,75	0,957	0,50	0,0	2,0	0,0	4	-4,75	2,500	-4,50	-8,0	-2,0	0,0
	Pre-cycle 13 (n=3)	0,33	0,577	0,00	0,0	1,0	25,0	3	-4,00	1,732	-5,00	-5,0	-2,0	25,0
	Pre-cycle 25 (n=3)	0,33	0,577	0,00	0,0	1,0	25,0	3	-4,00	1,732	-5,00	-5,0	-2,0	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	0,0	1,0	50,0	2	NC	NC	NC	-5,0	-5,0	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	1,0	50,0	2	NC	NC	NC	-5,0	-5,0	50,0
Physician-selected target tumour pain [c]	Baseline (n=4)	2,25	0,957	2,50	1,0	3,0	0,0							
	Pre-cycle 3 (n=4)	0,75	0,957	0,50	0,0	2,0	0,0	4	-1,50	1,000	-1,00	-3,0	-1,0	0,0
	Pre-cycle 5 (n=4)	1,00	2,000	0,00	0,0	4,0	0,0	4	-1,25	1,708	-1,50	-3,0	1,0	0,0
	Pre-cycle 9 (n=4)	0,50	0,577	0,50	0,0	1,0	0,0	4	-1,75	1,258	-2,00	-3,0	0,0	0,0
	Pre-cycle 13 (n=3)	0,00	0,000	0,00	0,0	0,0	25,0	3	-2,00	1,000	-2,00	-3,0	-1,0	25,0
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	0,0	50,0	2	NC	NC	NC	-3,0	-1,0	50,0
	Pre-cycle 37 (n=2)	NC	NC	NC	0,0	5,0	50,0	2	NC	NC	NC	-3,0	4,0	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	0,0	50,0	2	NC	NC	NC	-3,0	-1,0	50,0

[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.

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Table 2.2.3.6.4 NRS-11 pain intensity scores over time and change from baseline over time - Patients whose self-selected and target (physician-selected) PN were not the same - PN status at enrollment = Non-progressive
SPRINT Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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=4)	4,50	3,109	5,50	0,0	7,0	0,0							
	Pre-cycle 3 (n=4)	1,25	1,258	1,00	0,0	3,0	0,0	4	-3,25	3,096	-4,00	-6,0	1,0	0,0
	Pre-cycle 5 (n=4)	0,00	0,000	0,00	0,0	0,0	0,0	4	-4,50	3,109	-5,50	-7,0	0,0	0,0
	Pre-cycle 9 (n=4)	1,00	1,155	1,00	0,0	2,0	0,0	4	-3,50	2,380	-4,50	-5,0	0,0	0,0
	Pre-cycle 13 (n=3)	0,00	0,000	0,00	0,0	0,0	25,0	3	-4,00	3,606	-5,00	-7,0	0,0	25,0
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	0,0	50,0	2	NC	NC	NC	-5,0	0,0	50,0
	Pre-cycle 37 (n=2)	NC	NC	NC	0,0	1,0	50,0	2	NC	NC	NC	-6,0	-5,0	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	0,0	50,0	2	NC	NC	NC	-7,0	-5,0	50,0
Other pain	Baseline (n=4)	6,00	2,828	7,00	2,0	8,0	0,0							
	Pre-cycle 3 (n=4)	2,50	1,291	2,50	1,0	4,0	0,0	4	-3,50	2,380	-3,50	-6,0	-1,0	0,0
	Pre-cycle 5 (n=3)	2,67	1,155	2,00	2,0	4,0	25,0	3	-3,33	3,055	-4,00	-6,0	0,0	25,0
	Pre-cycle 9 (n=3)	3,67	0,577	4,00	3,0	4,0	25,0	3	-3,67	0,577	-4,00	-4,0	-3,0	25,0
	Pre-cycle 13 (n=1)	NC	NC	NC	3,0	3,0	75,0	1	NC	NC	NC	-5,0	-5,0	75,0
	Pre-cycle 25 (n=1)	NC	NC	NC	2,0	2,0	75,0	1	NC	NC	NC	-6,0	-6,0	75,0
	Pre-cycle 37 (n=1)	NC	NC	NC	2,0	2,0	75,0	1	NC	NC	NC	-6,0	-6,0	75,0
	Pre-cycle 49 (n=1)	NC	NC	NC	6,0	6,0	75,0	1	NC	NC	NC	-2,0	-2,0	75,0

[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.

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Table 2.2.3.6.5 NRS-11 pain intensity scores over time and change from baseline over time - Patients whose self-selected and target (physician-selected) PN were not the same - PN status at enrollment = Unknown
SPRINT Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [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=3)	3,33	1,528	3,00	2,0	5,0	0,0							
	Pre-cycle 3 (n=3)	2,00	3,464	0,00	0,0	6,0	0,0	3	-1,33	2,082	-2,00	-3,0	1,0	0,0
	Pre-cycle 5 (n=3)	1,33	1,528	1,00	0,0	3,0	0,0	3	-2,00	0,000	-2,00	-2,0	-2,0	0,0
	Pre-cycle 9 (n=3)	1,67	2,082	1,00	0,0	4,0	0,0	3	-1,67	0,577	-2,00	-2,0	-1,0	0,0
	Pre-cycle 13 (n=3)	1,33	2,309	0,00	0,0	4,0	0,0	3	-2,00	1,000	-2,00	-3,0	-1,0	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	5,0	33,3	2	NC	NC	NC	-2,0	0,0	33,3
	Pre-cycle 37 (n=2)	NC	NC	NC	3,0	6,0	33,3	2	NC	NC	NC	1,0	1,0	33,3
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	1,0	33,3	2	NC	NC	NC	-4,0	-2,0	33,3
Physician-selected target tumour pain [c]	Baseline (n=3)	2,00	1,732	1,00	1,0	4,0	0,0							
	Pre-cycle 3 (n=3)	1,33	0,577	1,00	1,0	2,0	0,0	3	-0,67	1,155	0,00	-2,0	0,0	0,0
	Pre-cycle 5 (n=3)	2,00	2,646	1,00	0,0	5,0	0,0	3	0,00	1,000	0,00	-1,0	1,0	0,0
	Pre-cycle 9 (n=3)	0,67	1,155	0,00	0,0	2,0	0,0	3	-1,33	0,577	-1,00	-2,0	-1,0	0,0
	Pre-cycle 13 (n=3)	0,67	1,155	0,00	0,0	2,0	0,0	3	-1,33	2,517	-1,00	-4,0	1,0	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	1,0	33,3	2	NC	NC	NC	-3,0	-1,0	33,3
	Pre-cycle 37 (n=2)	NC	NC	NC	0,0	4,0	33,3	2	NC	NC	NC	-1,0	0,0	33,3
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	1,0	33,3	2	NC	NC	NC	-3,0	-1,0	33,3

[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.

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Table 2.2.3.6.5 NRS-11 pain intensity scores over time and change from baseline over time - Patients whose self-selected and target (physician-selected) PN were not the same - PN status at enrollment = Unknown
SPRINT Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [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=3)	3,00	2,000	3,00	1,0	5,0	0,0							
	Pre-cycle 3 (n=3)	3,67	2,517	4,00	1,0	6,0	0,0	3	0,67	0,577	1,00	0,0	1,0	0,0
	Pre-cycle 5 (n=3)	3,00	2,000	3,00	1,0	5,0	0,0	3	0,00	2,000	0,00	-2,0	2,0	0,0
	Pre-cycle 9 (n=3)	2,67	1,155	2,00	2,0	4,0	0,0	3	-0,33	1,155	-1,00	-1,0	1,0	0,0
	Pre-cycle 13 (n=3)	1,00	1,000	1,00	0,0	2,0	0,0	3	-2,00	1,732	-3,00	-3,0	0,0	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	0,0	3,0	33,3	2	NC	NC	NC	-3,0	-2,0	33,3
	Pre-cycle 37 (n=2)	NC	NC	NC	4,0	5,0	33,3	2	NC	NC	NC	0,0	1,0	33,3
	Pre-cycle 49 (n=2)	NC	NC	NC	0,0	1,0	33,3	2	NC	NC	NC	-4,0	-3,0	33,3
Other pain	Baseline (n=2)	NC	NC	NC	1,0	4,0	33,3							
	Pre-cycle 3 (n=3)	4,33	3,055	5,00	1,0	7,0	0,0	2	NC	NC	NC	3,0	4,0	33,3
	Pre-cycle 5 (n=2)	NC	NC	NC	0,0	4,0	33,3	1	NC	NC	NC	3,0	3,0	66,7
	Pre-cycle 9 (n=2)	NC	NC	NC	2,0	3,0	33,3	1	NC	NC	NC	2,0	2,0	66,7
	Pre-cycle 13 (n=2)	NC	NC	NC	4,0	4,0	33,3	1	NC	NC	NC	0,0	0,0	66,7
	Pre-cycle 25 (n=1)	NC	NC	NC	5,0	5,0	66,7	1	NC	NC	NC	1,0	1,0	66,7
	Pre-cycle 37 (n=2)	NC	NC	NC	5,0	6,0	33,3	2	NC	NC	NC	2,0	4,0	33,3
	Pre-cycle 49 (n=2)	NC	NC	NC	1,0	2,0	33,3	2	NC	NC	NC	-3,0	1,0	33,3

[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.

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1.4.1.2 Subgruppenanalyse zur NRS-11-Schmerzskala: Responderanalyse

Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 3 (n=19)	Categories of change - literature-based [d]			
		Improvement	7	36.8	16.3, 61.6
		Deterioration	0	0	0, 17.6
		No improvement or deterioration	12	63.2	38.4, 83.7
	Pre-cycle 5 (n=19)	Categories of change - literature-based [d]			
		Improvement	12	63.2	38.4, 83.7
		Deterioration	1	5.3	0.1, 26.0
		No improvement or deterioration	6	31.6	12.6, 56.6
	Pre-cycle 9 (n=19)	Categories of change - literature-based [d]			
		Improvement	11	57.9	33.5, 79.7
		Deterioration	0	0	0, 17.6
		No improvement or deterioration	8	42.1	20.3, 66.5

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 13 (n=18)	Categories of change - literature-based [d]			
		Improvement	11	61.1	35.7, 82.7
		Deterioration	0	0	0, 18.5
		No improvement or deterioration	7	38.9	17.3, 64.3
	Pre-cycle 25 (n=13)	Categories of change - literature-based [d]			
		Improvement	7	53.8	25.1, 80.8
		Deterioration	0	0	0, 24.7
		No improvement or deterioration	6	46.2	19.2, 74.9
	Pre-cycle 37 (n=12)	Categories of change - literature-based [d]			
		Improvement	6	50.0	21.1, 78.9
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	6	50.0	21.1, 78.9

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 49 (n=12)	Categories of change - literature-based [d]			
		Improvement	7	58.3	27.7, 84.8
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	5	41.7	15.2, 72.3
	Overall (n=19)	Categories of change - literature-based [d]			
		Improvement	13	68.4	43.4, 87.4
		Deterioration	1	5.3	0.1, 26.0
		No improvement or deterioration	5	26.3	9.1, 51.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 3 (n=14)	Categories of change - literature-based [d]			
		Improvement	4	28.6	8.4, 58.1
		Deterioration	0	0	0, 23.2
		No improvement or deterioration	10	71.4	41.9, 91.6
	Pre-cycle 5 (n=14)	Categories of change - literature-based [d]			
		Improvement	6	42.9	17.7, 71.1
		Deterioration	1	7.1	0.2, 33.9
		No improvement or deterioration	7	50.0	23.0, 77.0
	Pre-cycle 9 (n=14)	Categories of change - literature-based [d]			
		Improvement	7	50.0	23.0, 77.0
		Deterioration	0	0	0, 23.2
		No improvement or deterioration	7	50.0	23.0, 77.0

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 13 (n=13)	Categories of change - literature-based [d]			
		Improvement	7	53.8	25.1, 80.8
		Deterioration	0	0	0, 24.7
		No improvement or deterioration	6	46.2	19.2, 74.9
	Pre-cycle 25 (n=9)	Categories of change - literature-based [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 37 (n=9)	Categories of change - literature-based [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	5	55.6	21.2, 86.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 49 (n=9)	Categories of change - literature-based [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	4	44.4	13.7, 78.8
	Overall (n=14)	Categories of change - literature-based [d]			
		Improvement	9	64.3	35.1, 87.2
		Deterioration	1	7.1	0.2, 33.9
		No improvement or deterioration	4	28.6	8.4, 58.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 3 (n=13)	Categories of change - literature-based [d]			
		Improvement	5	38.5	13.9, 68.4
		Deterioration	2	15.4	1.9, 45.4
		No improvement or deterioration	6	46.2	19.2, 74.9
	Pre-cycle 5 (n=13)	Categories of change - literature-based [d]			
		Improvement	5	38.5	13.9, 68.4
		Deterioration	3	23.1	5.0, 53.8
		No improvement or deterioration	5	38.5	13.9, 68.4
	Pre-cycle 9 (n=14)	Categories of change - literature-based [d]			
		Improvement	6	42.9	17.7, 71.1
		Deterioration	0	0	0, 23.2
		No improvement or deterioration	8	57.1	28.9, 82.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 13 (n=13)	Categories of change - literature-based [d]			
		Improvement	5	38.5	13.9, 68.4
		Deterioration	1	7.7	0.2, 36.0
		No improvement or deterioration	7	53.8	25.1, 80.8
	Pre-cycle 25 (n=9)	Categories of change - literature-based [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 37 (n=7)	Categories of change - literature-based [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 49 (n=6)	Categories of change - literature-based [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Overall (n=14)	Categories of change - literature-based [d]			
		Improvement	7	50.0	23.0, 77.0
		Deterioration	3	21.4	4.7, 50.8
		No improvement or deterioration	6	42.9	17.7, 71.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 3 (n=15)	Categories of change - literature-based [d]			
		Improvement	4	26.7	7.8, 55.1
		Deterioration	3	20.0	4.3, 48.1
		No improvement or deterioration	8	53.3	26.6, 78.7
	Pre-cycle 5 (n=13)	Categories of change - literature-based [d]			
		Improvement	4	30.8	9.1, 61.4
		Deterioration	2	15.4	1.9, 45.4
		No improvement or deterioration	7	53.8	25.1, 80.8
	Pre-cycle 9 (n=14)	Categories of change - literature-based [d]			
		Improvement	6	42.9	17.7, 71.1
		Deterioration	3	21.4	4.7, 50.8
		No improvement or deterioration	5	35.7	12.8, 64.9

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 13 (n=9)	Categories of change - literature-based [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	7	77.8	40.0, 97.2
	Pre-cycle 25 (n=6)	Categories of change - literature-based [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 37 (n=6)	Categories of change - literature-based [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 49 (n=7)	Categories of change - literature-based [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	4	57.1	18.4, 90.1
	Overall (n=16)	Categories of change - literature-based [d]			
		Improvement	9	56.3	29.9, 80.2
		Deterioration	5	31.3	11.0, 58.7
		No improvement or deterioration	4	25.0	7.3, 52.4

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 3 (n=12)	Categories of change - literature-based [d]			
		Improvement	6	50.0	21.1, 78.9
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	5	41.7	15.2, 72.3
	Pre-cycle 5 (n=12)	Categories of change - literature-based [d]			
		Improvement	8	66.7	34.9, 90.1
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	3	25.0	5.5, 57.2
	Pre-cycle 9 (n=12)	Categories of change - literature-based [d]			
		Improvement	7	58.3	27.7, 84.8
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	5	41.7	15.2, 72.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 13 (n=11)	Categories of change - literature-based [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 25 (n=9)	Categories of change - literature-based [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	3	33.3	7.5, 70.1
	Pre-cycle 37 (n=9)	Categories of change - literature-based [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	3	33.3	7.5, 70.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 49 (n=7)	Categories of change - literature-based [d]			
		Improvement	5	71.4	29.0, 96.3
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	1	14.3	0.4, 57.9
	Overall (n=12)	Categories of change - literature-based [d]			
		Improvement	8	66.7	34.9, 90.1
		Deterioration	3	25.0	5.5, 57.2
		No improvement or deterioration	1	8.3	0.2, 38.5

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 3 (n=11)	Categories of change - literature-based [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 5 (n=11)	Categories of change - literature-based [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	4	36.4	10.9, 69.2
	Pre-cycle 9 (n=11)	Categories of change - literature-based [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	5	45.5	16.7, 76.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 13 (n=11)	Categories of change - literature-based [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	6	54.5	23.4, 83.3
	Pre-cycle 25 (n=9)	Categories of change - literature-based [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 37 (n=9)	Categories of change - literature-based [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	3	33.3	7.5, 70.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 49 (n=7)	Categories of change - literature-based [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	3	42.9	9.9, 81.6
	Overall (n=11)	Categories of change - literature-based [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	4	36.4	10.9, 69.2
		No improvement or deterioration	1	9.1	0.2, 41.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 3 (n=12)	Categories of change - literature-based [d]			
		Improvement	5	41.7	15.2, 72.3
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	7	58.3	27.7, 84.8
	Pre-cycle 5 (n=11)	Categories of change - literature-based [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 9 (n=12)	Categories of change - literature-based [d]			
		Improvement	6	50.0	21.1, 78.9
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	6	50.0	21.1, 78.9

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 13 (n=10)	Categories of change - literature-based [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	4	40.0	12.2, 73.8
	Pre-cycle 25 (n=6)	Categories of change - literature-based [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 37 (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	3	42.9	9.9, 81.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 49 (n=6)	Categories of change - literature-based [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1
	Overall (n=12)	Categories of change - literature-based [d]			
		Improvement	7	58.3	27.7, 84.8
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	4	33.3	9.9, 65.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 3 (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 5 (n=6)	Categories of change - literature-based [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 9 (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 13 (n=9)	Categories of change - literature-based [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	3	33.3	7.5, 70.1
	Pre-cycle 25 (n=6)	Categories of change - literature-based [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 37 (n=5)	Categories of change - literature-based [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 49 (n=3)	Categories of change - literature-based [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
	Overall (n=10)	Categories of change - literature-based [d]			
		Improvement	8	80.0	44.4, 97.5
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	1	10.0	0.3, 44.5

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 3 (n=11)	Categories of change - literature-based [d]			
		Improvement	3	27.3	6.0, 61.0
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	8	72.7	39.0, 94.0
	Pre-cycle 5 (n=11)	Categories of change - literature-based [d]			
		Improvement	7	63.6	30.8, 89.1
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	3	27.3	6.0, 61.0
	Pre-cycle 9 (n=11)	Categories of change - literature-based [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	5	45.5	16.7, 76.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 13 (n=10)	Categories of change - literature-based [d]			
		Improvement	7	70.0	34.8, 93.3
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	3	30.0	6.7, 65.2
	Pre-cycle 25 (n=6)	Categories of change - literature-based [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 37 (n=6)	Categories of change - literature-based [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 49 (n=6)	Categories of change - literature-based [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Overall (n=11)	Categories of change - literature-based [d]			
		Improvement	7	63.6	30.8, 89.1
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	3	27.3	6.0, 61.0

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 3 (n=7)	Categories of change - literature-based [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 5 (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 9 (n=7)	Categories of change - literature-based [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	4	57.1	18.4, 90.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 13 (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 25 (n=4)	Categories of change - literature-based [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 37 (n=4)	Categories of change - literature-based [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 49 (n=4)	Categories of change - literature-based [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Overall (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 3 (n=8)	Categories of change - literature-based [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	2	25.0	3.2, 65.1
	Pre-cycle 5 (n=7)	Categories of change - literature-based [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 9 (n=8)	Categories of change - literature-based [d]			
		Improvement	5	62.5	24.5, 91.5
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	3	37.5	8.5, 75.5

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 13 (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 25 (n=3)	Categories of change - literature-based [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 37 (n=3)	Categories of change - literature-based [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 49 (n=3)	Categories of change - literature-based [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Overall (n=8)	Categories of change - literature-based [d]			
		Improvement	5	62.5	24.5, 91.5
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	2	25.0	3.2, 65.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 3 (n=9)	Categories of change - literature-based [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	3	33.3	7.5, 70.1
	Pre-cycle 5 (n=8)	Categories of change - literature-based [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	4	50.0	15.7, 84.3
	Pre-cycle 9 (n=9)	Categories of change - literature-based [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	3	33.3	7.5, 70.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 13 (n=6)	Categories of change - literature-based [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 25 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (n=3)	Categories of change - literature-based [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 49 (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Overall (n=10)	Categories of change - literature-based [d]			
		Improvement	8	80.0	44.4, 97.5
		Deterioration	3	30.0	6.7, 65.2
		No improvement or deterioration	1	10.0	0.3, 44.5

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 3 (n=10)	Categories of change - literature-based [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	4	40.0	12.2, 73.8
	Pre-cycle 5 (n=10)	Categories of change - literature-based [d]			
		Improvement	7	70.0	34.8, 93.3
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	3	30.0	6.7, 65.2
	Pre-cycle 9 (n=10)	Categories of change - literature-based [d]			
		Improvement	7	70.0	34.8, 93.3
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 13 (n=9)	Categories of change - literature-based [d]			
		Improvement	6	66.7	29.9, 92.5
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	3	33.3	7.5, 70.1
	Pre-cycle 25 (n=9)	Categories of change - literature-based [d]			
		Improvement	6	66.7	29.9, 92.5
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	3	33.3	7.5, 70.1
	Pre-cycle 37 (n=8)	Categories of change - literature-based [d]			
		Improvement	6	75.0	34.9, 96.8
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	2	25.0	3.2, 65.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 49 (n=8)	Categories of change - literature-based [d]			
		Improvement	6	75.0	34.9, 96.8
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	2	25.0	3.2, 65.1
	Overall (n=10)	Categories of change - literature-based [d]			
		Improvement	8	80.0	44.4, 97.5
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 3 (n=9)	Categories of change - literature-based [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 5 (n=9)	Categories of change - literature-based [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 9 (n=9)	Categories of change - literature-based [d]			
		Improvement	6	66.7	29.9, 92.5
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	3	33.3	7.5, 70.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 13 (n=8)	Categories of change - literature-based [d]			
		Improvement	5	62.5	24.5, 91.5
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 25 (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 37 (n=7)	Categories of change - literature-based [d]			
		Improvement	5	71.4	29.0, 96.3
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	1	14.3	0.4, 57.9

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 49 (n=7)	Categories of change - literature-based [d]			
		Improvement	5	71.4	29.0, 96.3
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	2	28.6	3.7, 71.0
	Overall (n=9)	Categories of change - literature-based [d]			
		Improvement	7	77.8	40.0, 97.2
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	1	11.1	0.3, 48.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 3 (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 5 (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 9 (n=8)	Categories of change - literature-based [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 13 (n=7)	Categories of change - literature-based [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 25 (n=6)	Categories of change - literature-based [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 37 (n=6)	Categories of change - literature-based [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 49 (n=5)	Categories of change - literature-based [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3
	Overall (n=8)	Categories of change - literature-based [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 3 (n=8)	Categories of change - literature-based [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	4	50.0	15.7, 84.3
	Pre-cycle 5 (n=7)	Categories of change - literature-based [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 9 (n=7)	Categories of change - literature-based [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 13 (n=5)	Categories of change - literature-based [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 25 (n=4)	Categories of change - literature-based [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 37 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 49 (n=4)	Categories of change - literature-based [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Overall (n=8)	Categories of change - literature-based [d]			
		Improvement	5	62.5	24.5, 91.5
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	2	25.0	3.2, 65.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 3 (n=10)	Categories of change - literature-based [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 5 (n=10)	Categories of change - literature-based [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	3	30.0	6.7, 65.2
	Pre-cycle 9 (n=10)	Categories of change - literature-based [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	5	50.0	18.7, 81.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 13 (n=10)	Categories of change - literature-based [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 25 (n=7)	Categories of change - literature-based [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 37 (n=7)	Categories of change - literature-based [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	4	57.1	18.4, 90.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 49 (n=5)	Categories of change - literature-based [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	1	20.0	0.5, 71.6
	Overall (n=10)	Categories of change - literature-based [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	3	30.0	6.7, 65.2
		No improvement or deterioration	1	10.0	0.3, 44.5

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 3 (n=9)	Categories of change - literature-based [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 5 (n=9)	Categories of change - literature-based [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 9 (n=9)	Categories of change - literature-based [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	5	55.6	21.2, 86.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 13 (n=9)	Categories of change - literature-based [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 25 (n=7)	Categories of change - literature-based [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 37 (n=7)	Categories of change - literature-based [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	4	57.1	18.4, 90.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 49 (n=5)	Categories of change - literature-based [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Overall (n=9)	Categories of change - literature-based [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	3	33.3	7.5, 70.1
		No improvement or deterioration	2	22.2	2.8, 60.0

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 3 (n=10)	Categories of change - literature-based [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 5 (n=10)	Categories of change - literature-based [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 9 (n=10)	Categories of change - literature-based [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	7	70.0	34.8, 93.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 13 (n=9)	Categories of change - literature-based [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 25 (n=6)	Categories of change - literature-based [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 37 (n=5)	Categories of change - literature-based [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 49 (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	0	0	0, 60.2
	Overall (n=10)	Categories of change - literature-based [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	4	40.0	12.2, 73.8

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 3 (n=5)	Categories of change - literature-based [d]			
		Improvement	0	0	0, 52.2
		Deterioration	2	40.0	5.3, 85.3
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 5 (n=4)	Categories of change - literature-based [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 9 (n=5)	Categories of change - literature-based [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	2	40.0	5.3, 85.3
		No improvement or deterioration	2	40.0	5.3, 85.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 13 (n=7)	Categories of change - literature-based [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 25 (n=5)	Categories of change - literature-based [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 37 (n=5)	Categories of change - literature-based [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	2	40.0	5.3, 85.3
		No improvement or deterioration	2	40.0	5.3, 85.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.1.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=8)	Categories of change - literature-based [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	3	37.5	8.5, 75.5
		No improvement or deterioration	2	25.0	3.2, 65.1

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 3 (n=5)	Categories of change - literature-based [d]			
		Improvement	4	80.0	28.4, 99.5
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	1	20.0	0.5, 71.6
	Pre-cycle 5 (n=5)	Categories of change - literature-based [d]			
		Improvement	5	100	47.8, 100
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	0	0	0, 52.2
	Pre-cycle 9 (n=5)	Categories of change - literature-based [d]			
		Improvement	5	100	47.8, 100
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	0	0	0, 52.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 13 (n=4)	Categories of change - literature-based [d]			
		Improvement	4	100	39.8, 100
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	0	0	0, 60.2
	Pre-cycle 25 (n=3)	Categories of change - literature-based [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=5)	Categories of change - literature-based [d]			
		Improvement	5	100	47.8, 100
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	0	0	0, 52.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 3 (n=5)	Categories of change - literature-based [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 5 (n=5)	Categories of change - literature-based [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 9 (n=5)	Categories of change - literature-based [d]			
		Improvement	4	80.0	28.4, 99.5
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	1	20.0	0.5, 71.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 13 (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 25 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=5)	Categories of change - literature-based [d]			
		Improvement	4	80.0	28.4, 99.5
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	1	20.0	0.5, 71.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 3 (n=5)	Categories of change - literature-based [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 5 (n=5)	Categories of change - literature-based [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 9 (n=5)	Categories of change - literature-based [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 13 (n=4)	Categories of change - literature-based [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 25 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=5)	Categories of change - literature-based [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 3 (n=4)	Categories of change - literature-based [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 5 (n=3)	Categories of change - literature-based [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 9 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.1 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=21) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 37 (n=1)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=4)	Categories of change - literature-based [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 3 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 5 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 9 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 13 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 25 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 3 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 5 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 9 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 13 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 25 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	1	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Overall (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	1	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 3 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 5 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 9 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 13 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 25 (n=1)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 3 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 5 (n=1)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 9 (n=1)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 13 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 25 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.2 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.3 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

INSUFFICIENT DATA

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 3 (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 5 (n=4)	Categories of change - literature-based [d]			
		Improvement	4	100	39.8, 100
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	0	0	0, 60.2
	Pre-cycle 9 (n=4)	Categories of change - literature-based [d]			
		Improvement	4	100	39.8, 100
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	0	0	0, 60.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 13 (n=3)	Categories of change - literature-based [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
	Pre-cycle 25 (n=3)	Categories of change - literature-based [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=4)	Categories of change - literature-based [d]			
		Improvement	4	100	39.8, 100
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	0	0	0, 60.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 3 (n=4)	Categories of change - literature-based [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 5 (n=4)	Categories of change - literature-based [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 9 (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 13 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	0	0	0, 60.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 3 (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 5 (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 9 (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 13 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 3 (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 5 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 9 (n=3)	Categories of change - literature-based [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 13 (n=1)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 25 (n=1)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.4 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 49 (n=1)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=4)	Categories of change - literature-based [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 3 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 5 (n=3)	Categories of change - literature-based [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
	Pre-cycle 9 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 13 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Self-selected tumour pain score	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=3)	Categories of change - literature-based [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 3 (n=3)	Categories of change - literature-based [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 5 (n=3)	Categories of change - literature-based [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 9 (n=3)	Categories of change - literature-based [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 13 (n=3)	Categories of change - literature-based [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 25 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Physician-selected target tumour pain [e]	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=3)	Categories of change - literature-based [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 3 (n=3)	Categories of change - literature-based [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 5 (n=3)	Categories of change - literature-based [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 9 (n=3)	Categories of change - literature-based [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 13 (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Overall tumour pain	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=3)	Categories of change - literature-based [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 3 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	2	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 5 (n=1)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 9 (n=1)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 13 (n=1)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 25 (n=1)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change - literature-based [d]			
		Improvement	0	NC	NC
		Deterioration	2	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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Table 5.2.2.1.5 NRS-11 self-report score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Patients whose self-selected PN and target (physician-selected) PN differ - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Other pain	Pre-cycle 49 (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=2)	Categories of change - literature-based [d]			
		Improvement	1	NC	NC
		Deterioration	2	NC	NC
		No improvement or deterioration	0	NC	NC

[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 change/deterioration are defined using a threshold of 2 from literature (Farrar,et al. 2000, Kendrick, et al. 2005, Salaffi, F., et al. 2004, Voepel-Lewis et al. 2011).
[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 different.
NC = Not Calculated.

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1.5 Endpunkt Schmerz: Zeit bis zur Schmerzlinderung

1.5.1 Subgruppenanalysen zur Zeit bis zur Schmerzlinderung

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: 31 March 2021 (DC02)

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.

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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: 31 March 2021 (DC02)

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, NC
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.

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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: 31 March 2021 (DC02)

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, NC
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.

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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: 31 March 2021 (DC02)

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.

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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: 31 March 2021 (DC02)

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, NC
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.

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1.6 Endpunkt Schmerz: Pain Interference Index (PII)

1.6.1 Subgruppenanalysen zum PII

1.6.1.1 Subgruppenanalyyse zum PII: Veränderung gegenüber Baseline – Selbstberichtet

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: 31 March 2021 (DC02)

		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=12)	0,18	0,575	0,00	0,0	2,0	42,9	12	-0,58	0,694	-0,25	-2,0	0,0	42,9
	Pre-cycle 49 (n=12)	0,10	0,166	0,00	0,0	0,5	42,9	12	-0,67	1,082	-0,08	-3,3	0,3	42,9
	Pre-cycle 61 (n=2)	NC	NC	NC	0,0	0,0	90,5	2	NC	NC	NC	-0,2	0,0	90,5

[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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=9)	0,52	0,860	0,17	0,0	2,7	30,8	9	-0,93	1,377	-0,33	-4,0	0,5	30,8
	Pre-cycle 49 (n=6)	0,94	1,311	0,33	0,0	3,5	53,8	6	-0,31	0,386	-0,17	-1,0	0,0	53,8

[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.

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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: 31 March 2021 (DC02)

		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=6)	0,00	0,000	0,00	0,0	0,0	45,5	6	-0,47	0,770	-0,17	-2,0	0,0	45,5
	Pre-cycle 49 (n=6)	0,11	0,202	0,00	0,0	0,5	45,5	6	-0,36	0,846	0,00	-2,0	0,3	45,5
	Pre-cycle 61 (n=1)	NC	NC	NC	0,0	0,0	90,9	1	NC	NC	NC	-0,2	-0,2	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.

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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: 31 March 2021 (DC02)

		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=8)	0,06	0,086	0,00	0,0	0,2	27,3	8	-0,52	0,552	-0,33	-1,2	0,0	27,3
	Pre-cycle 49 (n=8)	0,23	0,408	0,00	0,0	1,2	27,3	8	-0,35	0,507	-0,17	-1,2	0,0	27,3
	Pre-cycle 61 (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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	0,90	1,045	0,67	0,0	2,7	41,7	7	-1,19	1,514	-1,33	-4,0	0,5	41,7
	Pre-cycle 49 (n=4)	1,08	1,613	0,33	0,2	3,5	66,7	4	-1,21	1,474	-0,75	-3,3	0,0	66,7

[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.

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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: 31 March 2021 (DC02)

		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=20)	0,28	0,607	0,00	0,0	2,3	28,6	19	-0,99	1,058	-0,50	-3,0	0,0	32,1
	Pre-cycle 37 (n=17)	0,19	0,448	0,00	0,0	1,8	39,3	16	-1,13	1,216	-0,67	-3,7	0,0	42,9
	Pre-cycle 49 (n=17)	0,38	1,010	0,00	0,0	4,0	39,3	16	-1,16	1,155	-1,08	-3,8	0,0	42,9
	Pre-cycle 61 (n=3)	0,39	0,674	0,00	0,0	1,2	89,3	3	-1,06	2,275	0,00	-3,7	0,5	89,3

[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.

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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: 31 March 2021 (DC02)

		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=12)	0,67	0,788	0,33	0,0	2,0	40,0	12	-0,57	0,973	-0,33	-2,8	0,7	40,0
	Pre-cycle 49 (n=8)	0,48	0,888	0,00	0,0	2,0	60,0	8	-0,23	1,054	-0,17	-1,5	1,8	60,0

[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.

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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: 31 March 2021 (DC02)

		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=14)	0,67	0,967	0,17	0,0	3,0	30,0	13	-0,72	1,218	-0,17	-3,0	1,2	35,0
	Pre-cycle 37 (n=11)	0,21	0,495	0,00	0,0	1,7	45,0	10	-1,30	1,344	-1,00	-3,7	0,0	50,0
	Pre-cycle 49 (n=10)	0,53	1,288	0,00	0,0	4,0	50,0	9	-1,20	1,320	-0,67	-3,8	0,0	55,0
	Pre-cycle 61 (n=2)	NC	NC	NC	0,0	1,2	90,0	2	NC	NC	NC	-3,7	0,5	90,0

[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.

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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: 31 March 2021 (DC02)

		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=9)	0,02	0,056	0,00	0,0	0,2	35,7	9	-0,69	0,880	-0,33	-2,3	0,0	35,7
	Pre-cycle 49 (n=8)	0,02	0,059	0,00	0,0	0,2	42,9	8	-0,73	0,930	-0,25	-2,3	0,0	42,9
	Pre-cycle 61 (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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=9)	0,96	0,763	0,67	0,0	2,0	35,7	9	-0,63	1,095	-0,33	-2,8	0,7	35,7
	Pre-cycle 49 (n=7)	0,69	0,915	0,00	0,0	2,0	50,0	7	-0,52	1,317	-1,00	-1,8	1,8	50,0

[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.

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1.6.1.1 Subgruppenanalyyse zum PII: Veränderung gegenüber Baseline – Elternberichtet

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: 31 March 2021 (DC02)

		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=20)	0,28	0,607	0,00	0,0	2,3	28,6	19	-0,99	1,058	-0,50	-3,0	0,0	32,1
	Pre-cycle 37 (n=17)	0,19	0,448	0,00	0,0	1,8	39,3	16	-1,13	1,216	-0,67	-3,7	0,0	42,9
	Pre-cycle 49 (n=17)	0,38	1,010	0,00	0,0	4,0	39,3	16	-1,16	1,155	-1,08	-3,8	0,0	42,9
	Pre-cycle 61 (n=3)	0,39	0,674	0,00	0,0	1,2	89,3	3	-1,06	2,275	0,00	-3,7	0,5	89,3

[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.

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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: 31 March 2021 (DC02)

		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=12)	0,67	0,788	0,33	0,0	2,0	40,0	12	-0,57	0,973	-0,33	-2,8	0,7	40,0
	Pre-cycle 49 (n=8)	0,48	0,888	0,00	0,0	2,0	60,0	8	-0,23	1,054	-0,17	-1,5	1,8	60,0

[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.

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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: 31 March 2021 (DC02)

		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=14)	0,67	0,967	0,17	0,0	3,0	30,0	13	-0,72	1,218	-0,17	-3,0	1,2	35,0
	Pre-cycle 37 (n=11)	0,21	0,495	0,00	0,0	1,7	45,0	10	-1,30	1,344	-1,00	-3,7	0,0	50,0
	Pre-cycle 49 (n=10)	0,53	1,288	0,00	0,0	4,0	50,0	9	-1,20	1,320	-0,67	-3,8	0,0	55,0
	Pre-cycle 61 (n=2)	NC	NC	NC	0,0	1,2	90,0	2	NC	NC	NC	-3,7	0,5	90,0

[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.

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Table 2.3.2.1.4 PII parent-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: 31 March 2021 (DC02)

		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=9)	0,02	0,056	0,00	0,0	0,2	35,7	9	-0,69	0,880	-0,33	-2,3	0,0	35,7
	Pre-cycle 49 (n=8)	0,02	0,059	0,00	0,0	0,2	42,9	8	-0,73	0,930	-0,25	-2,3	0,0	42,9
	Pre-cycle 61 (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.

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Table 2.3.2.1.5 PII parent-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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=9)	0,96	0,763	0,67	0,0	2,0	35,7	9	-0,63	1,095	-0,33	-2,8	0,7	35,7
	Pre-cycle 49 (n=7)	0,69	0,915	0,00	0,0	2,0	50,0	7	-0,52	1,317	-1,00	-1,8	1,8	50,0

[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.

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1.6.1.2 Subgruppenanalyyse zum PII: Responderanalyse – Selbstberichtet

Table 2.3.3.1.1 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: 31 March 2021 (DC02)

			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=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 49 (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 61 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	2	NC	NC
	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.

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Table 2.3.3.1.2 PII self-reported pain interference score categories of change over time - percentage of patients with Deterioration by >= 0.9 points - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	14	73,7	48,8, 90,9
		Deterioration	5	26,3	9,1, 51,2
	Pre-cycle 5 (N=19)	Categories of change [d]			
		No deterioration	17	89,5	66,9, 98,7
		Deterioration	2	10,5	1,3, 33,1
	Pre-cycle 9 (N=19)	Categories of change [d]			
		No deterioration	18	94,7	74,0, 99,9
		Deterioration	1	5,3	0,1, 26,0
	Pre-cycle 13 (N=18)	Categories of change [d]			
		No deterioration	18	100	81,5, 100
		Deterioration	0	0	0, 18,5
	Pre-cycle 25 (N=14)	Categories of change [d]			
		No deterioration	14	100	76,8, 100
		Deterioration	0	0	0, 23,2
	Pre-cycle 37 (N=12)	Categories of change [d]			
		No deterioration	12	100	73,5, 100
		Deterioration	0	0	0, 26,5
	Pre-cycle 49 (N=12)	Categories of change [d]			
		No deterioration	12	100	73,5, 100
		Deterioration	0	0	0, 26,5
	Pre-cycle 61 (N=2)	Categories of change [d]			
		No deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Overall (N=19)	Categories of change [d]			
		No deterioration	14	73,7	48,8, 90,9
		Deterioration	5	26,3	9,1, 51,2

[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] Deterioration/no Deterioration are defined using a threshold of 0.9 for Total score. NC - not calculated.

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Table 2.3.3.2.1 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: 31 March 2021 (DC02)

			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
	Pre-cycle 37 (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 49 (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=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.

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Table 2.3.3.2.2 PII self-reported pain interference score categories of change over time - percentage of patients with Deterioration by >= 0.9 points - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	12	100	73,5, 100
		Deterioration	0	0	0, 26,5
	Pre-cycle 5 (N=12)	Categories of change [d]			
		No deterioration	12	100	73,5, 100
		Deterioration	0	0	0, 26,5
	Pre-cycle 9 (N=12)	Categories of change [d]			
		No deterioration	12	100	73,5, 100
		Deterioration	0	0	0, 26,5
	Pre-cycle 13 (N=11)	Categories of change [d]			
		No deterioration	11	100	71,5, 100
		Deterioration	0	0	0, 28,5
	Pre-cycle 25 (N=9)	Categories of change [d]			
		No deterioration	9	100	66,4, 100
		Deterioration	0	0	0, 33,6
	Pre-cycle 37 (N=9)	Categories of change [d]			
		No deterioration	9	100	66,4, 100
		Deterioration	0	0	0, 33,6
	Pre-cycle 49 (N=6)	Categories of change [d]			
		No deterioration	6	100	54,1, 100
		Deterioration	0	0	0, 45,9
	Overall (N=12)	Categories of change [d]			
		No deterioration	12	100	73,5, 100
		Deterioration	0	0	0, 26,5

[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] Deterioration/no Deterioration are defined using a threshold of 0.9 for Total score. NC - not calculated.

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Table 2.3.3.3.1 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: 31 March 2021 (DC02)

			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=6)	Categories of change [d]			
		Improvement	1	16,7	0,4, 64,1
		No improvement	5	83,3	35,9, 99,6
	Pre-cycle 49 (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 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	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.

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Table 2.3.3.3.2 PII self-reported pain interference score categories of change over time - percentage of patients with Deterioration by >= 0.9 points - PN status at enrollment = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	7	63,6	30,8, 89,1
		Deterioration	4	36,4	10,9, 69,2
	Pre-cycle 5 (N=11)	Categories of change [d]			
		No deterioration	10	90,9	58,7, 99,8
		Deterioration	1	9,1	0,2, 41,3
	Pre-cycle 9 (N=11)	Categories of change [d]			
		No deterioration	11	100	71,5, 100
		Deterioration	0	0	0, 28,5
	Pre-cycle 13 (N=10)	Categories of change [d]			
		No deterioration	10	100	69,2, 100
		Deterioration	0	0	0, 30,8
	Pre-cycle 25 (N=6)	Categories of change [d]			
		No deterioration	6	100	54,1, 100
		Deterioration	0	0	0, 45,9
	Pre-cycle 37 (N=6)	Categories of change [d]			
		No deterioration	6	100	54,1, 100
		Deterioration	0	0	0, 45,9
	Pre-cycle 49 (N=6)	Categories of change [d]			
		No deterioration	6	100	54,1, 100
		Deterioration	0	0	0, 45,9
	Pre-cycle 61 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (N=11)	Categories of change [d]			
		No deterioration	7	63,6	30,8, 89,1
		Deterioration	4	36,4	10,9, 69,2

[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] Deterioration/no Deterioration are defined using a threshold of 0.9 for Total score. NC - not calculated.

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Table 2.3.3.4.1 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: 31 March 2021 (DC02)

			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=8)	Categories of change [d]			
		Improvement	3	37,5	8,5, 75,5
		No improvement	5	62,5	24,5, 91,5
	Pre-cycle 49 (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 61 (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.

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Table 2.3.3.4.2 PII self-reported pain interference score categories of change over time - percentage of patients with Deterioration by >= 0.9 points - PN status at enrollment = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	9	90,0	55,5, 99,7
		Deterioration	1	10,0	0,3, 44,5
	Pre-cycle 5 (N=10)	Categories of change [d]			
		No deterioration	9	90,0	55,5, 99,7
		Deterioration	1	10,0	0,3, 44,5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		No deterioration	9	90,0	55,5, 99,7
		Deterioration	1	10,0	0,3, 44,5
	Pre-cycle 13 (N=9)	Categories of change [d]			
		No deterioration	9	100	66,4, 100
		Deterioration	0	0	0, 33,6
	Pre-cycle 25 (N=9)	Categories of change [d]			
		No deterioration	9	100	66,4, 100
		Deterioration	0	0	0, 33,6
	Pre-cycle 37 (N=8)	Categories of change [d]			
		No deterioration	8	100	63,1, 100
		Deterioration	0	0	0, 36,9
	Pre-cycle 49 (N=8)	Categories of change [d]			
		No deterioration	8	100	63,1, 100
		Deterioration	0	0	0, 36,9
	Pre-cycle 61 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (N=10)	Categories of change [d]			
		No deterioration	9	90,0	55,5, 99,7
		Deterioration	1	10,0	0,3, 44,5

[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] Deterioration/no Deterioration are defined using a threshold of 0.9 for Total score. NC - not calculated.

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Table 2.3.3.5.1 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: 31 March 2021 (DC02)

			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
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	4	57,1	18,4, 90,1
		No improvement	3	42,9	9,9, 81,6
	Pre-cycle 49 (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=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.

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Table 2.3.3.5.2 PII self-reported pain interference score categories of change over time - percentage of patients with Deterioration by >= 0.9 points - PN status at enrollment = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	Selumetinib 25 mg/m² BID (N=12) [a] n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		No deterioration	10	100	69,2, 100
		Deterioration	0	0	0, 30,8
	Pre-cycle 5 (N=10)	Categories of change [d]			
		No deterioration	10	100	69,2, 100
		Deterioration	0	0	0, 30,8
	Pre-cycle 9 (N=10)	Categories of change [d]			
		No deterioration	10	100	69,2, 100
		Deterioration	0	0	0, 30,8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		No deterioration	10	100	69,2, 100
		Deterioration	0	0	0, 30,8
	Pre-cycle 25 (N=8)	Categories of change [d]			
		No deterioration	8	100	63,1, 100
		Deterioration	0	0	0, 36,9
	Pre-cycle 37 (N=7)	Categories of change [d]			
		No deterioration	7	100	59,0, 100
		Deterioration	0	0	0, 41,0
	Pre-cycle 49 (N=4)	Categories of change [d]			
		No deterioration	4	100	39,8, 100
		Deterioration	0	0	0, 60,2
	Overall (N=10)	Categories of change [d]			
		No deterioration	10	100	69,2, 100
		Deterioration	0	0	0, 30,8

[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] Deterioration/no Deterioration are defined using a threshold of 0.9 for Total score. NC - not calculated.

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1.6.1.3 Subgruppenanalyyse zum PII: Responderanalyse –Elternberichtet

Table 2.3.4.1.1 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: 31 March 2021 (DC02)

			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=19)	Categories of change [d]			
		Improvement	9	47,4	24,4, 71,1
		No improvement	10	52,6	28,9, 75,6
	Pre-cycle 37 (N=16)	Categories of change [d]			
		Improvement	7	43,8	19,8, 70,1
		No improvement	9	56,3	29,9, 80,2
	Pre-cycle 49 (N=16)	Categories of change [d]			
		Improvement	8	50,0	24,7, 75,3
		No improvement	8	50,0	24,7, 75,3
	Pre-cycle 61 (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=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.

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Table 2.3.4.1.2 PII parent-reported pain interference score categories of change over time - percentage of patients with Deterioration by >= 0.9 points - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	24	92,3	74,9, 99,1
		Deterioration	2	7,7	0,9, 25,1
	Pre-cycle 5 (N=25)	Categories of change [d]			
		No deterioration	22	88,0	68,8, 97,5
		Deterioration	3	12,0	2,5, 31,2
	Pre-cycle 9 (N=26)	Categories of change [d]			
		No deterioration	22	84,6	65,1, 95,6
		Deterioration	4	15,4	4,4, 34,9
	Pre-cycle 13 (N=25)	Categories of change [d]			
		No deterioration	22	88,0	68,8, 97,5
		Deterioration	3	12,0	2,5, 31,2
	Pre-cycle 25 (N=19)	Categories of change [d]			
		No deterioration	19	100	82,4, 100
		Deterioration	0	0	0, 17,6
	Pre-cycle 37 (N=16)	Categories of change [d]			
		No deterioration	16	100	79,4, 100
		Deterioration	0	0	0, 20,6
	Pre-cycle 49 (N=16)	Categories of change [d]			
		No deterioration	16	100	79,4, 100
		Deterioration	0	0	0, 20,6
	Pre-cycle 61 (N=3)	Categories of change [d]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8
	Overall (N=26)	Categories of change [d]			
		No deterioration	20	76,9	56,4, 91,0
		Deterioration	6	23,1	9,0, 43,6

[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] Deterioration/no Deterioration are defined using a threshold of 0.9 for Total score. NC - not calculated.

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Table 2.3.4.2.1 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: 31 March 2021 (DC02)

Parameter	Time point	Response category	Selumetinib 25 mg/m² BID (N=20) [a] 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=12)	Categories of change [d]			
		Improvement	4	33,3	9,9, 65,1
		No improvement	8	66,7	34,9, 90,1
	Pre-cycle 49 (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=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.

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Table 2.3.4.2.2 PII parent-reported pain interference score categories of change over time - percentage of patients with Deterioration by >= 0.9 points - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	16	84,2	60,4, 96,6
		Deterioration	3	15,8	3,4, 39,6
	Pre-cycle 5 (N=18)	Categories of change [d]			
		No deterioration	18	100	81,5, 100
		Deterioration	0	0	0, 18,5
	Pre-cycle 9 (N=19)	Categories of change [d]			
		No deterioration	17	89,5	66,9, 98,7
		Deterioration	2	10,5	1,3, 33,1
	Pre-cycle 13 (N=17)	Categories of change [d]			
		No deterioration	16	94,1	71,3, 99,9
		Deterioration	1	5,9	0,1, 28,7
	Pre-cycle 25 (N=15)	Categories of change [d]			
		No deterioration	12	80,0	51,9, 95,7
		Deterioration	3	20,0	4,3, 48,1
	Pre-cycle 37 (N=12)	Categories of change [d]			
		No deterioration	12	100	73,5, 100
		Deterioration	0	0	0, 26,5
	Pre-cycle 49 (N=8)	Categories of change [d]			
		No deterioration	7	87,5	47,3, 99,7
		Deterioration	1	12,5	0,3, 52,7
	Overall (N=19)	Categories of change [d]			
		No deterioration	16	84,2	60,4, 96,6
		Deterioration	3	15,8	3,4, 39,6

[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] Deterioration/no Deterioration are defined using a threshold of 0.9 for Total score. NC - not calculated.

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Table 2.3.4.3.1 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: 31 March 2021 (DC02)

			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=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=10)	Categories of change [d]			
		Improvement	5	50,0	18,7, 81,3
		No improvement	5	50,0	18,7, 81,3
	Pre-cycle 49 (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 61 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
	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.

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Table 2.3.4.3.2 PII parent-reported pain interference score categories of change over time - percentage of patients with Deterioration by >= 0.9 points - PN status at enrollment = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	18	94,7	74,0, 99,9
		Deterioration	1	5,3	0,1, 26,0
	Pre-cycle 5 (N=18)	Categories of change [d]			
		No deterioration	17	94,4	72,7, 99,9
		Deterioration	1	5,6	0,1, 27,3
	Pre-cycle 9 (N=19)	Categories of change [d]			
		No deterioration	17	89,5	66,9, 98,7
		Deterioration	2	10,5	1,3, 33,1
	Pre-cycle 13 (N=18)	Categories of change [d]			
		No deterioration	16	88,9	65,3, 98,6
		Deterioration	2	11,1	1,4, 34,7
	Pre-cycle 25 (N=13)	Categories of change [d]			
		No deterioration	12	92,3	64,0, 99,8
		Deterioration	1	7,7	0,2, 36,0
	Pre-cycle 37 (N=10)	Categories of change [d]			
		No deterioration	10	100	69,2, 100
		Deterioration	0	0	0, 30,8
	Pre-cycle 49 (N=9)	Categories of change [d]			
		No deterioration	9	100	66,4, 100
		Deterioration	0	0	0, 33,6
	Pre-cycle 61 (N=2)	Categories of change [d]			
		No deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Overall (N=19)	Categories of change [d]			
		No deterioration	15	78,9	54,4, 93,9
		Deterioration	4	21,1	6,1, 45,6

[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] Deterioration/no Deterioration are defined using a threshold of 0.9 for Total score. NC - not calculated.

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Table 2.3.4.4.1 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: 31 March 2021 (DC02)

			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=9)	Categories of change [d]			
		Improvement	3	33,3	7,5, 70,1
		No improvement	6	66,7	29,9, 92,5
	Pre-cycle 49 (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 61 (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.

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Table 2.3.4.4.2 PII parent-reported pain interference score categories of change over time - percentage of patients with Deterioration by >= 0.9 points - PN status at enrollment = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	12	92,3	64,0, 99,8
		Deterioration	1	7,7	0,2, 36,0
	Pre-cycle 5 (N=13)	Categories of change [d]			
		No deterioration	12	92,3	64,0, 99,8
		Deterioration	1	7,7	0,2, 36,0
	Pre-cycle 9 (N=13)	Categories of change [d]			
		No deterioration	11	84,6	54,6, 98,1
		Deterioration	2	15,4	1,9, 45,4
	Pre-cycle 13 (N=11)	Categories of change [d]			
		No deterioration	11	100	71,5, 100
		Deterioration	0	0	0, 28,5
	Pre-cycle 25 (N=11)	Categories of change [d]			
		No deterioration	11	100	71,5, 100
		Deterioration	0	0	0, 28,5
	Pre-cycle 37 (N=9)	Categories of change [d]			
		No deterioration	9	100	66,4, 100
		Deterioration	0	0	0, 33,6
	Pre-cycle 49 (N=8)	Categories of change [d]			
		No deterioration	8	100	63,1, 100
		Deterioration	0	0	0, 36,9
	Pre-cycle 61 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (N=13)	Categories of change [d]			
		No deterioration	11	84,6	54,6, 98,1
		Deterioration	2	15,4	1,9, 45,4

[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] Deterioration/no Deterioration are defined using a threshold of 0.9 for Total score. NC - not calculated.

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Table 2.3.4.5.1 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: 31 March 2021 (DC02)

			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
	Pre-cycle 37 (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 49 (N=7)	Categories of change [d]			
		Improvement	4	57,1	18,4, 90,1
		No improvement	3	42,9	9,9, 81,6
	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.

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Table 2.3.4.5.2 PII parent-reported pain interference score categories of change over time - percentage of patients with Deterioration by >= 0.9 points - PN status at enrollment = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	10	76,9	46,2, 95,0
		Deterioration	3	23,1	5,0, 53,8
	Pre-cycle 5 (N=12)	Categories of change [d]			
		No deterioration	11	91,7	61,5, 99,8
		Deterioration	1	8,3	0,2, 38,5
	Pre-cycle 9 (N=13)	Categories of change [d]			
		No deterioration	11	84,6	54,6, 98,1
		Deterioration	2	15,4	1,9, 45,4
	Pre-cycle 13 (N=13)	Categories of change [d]			
		No deterioration	11	84,6	54,6, 98,1
		Deterioration	2	15,4	1,9, 45,4
	Pre-cycle 25 (N=10)	Categories of change [d]			
		No deterioration	8	80,0	44,4, 97,5
		Deterioration	2	20,0	2,5, 55,6
	Pre-cycle 37 (N=9)	Categories of change [d]			
		No deterioration	9	100	66,4, 100
		Deterioration	0	0	0, 33,6
	Pre-cycle 49 (N=7)	Categories of change [d]			
		No deterioration	6	85,7	42,1, 99,6
		Deterioration	1	14,3	0,4, 57,9
	Overall (N=13)	Categories of change [d]			
		No deterioration	10	76,9	46,2, 95,0
		Deterioration	3	23,1	5,0, 53,8

[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] Deterioration/no Deterioration are defined using a threshold of 0.9 for Total score. NC - not calculated.

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1.7 Endpunkt Motorfunktion: Patient-reported Outcome Measurement Information System (PROMIS)

1.7.1 Rücklaufquoten für den PROMIS

1.7.1.1 Rücklaufquoten für den PROMIS – Elternberichtet (5–18 Jahre)

Tabelle 1: Rücklaufquoten für den PROMIS – Elternberichtet (5–18 Jahre)

Studie	Selumetinib 25 mg/m² BID		
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Alle Patienten im Alter von 5–18 Jahren (FAS) N = 33**		
	Erwartete Antworten, N*	**Alle Fragen beantwortet, n (%)**	**Mindestens eine Frage beantwortet, n (%)**
PROMIS – elternberichtet – Itembank Mobilität			
Baseline	33	25 (75,8)	32 (97,0)
Zyklus 3	32	29 (90,6)	31 (96,9)
Zyklus 5	32	29 (90,6)	31 (96,9)
Zyklus 9	29	28 (96,6)	29 (100,0)
Zyklus 13	29	29 (100,0)	29 (100,0)
Zyklus 25	21	20 (95,2)	20 (95,2)
Zyklus 37	16	13 (81,3)	15 (93,8)
Zyklus 49	13	10 (76,9)	12 (92,3)
PROMIS – elternberichtet – Itembank obere Extremitäten			
Baseline	33	27 (81,8)	31 (93,9)
Zyklus 3	32	29 (90,6)	31 (96,9)
Zyklus 5	32	30 (93,8)	31 (96,9)
Zyklus 9	29	29 (100,0)	29 (100,0)
Zyklus 13	29	29 (100,0)	29 (100,0)
Zyklus 25	21	20 (95,2)	20 (95,2)
Zyklus 37	16	15 (93,8)	15 (93,8)
Zyklus 49	13	11 (84,6)	11 (84,6)

BID: Zweimal täglich; FAS: Full Analysis Set; n: Patienten mit Antwort; N*: Patienten mit erwarteter Antwort; PROMIS: Patient-Reported Outcomes Measurement Information System
Quelle: AstraZeneca. Studie SPRINT - Phase II: CSR all tables. Stand: 25.03.2022. 2022.

1.7.1.2 Rücklaufquoten für den PROMIS – Elternberichtet (8–18 Jahre)

Tabelle 2: Rücklaufquoten für den PROMIS – Elternberichtet (8–18 Jahre)

Studie	Selumetinib 25 mg/m² BID		
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	Alle Patienten im Alter von 8–18 Jahren (FAS) N = 24		
	Erwartete Antworten, N*	Alle Fragen beantwortet, n (%)	Mindestens eine Frage beantwortet, n (%)
PROMIS – elternberichtet – Itembank Mobilität			
Baseline	24	18 (75,0)	24 (100,0)
Zyklus 3	23	20 (87,0)	22 (95,7)
Zyklus 5	23	21 (91,3)	23 (100,0)
Zyklus 9	21	20 (95,2)	21 (100,0)
Zyklus 13	21	21 (100,0)	21 (100,0)
Zyklus 25	14	14 (100,0)	14 (100,0)
Zyklus 37	11	10 (90,9)	11 (100,0)
Zyklus 49	10	7 (70,0)	9 (90,0)
PROMIS – elternberichtet – Itembank obere Extremitäten			
Baseline	24	20 (83,3)	23 (95,8)
Zyklus 3	23	20 (87,0)	22 (95,7)
Zyklus 5	23	22 (95,7)	23 (100,0)
Zyklus 9	21	21 (100,0)	21 (100,0)
Zyklus 13	21	21 (100,0)	21 (100,0)
Zyklus 25	14	14 (100,0)	14 (100,0)
Zyklus 37	11	11 (100,0)	11 (100,0)
Zyklus 49	10	8 (80,0)	8 (80,0)

BID: Zweimal täglich; FAS: Full Analysis Set; n: Patienten mit Antwort; N*: Patienten mit erwarteter Antwort; PROMIS: Patient-Reported Outcomes Measurement Information System
Quelle: AstraZeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 1. Stand: 04.2023. 2023.

1.7.2 PROMIS Veränderung gegenüber Baseline

1.7.2.1 PROMIS Veränderung gegenüber Baseline – Elternberichtet (5–18 Jahre)

Tabelle 3: Ergebnisse für PROMIS Veränderung gegenüber Baseline – Elternberichtet (5–18 Jahre)

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Elternberichtet 5–18 Jahre mit PN-assoziierter Morbidität der Motorfunktion N = 33**	
	Absoluter Wert N* Mittelwert ± s Median Min–Max	**Veränderung gegenüber Baseline** N* Mittelwert ± s Median Min–Max
Itembank Mobilität – T-Score		
Baseline	32 37,43 ± 7,323 37,85 19,8–56,5	–
Zyklus 3	31 38,75 ± 6,116 40,10 27,5–56,5	30 2,04 ± 2,944 1,75 -3,9–10,0
Zyklus 5	31 39,31 ± 8,087 39,60 17,5–56,5	30 1,75 ± 5,790 1,70 -9,7–16,0
Zyklus 9	32 39,86 ± 7,416 40,25 17,5–56,5	31 2,36 ± 5,754 2,60 -9,7–18,5
Zyklus 13	29 41,14 ± 8,958 40,10 21,1–56,5	28 3,03 ± 4,358 2,25 -3,4–15,4
Zyklus 25	20 43,02 ± 7,442 41,50 28,0–56,5	19 4,51 ± 5,225 3,20 -3,7–17,9
Zyklus 37	16 43,11 ± 7,891 41,55 31,8–56,5	15 3,82 ± 3,588 4,40 -2,4–12,2
Zyklus 49	12 42,47 ± 8,571 41,85 28,4–56,5	11 4,39 ± 4,485 2,70 0,0–12,2
Itembank Mobilität – Rohwert		
Baseline	32 22,5 ± 6,71 22,5 3–32	–
Zyklus 3	31 24,3 ± 5,76 26,0 10–32	30 2,2 ± 3,13 2,5 -3–10
Zyklus 5	31 24,4 ± 7,22 26,0 0–32	30 1,8 ± 4,21 2,0 -7–9
Zyklus 9	32 25,2 ± 6,50 26,5 1–32	31 2,7 ± 4,03 3,0 -8–11
Zyklus 13	29 25,2 ± 6,52 26,0 4–32	28 2,6 ± 3,19 2,0 -3–11

Studie	Selumetinib 25 mg/m² BID	
SPRINT **Phase II, Stratum 1** **Datenschnitt: 31. März 2021**	**Elternberichtet** **5–18 Jahre mit PN-assoziierter Morbidität der Motorfunktion** **N = 33**	
	Absoluter Wert N* Mittelwert ± s Median Min–Max	**Veränderung gegenüber Baseline** N* Mittelwert ± s Median Min–Max
Zyklus 25	20 27,3 ± 5,33 29,0 11–32	19 3,4 ± 3,59 3,0 -5–10
Zyklus 37	16 26,8 ± 4,65 28,0 17–32	15 3,0 ± 3,46 4,0 -4–7
Zyklus 49	12 26,1 ± 6,37 28,0 11–32	11 2,9 ± 2,63 2,0 0–9
Itembank obere Extremitäten – T-Score		
Baseline	31 38,15 ± 12,355 36,90 14,0–54,8	–
Zyklus 3	31 37,49 ± 11,597 35,10 16,6–54,8	30 -0,24 ± 6,968 0,00 -20,9–15,5
Zyklus 5	31 38,55 ± 12,000 35,10 16,6–54,8	29 0,79 ± 4,974 0,00 -13,5–10,5
Zyklus 9	32 38,35 ± 11,607 36,90 15,8–54,8	30 -0,34 ± 7,092 0,10 -25,3–8,9
Zyklus 13	29 40,58 ± 12,531 38,30 14,0–54,8	27 1,85 ± 6,545 0,90 -16,7–17,9
Zyklus 25	20 42,26 ± 11,831 41,25 18,0–54,8	18 4,49 ± 5,433 3,90 -3,3–17,9
Zyklus 37	16 42,95 ± 12,082 42,10 18,8–54,8	14 5,51 ± 6,448 5,40 -6,0–17,9
Zyklus 49	11 39,14 ± 11,621 35,90 18,7–54,8	10 5,17 ± 6,317 5,25 -8,4–15,5
Itembank obere Extremitäten – Rohwert		
Baseline	31 23,7 ± 9,27 28,0 0–32	–
Zyklus 3	31 23,5 ± 8,86 27,0 1–32	30 -0,1 ± 3,67 0,0 -9–8
Zyklus 5	31 24,5 ± 8,89 28,0 1–32	29 0,9 ± 2,78 0,0 -3–11
Zyklus 9	32 24,5 ± 8,58 28,0 1–32	30 0,6 ± 5,45 0,5 -17–10

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT **Phase II, Stratum 1** **Datenschnitt: 31. März 2021**	**Elternberichtet** **5–18 Jahre mit PN-assoziierter Morbidität der Motorfunktion** **N = 33**	
	Absoluter Wert	**Veränderung gegenüber Baseline**
	N* Mittelwert ± s Median Min–Max	N* Mittelwert ± s Median Min–Max
Zyklus 13	29 25,9 ± 8,57 29,0 0–32	27 1,7 ± 3,74 0,0 -4–10
Zyklus 25	20 27,2 ± 7,28 30,0 2–32	18 2,7 ± 3,36 1,5 0–10
Zyklus 37	16 27,5 ± 7,30 30,5 4–32	14 3,8 ± 4,17 3,5 -1–13
Zyklus 49	11 25,9 ± 8,30 28,0 3–32	10 4,1 ± 4,82 3,0 -3–12

BID: Zweimal täglich; FAS: Full Analysis Set; Max: Maximum; Min: Minimum; PN: Plexiformes Neurofibrom; PROMIS: Patient-Reported Outcomes Measurement Information System; s: Standardabweichung
N*: Anzahl der in die Analyse mit eingeschlossenen Patienten. Patienten mit erhobenen Werten bei der jeweiligen Visite gingen in die Analyse mit ein
Quelle: AstraZeneca. Studie SPRINT - Phase II: CSR all tables. Stand: 25.03.2022. 2022.

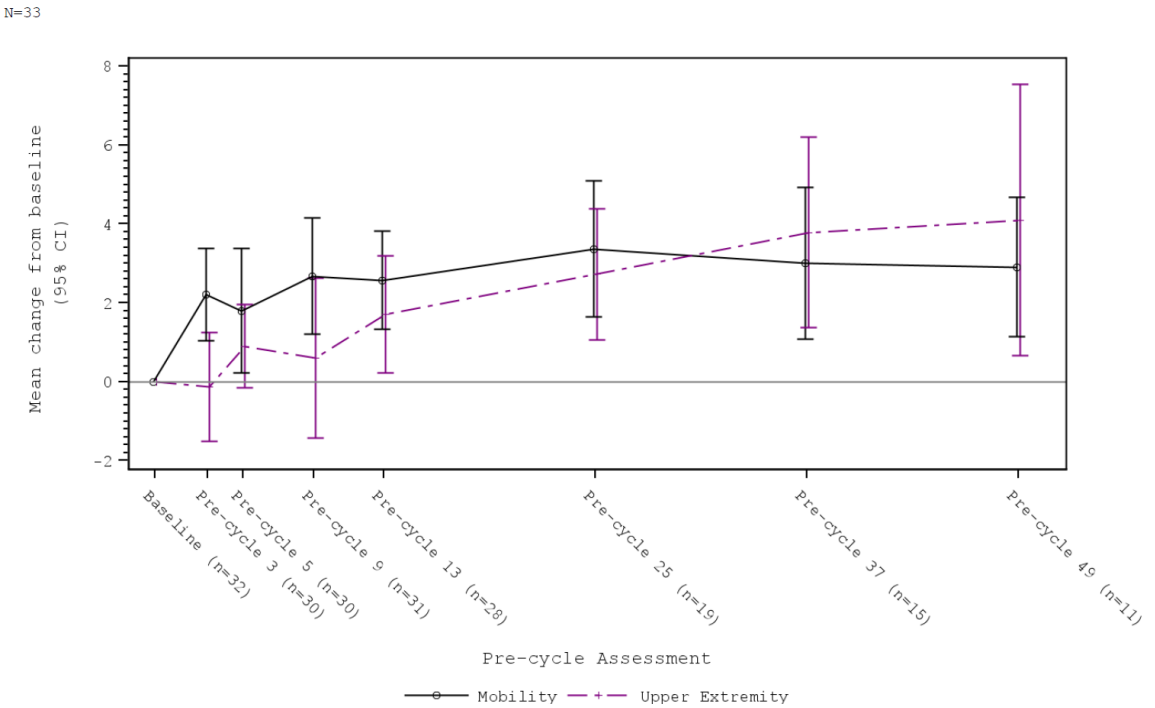

Abbildung 1: Elternberichteter (5–18 Jahre) PROMIS – Rohwert – Mittlere Veränderung gegenüber Baseline
Quelle: AstraZeneca. Studie SPRINT - Phase II: CSR all figures. Stand: 25.03.2022. 2022.

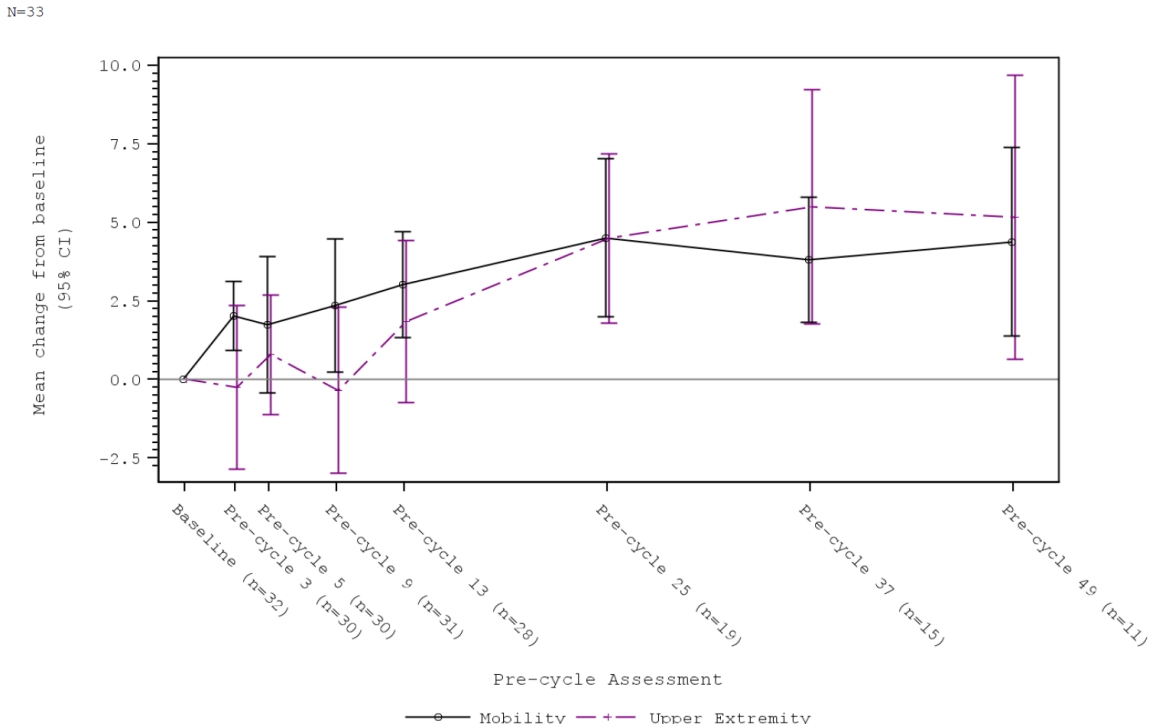

Abbildung 2: Elternberichteter (5–18 Jahre) PROMIS – T-Score – Mittlere Veränderung gegenüber Baseline
Quelle: AstraZeneca. Studie SPRINT - Phase II: CSR all figures. Stand: 25.03.2022. 2022.

1.7.2.2 PROMIS Veränderung gegenüber Baseline – Elternberichtet (8–18 Jahre)

Tabelle 4: Ergebnisse für PROMIS Veränderung gegenüber Baseline – Elternberichtet (8–18 Jahre)

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Elternberichtet 8–18 Jahre mit PN-assoziierter Morbidität der Motorfunktion N = 24**	
	Absoluter Wert N* Mittelwert ± s Median Min–Max	**Veränderung gegenüber Baseline** N* Mittelwert ± s Median Min–Max
Itembank Mobilität – T-Score		
Baseline	24 37,86 ± 7,812 37,85 19,8–56,5	–
Zyklus 3	22 38,87 ± 6,401 39,50 27,5–56,5	22 2,05 ± 2,881 2,20 -3,9–7,7
Zyklus 5	23 38,25 ± 7,689 38,80 17,5–56,5	23 0,58 ± 5,210 0,00 -9,7–15,4
Zyklus 9	23 39,23 ± 7,404 39,60 17,5–56,5	23 1,56 ± 5,660 2,60 -9,7–18,5
Zyklus 13	21 40,51 ± 9,503 38,30 21,1–56,5	21 2,72 ± 4,516 2,20 -3,4–15,4
Zyklus 25	14 44,80 ± 7,286 42,75 32,0–56,5	14 5,61 ± 5,125 3,45 0,0–17,9
Zyklus 37	12 43,64 ± 7,235 41,95 31,8–56,5	12 4,51 ± 3,391 4,45 0,0–12,2
Zyklus 49	9 44,41 ± 8,436 44,10 31,1–56,5	9 5,14 ± 4,651 3,50 0,0–12,2
Itembank Mobilität – Rohwert		
Baseline	24 22,7 ± 6,78 22,5 3–32	–
Zyklus 3	22 24,3 ± 5,42 25,0 10–32	22 2,3 ± 2,96 3,0 -3–8
Zyklus 5	23 23,7 ± 7,07 25,0 0–32	23 1,3 ± 4,16 1,0 -7–9
Zyklus 9	23 24,7 ± 6,85 26,0 1–32	23 2,2 ± 4,03 3,0 -8–11
Zyklus 13	21 24,5 ± 6,79 25,0 4–32	21 2,2 ± 2,80 2,0 -3–8

Studie	Selumetinib 25 mg/m² BID	
SPRINT **Phase II, Stratum 1** **Datenschnitt: 31. März 2021**	**Elternberichtet** **8–18 Jahre mit PN-assoziierter Morbidität der Motorfunktion** **N = 24**	
	Absoluter Wert N* Mittelwert ± s Median Min–Max	**Veränderung gegenüber Baseline** N* Mittelwert ± s Median Min–Max
Zyklus 25	14 28,4 ± 3,91 29,5 18–32	14 3,9 ± 2,73 3,5 0–10
Zyklus 37	12 27,4 ± 3,92 28,0 18–32	12 3,4 ± 2,97 4,0 -3–7
Zyklus 49	9 27,4 ± 4,93 29,0 17–32	9 3,3 ± 2,74 3,0 0–9
Itembank obere Extremitäten – T-Score		
Baseline	23 39,16 ± 12,291 38,20 18,2–54,8	–
Zyklus 3	22 38,05 ± 12,102 34,90 21,0–54,8	22 -0,40 ± 7,760 0,00 -20,9–15,5
Zyklus 5	23 39,37 ± 11,660 39,30 16,6–54,8	22 0,21 ± 5,026 0,00 -13,5–10,5
Zyklus 9	23 38,00 ± 11,076 36,90 15,8–54,8	22 -1,21 ± 7,812 0,00 -25,3–7,7
Zyklus 13	21 40,69 ± 11,920 38,30 14,0–54,8	20 1,91 ± 7,300 0,80 -16,7–17,9
Zyklus 25	14 45,21 ± 10,600 48,40 28,8–54,8	13 4,86 ± 5,472 3,80 0,0–17,9
Zyklus 37	12 45,32 ± 10,643 50,35 29,7–54,8	11 6,20 ±6,926 6,10 -6,0–17,9
Zyklus 49	8 41,30 ± 11,268 35,05 31,1–54,8	8 4,94 ± 7,101 5,25 -8,4–15,5
Itembank obere Extremitäten – Rohwert		
Baseline	23 24,5 ± 8,76 28,0 4–32	–
Zyklus 3	22 23,5 ± 8,56 26,0 7–32	22 -0,6 ± 3,91 0,0 -9–8
Zyklus 5	23 25,3 ± 8,09 30,0 1–32	22 0,9 ± 2,95 0,0 -3–11

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT **Phase II, Stratum 1** **Datenschnitt: 31. März 2021**	**Elternberichtet** **8–18 Jahre mit PN-assoziierter Morbidität der Motorfunktion** **N = 24**	
	Absoluter Wert N* Mittelwert ± s Median Min–Max	**Veränderung gegenüber Baseline** N* Mittelwert ± s Median Min–Max
Zyklus 9	23 24,5 ± 8,07 28,0 1–32	22 0,0 ± 5,94 0,0 -17–10
Zyklus 13	21 26,2 ± 7,72 29,0 0–32	20 1,9 ± 3,94 0,0 -4–10
Zyklus 25	14 29,0 ± 4,24 31,5 21–32	13 2,8 ± 3,87 1,0 0–10
Zyklus 37	12 29,3 ± 3,70 31,5 22–32	11 4,1 ± 4,59 3,0 -1–13
Zyklus 49	8 27,8 ± 3,81 27,0 23–32	8 4,4 ± 5,42 3,0 -3–12

BID: Zweimal täglich; FAS: Full Analysis Set; Max: Maximum; Min: Minimum; PN: Plexiformes Neurofibrom; PROMIS: Patient-Reported Outcomes Measurement Information System; s: Standardabweichung
N*: Anzahl der in die Analyse mit eingeschlossenen Patienten. Patienten mit erhobenen Werten bei der jeweiligen Visite gingen in die Analyse mit ein.
Quelle: AstraZeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 1. Stand: 04.2023. 2023.

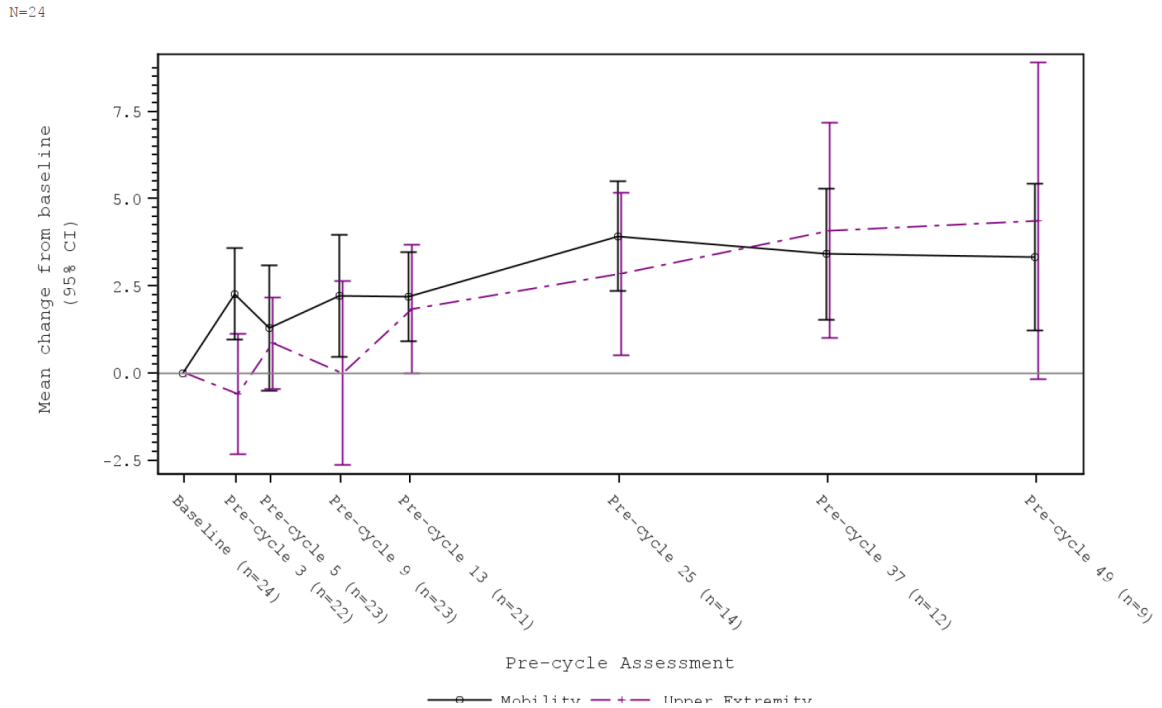

Abbildung 3: Elternberichteter (8–18 Jahre) PROMIS – Rohwert – Mittlere Veränderung gegenüber Baseline
Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 2 – 4. Stand: 17.03.2023. 2023.

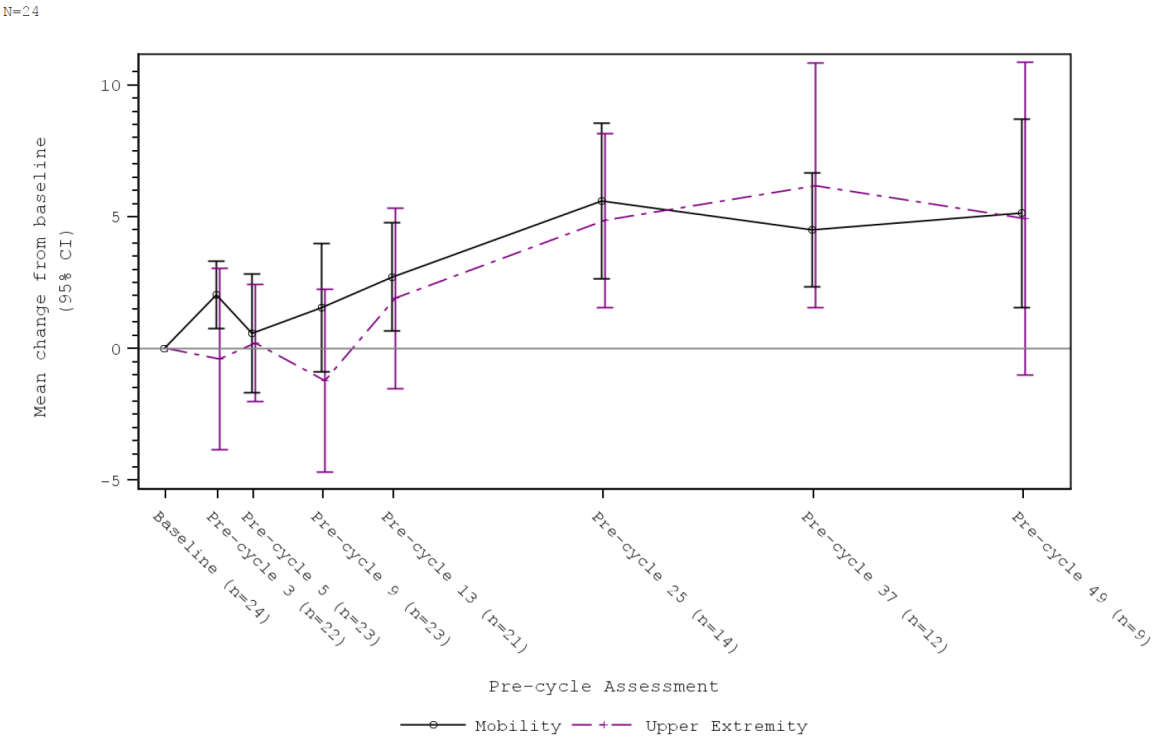

Abbildung 4: Elternberichteter (8–18 Jahre) PROMIS – T-Score – Mittlere Veränderung gegenüber Baseline
Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 2 – 4. Stand: 17.03.2023. 2023.

1.7.2.3 Subgruppenanalysen PROMIS Veränderung gegenüber Baseline

1.7.2.3.1 Subgruppenanalysen PROMIS Veränderung gegenüber Baseline – Selbstberichtet (8-18 Jahre)

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: 31 March 2021 (DC02)

		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=5)	47,80	9,494	50,00	33,2	58,5	64,3	5	2,10	9,272	0,00	-10,3	14,4	64,3
	Pre-cycle 49 (n=5)	50,84	8,765	52,30	37,6	58,5	64,3	5	5,14	9,471	1,50	-5,9	15,7	64,3
	Pre-cycle 61 (n=1)	NC	NC	NC	43,5	43,5	92,9	1	NC	NC	NC	-2,3	-2,3	92,9
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=5)	28,0	6,24	31,0	17	32	64,3	5	1,4	3,58	2,0	-4	5	64,3
	Pre-cycle 49 (n=5)	29,2	4,66	31,0	21	32	64,3	5	2,6	2,61	3,0	0	6	64,3
	Pre-cycle 61 (n=1)	NC	NC	NC	28	28	92,9	1	NC	NC	NC	1	1	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.

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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: 31 March 2021 (DC02)

		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=5)	47,06	10,882	48,80	30,9	56,7	64,3	5	8,88	8,613	10,50	0,0	18,7	64,3
	Pre-cycle 49 (n=5)	49,02	9,416	50,00	33,7	56,7	64,3	5	10,84	10,324	13,30	0,0	21,0	64,3
	Pre-cycle 61 (n=1)	NC	NC	NC	40,0	40,0	92,9	1	NC	NC	NC	13,0	13,0	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=5)	28,6	4,98	30,0	20	32	64,3	5	7,0	6,44	11,0	0	13	64,3
	Pre-cycle 49 (n=5)	29,6	4,28	31,0	22	32	64,3	5	8,0	7,38	12,0	0	15	64,3
	Pre-cycle 61 (n=1)	NC	NC	NC	28	28	92,9	1	NC	NC	NC	12	12	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	50,10	6,056	47,40	43,5	58,5	30,0	7	0,99	4,280	0,00	-3,8	8,5	30,0
	Pre-cycle 49 (n=5)	47,76	13,064	50,00	26,8	58,5	50,0	5	-3,32	13,038	0,00	-25,5	8,5	50,0
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
	Pre-cycle 37 (n=7)	30,1	1,57	30,0	28	32	30,0	7	0,3	1,60	0,0	-2	3	30,0
	Pre-cycle 49 (n=5)	27,0	9,03	31,0	11	32	50,0	5	-3,8	9,09	0,0	-20	1	50,0

[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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	52,50	7,437	56,70	38,6	56,7	30,0	6	4,55	12,831	8,40	-18,1	20,2	40,0
	Pre-cycle 49 (n=5)	51,88	6,621	56,70	43,9	56,7	50,0	4	1,00	10,016	4,20	-12,8	8,4	60,0
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
	Pre-cycle 37 (n=7)	31,0	1,91	32,0	27	32	30,0	6	0,8	3,82	1,0	-5	7	40,0
	Pre-cycle 49 (n=5)	31,2	1,10	32,0	30	32	50,0	4	0,0	1,41	0,5	-2	1	60,0

[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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 49 (n=1)	NC	NC	NC	47,3	47,3	83,3	1	NC	NC	NC	1,5	1,5	83,3
	Pre-cycle 61 (n=1)	NC	NC	NC	43,5	43,5	83,3	1	NC	NC	NC	-2,3	-2,3	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
	Pre-cycle 49 (n=1)	NC	NC	NC	30	30	83,3	1	NC	NC	NC	3	3	83,3
	Pre-cycle 61 (n=1)	NC	NC	NC	28	28	83,3	1	NC	NC	NC	1	1	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 49 (n=1)	NC	NC	NC	48,0	48,0	83,3	1	NC	NC	NC	21,0	21,0	83,3
	Pre-cycle 61 (n=1)	NC	NC	NC	40,0	40,0	83,3	1	NC	NC	NC	13,0	13,0	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
	Pre-cycle 49 (n=1)	NC	NC	NC	31	31	83,3	1	NC	NC	NC	15	15	83,3
	Pre-cycle 61 (n=1)	NC	NC	NC	28	28	83,3	1	NC	NC	NC	12	12	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=6)	52,13	5,740	51,15	43,5	58,5	25,0	6	2,58	6,912	0,00	-3,8	14,4	25,0
	Pre-cycle 49 (n=6)	50,77	12,302	55,40	26,8	58,5	25,0	6	1,22	14,849	1,35	-25,5	15,7	25,0
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
	Pre-cycle 37 (n=6)	30,8	1,47	31,0	28	32	25,0	6	1,2	2,71	0,0	-2	5	25,0
	Pre-cycle 49 (n=6)	28,2	8,42	31,5	11	32	25,0	6	-1,5	9,38	0,5	-20	6	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=6)	53,50	5,073	56,70	45,4	56,7	25,0	5	5,42	8,267	0,00	0,0	18,7	37,5
	Pre-cycle 49 (n=6)	53,70	4,870	56,70	45,4	56,7	25,0	5	5,66	8,752	0,00	0,0	19,9	37,5
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
	Pre-cycle 37 (n=6)	31,3	1,03	32,0	30	32	25,0	5	2,4	4,83	0,0	0	11	37,5
	Pre-cycle 49 (n=6)	31,5	0,84	32,0	30	32	25,0	5	2,6	5,27	0,0	0	12	37,5

[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.

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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: 31 March 2021 (DC02)

		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=5)	46,38	8,977	47,00	33,2	58,5	50,0	5	0,54	7,100	1,50	-10,3	8,5	50,0
	Pre-cycle 49 (n=3)	47,03	10,597	45,00	37,6	58,5	70,0	3	0,10	7,494	-2,30	-5,9	8,5	70,0
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=5)	27,4	5,94	29,0	17	32	50,0	5	0,0	2,65	1,0	-4	3	50,0
	Pre-cycle 49 (n=3)	27,3	5,69	29,0	21	32	70,0	3	0,0	1,00	0,0	-1	1	70,0

[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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=5)	47,92	12,327	56,70	30,9	56,7	50,0	5	5,88	14,267	8,40	-18,1	20,2	50,0
	Pre-cycle 49 (n=3)	44,77	11,524	43,90	33,7	56,7	70,0	3	2,97	13,872	8,40	-12,8	13,3	70,0
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
	Pre-cycle 37 (n=5)	28,6	5,27	32,0	20	32	50,0	5	3,0	6,16	1,0	-5	11	50,0
	Pre-cycle 49 (n=3)	28,0	5,29	30,0	22	32	70,0	3	4,0	7,94	1,0	-2	13	70,0

[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.

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Table 5.3.1.1.1 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=12)	Categories of change [d]			
		Improvement	3	25.0	5.5, 57.2
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	8	66.7	34.9, 90.1
	Pre-cycle 5 (n=12)	Categories of change [d]			
		Improvement	2	16.7	2.1, 48.4
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	9	75.0	42.8, 94.5
	Pre-cycle 9 (n=12)	Categories of change [d]			
		Improvement	4	33.3	9.9, 65.1
		Deterioration	2	16.7	2.1, 48.4
		No improvement or deterioration	6	50.0	21.1, 78.9
	Pre-cycle 13 (n=11)	Categories of change [d]			
		Improvement	1	9.1	0.2, 41.3
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	9	81.8	48.2, 97.7

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.1 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	6	85.7	42.1, 99.6
	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Overall (n=12)	Categories of change [d]			
		Improvement	5	41.7	15.2, 72.3
		Deterioration	2	16.7	2.1, 48.4
		No improvement or deterioration	5	41.7	15.2, 72.3

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.1 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=12)	Categories of change [d]			
		Improvement	4	33.3	9.9, 65.1
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	7	58.3	27.7, 84.8
	Pre-cycle 5 (n=12)	Categories of change [d]			
		Improvement	2	16.7	2.1, 48.4
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	9	75.0	42.8, 94.5
	Pre-cycle 9 (n=12)	Categories of change [d]			
		Improvement	1	8.3	0.2, 38.5
		Deterioration	2	16.7	2.1, 48.4
		No improvement or deterioration	9	75.0	42.8, 94.5
	Pre-cycle 13 (n=11)	Categories of change [d]			
		Improvement	3	27.3	6.0, 61.0
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	8	72.7	39.0, 94.0

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.1 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=12) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3
	Overall (n=12)	Categories of change [d]			
		Improvement	5	41.7	15.2, 72.3
		Deterioration	4	33.3	9.9, 65.1
		No improvement or deterioration	4	33.3	9.9, 65.1

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.2 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=9)	Categories of change [d]			
		Improvement	0	0	0, 33.6
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	9	100	66.4, 100
	Pre-cycle 5 (n=10)	Categories of change [d]			
		Improvement	1	10.0	0.3, 44.5
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	9	90.0	55.5, 99.7
	Pre-cycle 9 (n=10)	Categories of change [d]			
		Improvement	0	0	0, 30.8
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	10	100	69.2, 100
	Pre-cycle 13 (n=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	8	88.9	51.8, 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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.2 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	0	0	0, 41.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	7	100	59.0, 100
	Pre-cycle 37 (n=7)	Categories of change [d]			
		Improvement	0	0	0, 41.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	7	100	59.0, 100
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	4	80.0	28.4, 99.5
	Overall (n=10)	Categories of change [d]			
		Improvement	1	10.0	0.3, 44.5
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	8	80.0	44.4, 97.5

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.2 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=9)	Categories of change [d]			
		Improvement	0	0	0, 33.6
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	9	100	66.4, 100
	Pre-cycle 5 (n=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	8	88.9	51.8, 99.7
	Pre-cycle 9 (n=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	7	77.8	40.0, 97.2
	Pre-cycle 13 (n=8)	Categories of change [d]			
		Improvement	0	0	0, 36.9
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	7	87.5	47.3, 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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.2 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	0	0	0, 45.9
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 49 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Overall (n=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	6	66.7	29.9, 92.5

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.3 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 5 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 9 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 13 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	3	60.0	14.7, 94.7

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.
NC = not calculated.

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Table 5.3.1.1.3 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.
NC = not calculated.

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Table 5.3.1.1.3 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 5 (n=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 9 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 13 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.
NC = not calculated.

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Table 5.3.1.1.3 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	2	33.3	4.3, 77.7

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.
NC = not calculated.

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Table 5.3.1.1.4 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	6	85.7	42.1, 99.6
	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	0	0	0, 36.9
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	8	100	63.1, 100
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	1	12.5	0.3, 52.7
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	6	75.0	34.9, 96.8
	Pre-cycle 13 (n=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	6	85.7	42.1, 99.6

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.4 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	6	85.7	42.1, 99.6
	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 49 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	4	66.7	22.3, 95.7
	Overall (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	4	50.0	15.7, 84.3

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.4 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 5 (n=7)	Categories of change [d]			
		Improvement	0	0	0, 41.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	6	85.7	42.1, 99.6
	Pre-cycle 9 (n=7)	Categories of change [d]			
		Improvement	0	0	0, 41.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	6	85.7	42.1, 99.6
	Pre-cycle 13 (n=6)	Categories of change [d]			
		Improvement	0	0	0, 45.9
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	6	100	54.1, 100

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.4 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Overall (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	4	57.1	18.4, 90.1

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.5 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=8)	Categories of change [d]			
		Improvement	1	12.5	0.3, 52.7
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	7	87.5	47.3, 99.7
	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	1	12.5	0.3, 52.7
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	7	87.5	47.3, 99.7
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	6	75.0	34.9, 96.8
	Pre-cycle 13 (n=8)	Categories of change [d]			
		Improvement	0	0	0, 36.9
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	8	100	63.1, 100

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.5 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	0	0	0, 45.9
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	6	100	54.1, 100
	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	5	100	47.8, 100
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Overall (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.5 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=8)	Categories of change [d]			
		Improvement	0	0	0, 36.9
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	7	87.5	47.3, 99.7
	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	0	0	0, 36.9
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	8	100	63.1, 100
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	1	12.5	0.3, 52.7
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	6	75.0	34.9, 96.8
	Pre-cycle 13 (n=8)	Categories of change [d]			
		Improvement	1	12.5	0.3, 52.7
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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Table 5.3.1.1.5 PROMIS self-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Overall (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	4	50.0	15.7, 84.3

[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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility self report - 4.8; Upper extremity self report - 4.8.

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1.7.2.3.2 Subgruppenanalysen PROMIS Veränderung gegenüber Baseline – Elternberichtet (5-7 Jahre)

Table 2.5.2.1.1 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [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=4)	38.28	7.612	40.45	27.3	44.9	20.0							
	Pre-cycle 3 (n=5)	39.56	6.519	40.70	28.9	46.8	0.0	4	0.98	0.907	0.95	0.1	1.9	20.0
	Pre-cycle 5 (n=5)	45.12	8.634	46.70	32.5	56.5	0.0	4	7.35	6.062	5.75	1.9	16.0	20.0
	Pre-cycle 9 (n=5)	43.96	8.965	44.10	31.9	56.5	0.0	4	5.00	7.768	2.35	-0.8	16.1	20.0
	Pre-cycle 13 (n=5)	44.42	9.452	46.80	30.6	56.5	0.0	4	3.13	2.395	2.60	0.9	6.4	20.0
	Pre-cycle 25 (n=4)	39.23	7.968	41.05	28.0	46.8	20.0	3	0.63	0.503	0.70	0.1	1.1	40.0
	Pre-cycle 37 (n=3)	43.30	12.360	41.40	32.0	56.5	40.0	2	NC	NC	NC	0.9	4.7	60.0
	Pre-cycle 49 (n=3)	36.63	7.160	40.10	28.4	41.4	40.0	2	NC	NC	NC	0.9	1.1	60.0

[a] Parents/legal guardians of male children from 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\reqlb1.sas Executed: 2023-03-17T09:52

Table 2.5.2.1.1 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [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]
Raw Score	Baseline (n=4)	23.5	9.15	27.0	10	30	20.0							
	Pre-cycle 3 (n=5)	25.8	6.72	28.0	14	31	0.0	4	1.8	1.71	1.5	0	4	20.0
	Pre-cycle 5 (n=5)	28.2	6.30	31.0	17	32	0.0	4	4.3	2.50	4.5	1	7	20.0
	Pre-cycle 9 (n=5)	27.8	5.67	30.0	18	32	0.0	4	3.5	4.12	3.0	0	8	20.0
	Pre-cycle 13 (n=5)	27.6	7.13	31.0	15	32	0.0	4	3.0	2.31	3.0	1	5	20.0
	Pre-cycle 25 (n=4)	24.8	9.25	28.5	11	31	20.0	3	1.3	1.53	1.0	0	3	40.0
	Pre-cycle 37 (n=3)	26.0	7.94	29.0	17	32	40.0	2	NC	NC	NC	1	7	60.0
	Pre-cycle 49 (n=3)	22.0	9.64	26.0	11	29	40.0	2	NC	NC	NC	1	1	60.0

[a] Parents/legal guardians of male children from 5 to 7 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.

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Table 2.5.2.1.1 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [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=4)	32.90	16.762	31.40	14.0	54.8	20.0							
	Pre-cycle 3 (n=5)	37.24	14.034	40.70	16.6	54.8	0.0	4	3.25	3.609	2.30	0.0	8.4	20.0
	Pre-cycle 5 (n=5)	35.80	13.700	34.70	17.6	54.8	0.0	4	3.18	4.229	1.85	0.0	9.0	20.0
	Pre-cycle 9 (n=5)	39.62	15.965	36.90	16.6	54.8	0.0	4	2.93	2.156	3.55	0.0	4.6	20.0
	Pre-cycle 13 (n=5)	38.54	17.095	36.30	14.0	54.8	0.0	4	1.58	1.947	1.15	0.0	4.0	20.0
	Pre-cycle 25 (n=4)	31.83	10.595	34.20	18.0	40.9	20.0	3	3.73	5.005	4.00	-1.4	8.6	40.0
	Pre-cycle 37 (n=3)	37.30	18.021	38.30	18.8	54.8	40.0	2	NC	NC	NC	4.8	6.0	60.0
	Pre-cycle 49 (n=3)	33.37	12.734	39.80	18.7	41.6	40.0	2	NC	NC	NC	4.7	7.5	60.0

[a] Parents/legal guardians of male children from 5 to 7 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.

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Table 2.5.2.1.1 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [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]
Raw Score	Baseline (n=4)	19.0	13.90	22.0	0	32	20.0							
	Pre-cycle 3 (n=5)	23.6	13.01	30.0	1	32	0.0	4	2.8	2.75	2.5	0	6	20.0
	Pre-cycle 5 (n=5)	22.4	12.50	28.0	2	32	0.0	4	2.0	2.16	1.5	0	5	20.0
	Pre-cycle 9 (n=5)	24.2	13.14	29.0	1	32	0.0	4	3.3	4.03	2.0	0	9	20.0
	Pre-cycle 13 (n=5)	23.6	13.45	28.0	0	32	0.0	4	2.5	3.79	1.0	0	8	20.0
	Pre-cycle 25 (n=4)	21.0	13.22	26.0	2	30	20.0	3	3.3	1.15	4.0	2	4	40.0
	Pre-cycle 37 (n=3)	22.0	15.62	30.0	4	32	40.0	2	NC	NC	NC	4	4	60.0
	Pre-cycle 49 (n=3)	21.0	15.62	29.0	3	31	40.0	2	NC	NC	NC	3	3	60.0

[a] Parents/legal guardians of male children from 5 to 7 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.

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Table 2.5.2.1.2 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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=4)	34.03	3.241	33.30	31.0	38.5	0.0							
	Pre-cycle 3 (n=4)	37.05	5.056	37.45	30.8	42.5	0.0	4	3.03	4.698	1.15	-0.2	10.0	0.0
	Pre-cycle 5 (n=3)	37.80	8.984	40.80	27.7	44.9	25.0	3	3.27	7.100	2.30	-3.3	10.8	25.0
	Pre-cycle 9 (n=4)	38.38	5.008	40.55	30.9	41.5	0.0	4	4.35	4.044	4.25	-0.1	9.0	0.0
	Pre-cycle 13 (n=3)	40.10	3.000	40.10	37.1	43.1	25.0	3	5.07	6.054	6.00	-1.4	10.6	25.0
	Pre-cycle 25 (n=2)	NC	NC	NC	34.8	41.5	50.0	2	NC	NC	NC	-3.7	9.0	50.0
	Pre-cycle 37 (n=1)	NC	NC	NC	36.1	36.1	75.0	1	NC	NC	NC	-2.4	-2.4	75.0

[a] Parents/legal guardians of female children from 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\reqlb2.sas Executed: 2023-03-17T10:18

Table 2.5.2.1.2 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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]
Raw Score	Baseline (n=4)	20.3	4.57	20.0	15	26	0.0							
	Pre-cycle 3 (n=4)	22.5	7.59	24.5	12	29	0.0	4	2.3	5.50	1.0	-3	10	0.0
	Pre-cycle 5 (n=3)	23.0	10.44	28.0	11	30	25.0	3	2.3	6.51	2.0	-4	9	25.0
	Pre-cycle 9 (n=4)	24.8	5.91	27.0	16	29	0.0	4	4.5	4.36	3.5	1	10	0.0
	Pre-cycle 13 (n=3)	26.7	3.06	26.0	24	30	25.0	3	4.7	6.51	5.0	-2	11	25.0
	Pre-cycle 25 (n=2)	NC	NC	NC	21	29	50.0	2	NC	NC	NC	-5	10	50.0
	Pre-cycle 37 (n=1)	NC	NC	NC	22	22	75.0	1	NC	NC	NC	-4	-4	75.0

[a] Parents/legal guardians of female children from 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req1b2.sas Executed: 2023-03-17T10:18

Table 2.5.2.1.2 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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=4)	37.55	9.629	39.20	25.9	45.9	0.0							
	Pre-cycle 3 (n=4)	34.73	6.677	36.40	26.1	40.0	0.0	4	-2.83	3.071	-2.80	-5.9	0.2	0.0
	Pre-cycle 5 (n=3)	36.90	16.074	32.20	23.7	54.8	25.0	3	1.83	6.140	-1.20	-2.2	8.9	25.0
	Pre-cycle 9 (n=4)	38.73	12.205	37.00	26.1	54.8	0.0	4	1.18	5.625	0.20	-4.6	8.9	0.0
	Pre-cycle 13 (n=3)	43.23	13.105	45.90	29.0	54.8	25.0	3	1.80	6.696	0.90	-4.4	8.9	25.0
	Pre-cycle 25 (n=2)	NC	NC	NC	30.1	54.8	50.0	2	NC	NC	NC	-3.3	9.8	50.0
	Pre-cycle 37 (n=1)	NC	NC	NC	31.5	31.5	75.0	1	NC	NC	NC	-1.9	-1.9	75.0

[a] Parents/legal guardians of female children from 5 to 7 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.

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Table 2.5.2.1.2 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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]
Raw Score	Baseline (n=4)	24.0	8.37	26.0	13	31	0.0							
	Pre-cycle 3 (n=4)	23.5	6.81	25.0	15	29	0.0	4	-0.5	1.73	-1.0	-2	2	0.0
	Pre-cycle 5 (n=3)	21.7	11.06	23.0	10	32	25.0	3	-0.3	2.31	1.0	-3	1	25.0
	Pre-cycle 9 (n=4)	25.3	7.23	27.0	15	32	0.0	4	1.3	3.30	1.5	-3	5	0.0
	Pre-cycle 13 (n=3)	27.3	7.23	31.0	19	32	25.0	3	-0.3	2.31	1.0	-3	1	25.0
	Pre-cycle 25 (n=2)	NC	NC	NC	22	32	50.0	2	NC	NC	NC	0	2	50.0
	Pre-cycle 37 (n=1)	NC	NC	NC	22	22	75.0	1	NC	NC	NC	0	0	75.0

[a] Parents/legal guardians of female children from 5 to 7 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.

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Table 2.5.2.1.3 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [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=4)	39.08	5.140	39.45	32.5	44.9	20.0							
	Pre-cycle 3 (n=5)	42.04	2.880	40.80	39.4	46.8	0.0	4	3.28	4.532	1.40	0.3	10.0	20.0
	Pre-cycle 5 (n=4)	44.35	2.926	44.90	40.8	46.8	20.0	3	3.50	2.433	2.30	1.9	6.3	40.0
	Pre-cycle 9 (n=5)	45.92	6.356	44.10	40.8	56.5	0.0	4	6.65	7.511	5.65	-0.8	16.1	20.0
	Pre-cycle 13 (n=5)	46.06	7.056	46.80	37.1	56.5	0.0	4	4.38	5.239	4.15	-1.4	10.6	20.0
	Pre-cycle 25 (n=4)	41.15	4.916	41.50	34.8	46.8	20.0	3	2.13	6.413	1.10	-3.7	9.0	40.0
	Pre-cycle 37 (n=2)	NC	NC	NC	36.1	56.5	60.0	1	NC	NC	NC	-2.4	-2.4	80.0
	Pre-cycle 49 (n=1)	NC	NC	NC	40.1	40.1	80.0	0	NC	NC	NC	NC	NC	100.0

[a] Parents/legal guardians of children with a progressive PN status at baseline from 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req1b3.sas Executed: 2023-03-17T09:53

Table 2.5.2.1.3 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [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]
Raw Score	Baseline (n=4)	25.3	4.57	26.0	19	30	20.0							
	Pre-cycle 3 (n=5)	28.6	1.52	28.0	27	31	0.0	4	3.5	4.36	1.5	1	10	20.0
	Pre-cycle 5 (n=4)	30.0	1.41	30.5	28	31	20.0	3	2.7	2.08	2.0	1	5	40.0
	Pre-cycle 9 (n=5)	29.8	1.92	30.0	27	32	0.0	4	4.3	4.65	3.5	0	10	20.0
	Pre-cycle 13 (n=5)	29.6	3.21	31.0	24	32	0.0	4	3.8	5.62	3.0	-2	11	20.0
	Pre-cycle 25 (n=4)	27.5	4.43	29.0	21	31	20.0	3	2.7	7.51	3.0	-5	10	40.0
	Pre-cycle 37 (n=2)	NC	NC	NC	22	32	60.0	1	NC	NC	NC	-4	-4	80.0
	Pre-cycle 49 (n=1)	NC	NC	NC	26	26	80.0	0	NC	NC	NC	NC	NC	100.0

[a] Parents/legal guardians of children with a progressive PN status at baseline from 5 to 7 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.

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Table 2.5.2.1.3 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [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=4)	40.93	11.172	39.20	30.5	54.8	20.0							
	Pre-cycle 3 (n=5)	40.34	9.071	40.00	32.5	54.8	0.0	4	-0.90	2.951	-0.30	-5.0	2.0	20.0
	Pre-cycle 5 (n=4)	38.08	11.277	33.45	30.6	54.8	20.0	3	-0.37	0.723	0.00	-1.2	0.1	40.0
	Pre-cycle 9 (n=5)	43.72	10.428	40.40	33.6	54.8	0.0	4	0.03	3.717	0.10	-4.6	4.5	20.0
	Pre-cycle 13 (n=5)	43.46	12.102	45.90	29.0	54.8	0.0	4	-0.30	2.893	0.45	-4.4	2.3	20.0
	Pre-cycle 25 (n=4)	38.33	11.904	34.70	29.1	54.8	20.0	3	1.70	7.079	-1.40	-3.3	9.8	40.0
	Pre-cycle 37 (n=2)	NC	NC	NC	31.5	54.8	60.0	1	NC	NC	NC	-1.9	-1.9	80.0
	Pre-cycle 49 (n=1)	NC	NC	NC	41.6	41.6	80.0	0	NC	NC	NC	NC	NC	100.0

[a] Parents/legal guardians of children with a progressive PN status at baseline from 5 to 7 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.

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Table 2.5.2.1.3 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [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]
Raw Score	Baseline (n=4)	25.5	6.61	26.0	18	32	20.0							
	Pre-cycle 3 (n=5)	27.4	4.72	29.0	21	32	0.0	4	1.0	3.37	-0.5	-1	6	20.0
	Pre-cycle 5 (n=4)	25.5	5.69	25.5	19	32	20.0	3	0.7	0.58	1.0	0	1	40.0
	Pre-cycle 9 (n=5)	29.0	2.74	27.0	27	32	0.0	4	2.8	5.32	2.5	-3	9	20.0
	Pre-cycle 13 (n=5)	28.0	5.61	31.0	19	32	0.0	4	1.5	4.65	0.5	-3	8	20.0
	Pre-cycle 25 (n=4)	26.5	5.26	26.0	22	32	20.0	3	2.0	2.00	2.0	0	4	40.0
	Pre-cycle 37 (n=2)	NC	NC	NC	22	32	60.0	1	NC	NC	NC	0	0	80.0
	Pre-cycle 49 (n=1)	NC	NC	NC	31	31	80.0	0	NC	NC	NC	NC	NC	100.0

[a] Parents/legal guardians of children with a progressive PN status at baseline from 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\reqlb3.sas Executed: 2023-03-17T09:53

Table 2.5.2.1.4 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [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=3)	30.80	3.404	31.00	27.3	34.1	0.0							
	Pre-cycle 3 (n=3)	31.73	3.398	30.80	28.9	35.5	0.0	3	0.93	0.987	1.40	-0.2	1.6	0.0
	Pre-cycle 5 (n=3)	35.03	8.875	32.50	27.7	44.9	0.0	3	4.23	7.100	5.20	-3.3	10.8	0.0
	Pre-cycle 9 (n=3)	34.37	5.163	31.90	30.9	40.3	0.0	3	3.57	3.275	4.60	-0.1	6.2	0.0
	Pre-cycle 13 (n=2)	NC	NC	NC	30.6	40.1	33.3	2	NC	NC	NC	3.3	6.0	33.3
	Pre-cycle 25 (n=1)	NC	NC	NC	28.0	28.0	66.7	1	NC	NC	NC	0.7	0.7	66.7
	Pre-cycle 37 (n=1)	NC	NC	NC	32.0	32.0	66.7	1	NC	NC	NC	4.7	4.7	66.7
	Pre-cycle 49 (n=1)	NC	NC	NC	28.4	28.4	66.7	1	NC	NC	NC	1.1	1.1	66.7

[a] Parents/legal guardians of children with a non-progressive PN status at baseline from 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\reqlb4.sas Executed: 2023-03-17T09:53

Table 2.5.2.1.4 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [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]
Raw Score	Baseline (n=3)	15.3	5.51	15.0	10	21	0.0							
	Pre-cycle 3 (n=3)	16.0	5.29	14.0	12	22	0.0	3	0.7	3.51	1.0	-3	4	0.0
	Pre-cycle 5 (n=3)	19.3	9.71	17.0	11	30	0.0	3	4.0	7.00	7.0	-4	9	0.0
	Pre-cycle 9 (n=3)	20.3	5.86	18.0	16	27	0.0	3	5.0	3.61	6.0	1	8	0.0
	Pre-cycle 13 (n=2)	NC	NC	NC	15	26	33.3	2	NC	NC	NC	5	5	33.3
	Pre-cycle 25 (n=1)	NC	NC	NC	11	11	66.7	1	NC	NC	NC	1	1	66.7
	Pre-cycle 37 (n=1)	NC	NC	NC	17	17	66.7	1	NC	NC	NC	7	7	66.7
	Pre-cycle 49 (n=1)	NC	NC	NC	11	11	66.7	1	NC	NC	NC	1	1	66.7

[a] Parents/legal guardians of children with a non-progressive PN status at baseline from 5 to 7 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.

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Table 2.5.2.1.4 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [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=3)	28.60	16.120	25.90	14.0	45.9	0.0							
	Pre-cycle 3 (n=3)	27.57	11.769	26.10	16.6	40.0	0.0	3	-1.03	4.382	0.20	-5.9	2.6	0.0
	Pre-cycle 5 (n=3)	32.03	19.951	23.70	17.6	54.8	0.0	3	3.43	5.552	3.60	-2.2	8.9	0.0
	Pre-cycle 9 (n=3)	32.50	19.888	26.10	16.6	54.8	0.0	3	3.90	4.493	2.60	0.2	8.9	0.0
	Pre-cycle 13 (n=2)	NC	NC	NC	14.0	54.8	33.3	2	NC	NC	NC	0.0	8.9	33.3
	Pre-cycle 25 (n=1)	NC	NC	NC	18.0	18.0	66.7	1	NC	NC	NC	4.0	4.0	66.7
	Pre-cycle 37 (n=1)	NC	NC	NC	18.8	18.8	66.7	1	NC	NC	NC	4.8	4.8	66.7
	Pre-cycle 49 (n=1)	NC	NC	NC	18.7	18.7	66.7	1	NC	NC	NC	4.7	4.7	66.7

[a] Parents/legal guardians of children with a non-progressive PN status at baseline from 5 to 7 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.

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Table 2.5.2.1.4 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [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]
Raw Score	Baseline (n=3)	14.7	15.57	13.0	0	31	0.0							
	Pre-cycle 3 (n=3)	15.0	14.00	15.0	1	29	0.0	3	0.3	2.08	1.0	-2	2	0.0
	Pre-cycle 5 (n=3)	14.7	15.53	10.0	2	32	0.0	3	0.0	2.65	1.0	-3	2	0.0
	Pre-cycle 9 (n=3)	16.0	15.52	15.0	1	32	0.0	3	1.3	0.58	1.0	1	2	0.0
	Pre-cycle 13 (n=2)	NC	NC	NC	0	32	33.3	2	NC	NC	NC	0	1	33.3
	Pre-cycle 25 (n=1)	NC	NC	NC	2	2	66.7	1	NC	NC	NC	2	2	66.7
	Pre-cycle 37 (n=1)	NC	NC	NC	4	4	66.7	1	NC	NC	NC	4	4	66.7
	Pre-cycle 49 (n=1)	NC	NC	NC	3	3	66.7	1	NC	NC	NC	3	3	66.7

[a] Parents/legal guardians of children with a non-progressive PN status at baseline from 5 to 7 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.

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Table 2.5.2.1.5 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=1) [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=1)	NC	NC	NC	40.5	40.5	0.0							
	Pre-cycle 3 (n=1)	NC	NC	NC	40.6	40.6	0.0	1	NC	NC	NC	0.1	0.1	0.0
	Pre-cycle 5 (n=1)	NC	NC	NC	56.5	56.5	0.0	1	NC	NC	NC	16.0	16.0	0.0
	Pre-cycle 9 (n=1)	NC	NC	NC	40.6	40.6	0.0	1	NC	NC	NC	0.1	0.1	0.0
	Pre-cycle 13 (n=1)	NC	NC	NC	41.4	41.4	0.0	1	NC	NC	NC	0.9	0.9	0.0
	Pre-cycle 25 (n=1)	NC	NC	NC	40.6	40.6	0.0	1	NC	NC	NC	0.1	0.1	0.0
	Pre-cycle 37 (n=1)	NC	NC	NC	41.4	41.4	0.0	1	NC	NC	NC	0.9	0.9	0.0
	Pre-cycle 49 (n=1)	NC	NC	NC	41.4	41.4	0.0	1	NC	NC	NC	0.9	0.9	0.0

[a] Parents/legal guardians of children with an unknown PN status at baseline from 5 to 7 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 2.5.2.1.5 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=1) [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]
Raw Score	Baseline (n=1)	NC	NC	NC	28	28	0.0							
	Pre-cycle 3 (n=1)	NC	NC	NC	28	28	0.0	1	NC	NC	NC	0	0	0.0
	Pre-cycle 5 (n=1)	NC	NC	NC	32	32	0.0	1	NC	NC	NC	4	4	0.0
	Pre-cycle 9 (n=1)	NC	NC	NC	28	28	0.0	1	NC	NC	NC	0	0	0.0
	Pre-cycle 13 (n=1)	NC	NC	NC	29	29	0.0	1	NC	NC	NC	1	1	0.0
	Pre-cycle 25 (n=1)	NC	NC	NC	28	28	0.0	1	NC	NC	NC	0	0	0.0
	Pre-cycle 37 (n=1)	NC	NC	NC	29	29	0.0	1	NC	NC	NC	1	1	0.0
	Pre-cycle 49 (n=1)	NC	NC	NC	29	29	0.0	1	NC	NC	NC	1	1	0.0

[a] Parents/legal guardians of children with an unknown PN status at baseline from 5 to 7 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 2.5.2.1.5 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=1) [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=1)	NC	NC	NC	32.3	32.3	0.0							
	Pre-cycle 3 (n=1)	NC	NC	NC	40.7	40.7	0.0	1	NC	NC	NC	8.4	8.4	0.0
	Pre-cycle 5 (n=1)	NC	NC	NC	41.3	41.3	0.0	1	NC	NC	NC	9.0	9.0	0.0
	Pre-cycle 9 (n=1)	NC	NC	NC	36.9	36.9	0.0	1	NC	NC	NC	4.6	4.6	0.0
	Pre-cycle 13 (n=1)	NC	NC	NC	36.3	36.3	0.0	1	NC	NC	NC	4.0	4.0	0.0
	Pre-cycle 25 (n=1)	NC	NC	NC	40.9	40.9	0.0	1	NC	NC	NC	8.6	8.6	0.0
	Pre-cycle 37 (n=1)	NC	NC	NC	38.3	38.3	0.0	1	NC	NC	NC	6.0	6.0	0.0
	Pre-cycle 49 (n=1)	NC	NC	NC	39.8	39.8	0.0	1	NC	NC	NC	7.5	7.5	0.0

[a] Parents/legal guardians of children with an unknown PN status at baseline from 5 to 7 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 2.5.2.1.5 PROMIS parent-report scores and change from baseline over time - Ages 5-7 - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=1) [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]
Raw Score	Baseline (n=1)	NC	NC	NC	26	26	0.0							
	Pre-cycle 3 (n=1)	NC	NC	NC	30	30	0.0	1	NC	NC	NC	4	4	0.0
	Pre-cycle 5 (n=1)	NC	NC	NC	31	31	0.0	1	NC	NC	NC	5	5	0.0
	Pre-cycle 9 (n=1)	NC	NC	NC	29	29	0.0	1	NC	NC	NC	3	3	0.0
	Pre-cycle 13 (n=1)	NC	NC	NC	28	28	0.0	1	NC	NC	NC	2	2	0.0
	Pre-cycle 25 (n=1)	NC	NC	NC	30	30	0.0	1	NC	NC	NC	4	4	0.0
	Pre-cycle 37 (n=1)	NC	NC	NC	30	30	0.0	1	NC	NC	NC	4	4	0.0
	Pre-cycle 49 (n=1)	NC	NC	NC	29	29	0.0	1	NC	NC	NC	3	3	0.0

[a] Parents/legal guardians of children with an unknown PN status at baseline from 5 to 7 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\reqlb5.sas Executed: 2023-03-17T09:54

Table 5.3.1.2.1 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req25b1.sas Executed: 2023-05-31T17:36

Table 5.3.1.2.1 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req25b1.sas Executed: 2023-05-31T17:36

Table 5.3.1.2.1 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req25b1.sas Executed: 2023-05-31T17:36

Table 5.3.1.2.1 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.2 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.2 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
Upper Extremity	Pre-cycle 3 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.2 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.2 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.3 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.3 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
Upper Extremity	Pre-cycle 3 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.3 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.3 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=4) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.4 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=3) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.4 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=3) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.4 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=3) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.4 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=3) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.2.5 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=1) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC - not calculated.

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Table 5.3.1.2.5 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=1) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC - not calculated.

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Table 5.3.1.2.5 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=1) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC - not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req25b5.sas Executed: 2023-05-31T07:02

Table 5.3.1.2.5 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 5-7 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=1) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Children ages 5-7 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC - not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req25b5.sas Executed: 2023-05-31T07:02

1.7.2.3.3 Subgruppenanalysen PROMIS Veränderung gegenüber Baseline – Elternberichtet (8-18 Jahre)

Table 2.5.3.1.1 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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)	35.03	6.192	35.15	19.8	44.3	0.0							
	Pre-cycle 3 (n=13)	37.92	6.019	38.20	27.5	48.6	7.1	13	3.45	2.340	2.80	-0.5	7.7	7.1
	Pre-cycle 5 (n=13)	37.16	8.824	36.00	17.5	56.5	7.1	13	2.69	4.834	2.70	-2.7	15.4	7.1
	Pre-cycle 9 (n=13)	37.62	8.589	38.60	17.5	56.5	7.1	13	3.15	5.471	2.60	-4.1	18.5	7.1
	Pre-cycle 13 (n=12)	38.49	9.885	36.95	21.1	56.5	14.3	12	3.92	5.600	2.75	-3.4	15.4	14.3
	Pre-cycle 25 (n=7)	42.70	7.652	41.20	32.0	56.5	50.0	7	5.96	4.790	3.50	1.8	13.5	50.0
	Pre-cycle 37 (n=5)	41.42	9.230	38.90	31.8	56.5	64.3	5	5.80	3.953	4.50	1.6	12.2	64.3
	Pre-cycle 49 (n=5)	42.78	9.773	44.10	31.1	56.5	64.3	5	7.16	5.406	10.20	0.9	12.2	64.3

[a] Parents/legal guardians of male children from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req1c1.sas Executed: 2023-03-17T09:55

Table 2.5.3.1.1 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Raw Score	Baseline (n=14)	20.5	7.14	20.5	3	30	0.0							
	Pre-cycle 3 (n=13)	23.3	5.91	24.0	10	31	7.1	13	3.5	2.60	3.0	-1	8	7.1
	Pre-cycle 5 (n=13)	22.5	7.99	23.0	0	32	7.1	13	2.7	4.05	3.0	-3	9	7.1
	Pre-cycle 9 (n=13)	23.0	7.77	25.0	1	32	7.1	13	3.2	4.06	3.0	-5	11	7.1
	Pre-cycle 13 (n=12)	22.5	7.42	23.0	4	32	14.3	12	2.7	3.20	2.5	-3	8	14.3
	Pre-cycle 25 (n=7)	26.9	4.91	28.0	18	32	50.0	7	4.0	2.89	3.0	2	10	50.0
	Pre-cycle 37 (n=5)	25.6	5.13	25.0	18	32	64.3	5	4.4	1.82	4.0	2	7	64.3
	Pre-cycle 49 (n=5)	25.8	5.97	27.0	17	32	64.3	5	4.6	2.88	3.0	2	9	64.3

[a] Parents/legal guardians of male children from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req1c1.sas Executed: 2023-03-17T09:55

Table 2.5.3.1.1 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=14)	35.84	12.323	31.65	18.2	54.8	0.0							
	Pre-cycle 3 (n=13)	35.77	12.267	33.90	21.0	54.8	7.1	13	1.39	8.554	2.30	-20.9	15.5	7.1
	Pre-cycle 5 (n=13)	36.12	12.225	34.70	16.6	54.8	7.1	13	1.75	3.658	0.00	-1.9	10.5	7.1
	Pre-cycle 9 (n=13)	32.95	8.911	31.40	15.8	54.8	7.1	13	-1.42	8.797	0.00	-25.3	6.9	7.1
	Pre-cycle 13 (n=12)	36.64	11.447	35.30	14.0	54.8	14.3	12	1.88	7.595	2.80	-16.7	12.9	14.3
	Pre-cycle 25 (n=7)	40.69	10.609	39.30	28.8	54.8	50.0	7	3.67	4.062	2.30	0.0	10.5	50.0
	Pre-cycle 37 (n=5)	41.16	12.604	35.10	29.7	54.8	64.3	5	8.16	4.823	6.10	3.9	15.5	64.3
	Pre-cycle 49 (n=5)	41.44	12.246	34.20	31.1	54.8	64.3	5	8.44	4.713	7.50	3.9	15.5	64.3

[a] Parents/legal guardians of male children from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\reqlc1.sas Executed: 2023-03-17T09:55

Table 2.5.3.1.1 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Raw Score	Baseline (n=14)	22.1	9.62	24.0	4	32	0.0							
	Pre-cycle 3 (n=13)	21.6	9.01	20.0	7	32	7.1	13	0.3	4.21	1.0	-8	8	7.1
	Pre-cycle 5 (n=13)	22.7	9.33	23.0	1	32	7.1	13	1.4	3.33	0.0	-3	11	7.1
	Pre-cycle 9 (n=13)	21.5	8.30	20.0	1	32	7.1	13	0.2	7.34	0.0	-17	10	7.1
	Pre-cycle 13 (n=12)	24.3	9.00	26.5	0	32	14.3	12	2.8	4.65	1.0	-4	10	14.3
	Pre-cycle 25 (n=7)	27.6	4.79	30.0	21	32	50.0	7	3.0	4.47	1.0	0	10	50.0
	Pre-cycle 37 (n=5)	27.2	4.76	27.0	22	32	64.3	5	5.2	4.02	5.0	1	11	64.3
	Pre-cycle 49 (n=5)	27.4	4.34	26.0	23	32	64.3	5	5.4	4.56	4.0	1	12	64.3

[a] Parents/legal guardians of male children from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req1c1.sas Executed: 2023-03-17T09:55

Table 2.5.3.1.2 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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)	41.83	8.401	39.05	30.7	56.5	0.0							
	Pre-cycle 3 (n=9)	40.23	7.046	40.20	29.9	56.5	10.0	9	0.03	2.408	0.00	-3.9	3.5	10.0
	Pre-cycle 5 (n=10)	39.66	6.064	39.65	28.7	48.6	0.0	10	-2.17	4.510	-1.35	-9.7	4.8	0.0
	Pre-cycle 9 (n=10)	41.31	5.206	42.30	31.1	46.8	0.0	10	-0.52	5.469	2.45	-9.7	4.3	0.0
	Pre-cycle 13 (n=9)	43.21	8.780	42.30	30.8	56.5	10.0	9	1.13	1.699	0.10	-0.9	3.7	10.0
	Pre-cycle 25 (n=7)	46.90	6.796	42.80	41.5	56.5	30.0	7	5.26	5.804	3.40	0.0	17.9	30.0
	Pre-cycle 37 (n=7)	45.23	5.667	44.90	39.5	56.5	30.0	7	3.59	2.878	3.00	0.0	7.3	30.0
	Pre-cycle 49 (n=4)	46.45	7.244	44.55	40.2	56.5	60.0	4	2.63	1.868	3.10	0.0	4.3	60.0

[a] Parents/legal guardians of female children from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req1c2.sas Executed: 2023-03-17T09:56

Table 2.5.3.1.2 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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]
Raw Score	Baseline (n=10)	25.8	5.05	26.0	16	32	0.0							
	Pre-cycle 3 (n=9)	25.7	4.58	26.0	15	32	10.0	9	0.6	2.70	0.0	-3	4	10.0
	Pre-cycle 5 (n=10)	25.3	5.70	26.0	12	31	0.0	10	-0.5	3.75	-0.5	-7	5	0.0
	Pre-cycle 9 (n=10)	26.8	5.03	28.5	16	31	0.0	10	1.0	3.86	1.5	-8	5	0.0
	Pre-cycle 13 (n=9)	27.1	5.11	28.0	16	32	10.0	9	1.6	2.19	1.0	-1	5	10.0
	Pre-cycle 25 (n=7)	29.9	1.95	30.0	27	32	30.0	7	3.9	2.79	4.0	0	8	30.0
	Pre-cycle 37 (n=7)	28.7	2.43	28.0	25	32	30.0	7	2.7	3.55	3.0	-3	6	30.0
	Pre-cycle 49 (n=4)	29.5	2.65	30.0	26	32	60.0	4	1.8	1.71	1.5	0	4	60.0

[a] Parents/legal guardians of female children from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req1c2.sas Executed: 2023-03-17T09:56

Table 2.5.3.1.2 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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=9)	44.33	10.918	44.30	26.8	54.8	10.0							
	Pre-cycle 3 (n=9)	41.33	11.753	41.30	25.4	54.8	10.0	9	-3.00	5.956	-1.40	-13.5	6.8	10.0
	Pre-cycle 5 (n=10)	43.58	9.907	45.45	28.6	54.8	0.0	9	-2.00	6.076	0.00	-13.5	6.8	10.0
	Pre-cycle 9 (n=10)	44.57	10.454	45.10	27.8	54.8	0.0	9	-0.90	6.628	0.00	-13.5	7.7	10.0
	Pre-cycle 13 (n=9)	46.08	10.855	54.80	27.5	54.8	10.0	8	1.96	7.348	0.35	-8.4	17.9	20.0
	Pre-cycle 25 (n=7)	49.73	9.120	54.80	32.1	54.8	30.0	6	6.25	6.911	4.55	0.0	17.9	40.0
	Pre-cycle 37 (n=7)	48.29	8.779	54.80	34.6	54.8	30.0	6	4.57	8.383	3.85	-6.0	17.9	40.0
	Pre-cycle 49 (n=3)	41.07	12.014	35.90	32.5	54.8	70.0	3	-0.90	7.093	0.00	-8.4	5.7	70.0

[a] Parents/legal guardians of female children from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req1c2.sas Executed: 2023-03-17T09:56

Table 2.5.3.1.2 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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]
Raw Score	Baseline (n=9)	28.2	5.89	31.0	14	32	10.0							
	Pre-cycle 3 (n=9)	26.3	7.47	30.0	12	32	10.0	9	-1.9	3.22	-1.0	-9	2	10.0
	Pre-cycle 5 (n=10)	28.7	4.62	31.0	19	32	0.0	9	0.1	2.26	0.0	-3	5	10.0
	Pre-cycle 9 (n=10)	28.4	6.08	31.0	17	32	0.0	9	-0.2	3.46	0.0	-8	3	10.0
	Pre-cycle 13 (n=9)	28.7	5.07	32.0	17	32	10.0	8	0.5	2.14	0.0	-3	4	20.0
	Pre-cycle 25 (n=7)	30.4	3.36	32.0	23	32	30.0	6	2.7	3.44	1.5	0	9	40.0
	Pre-cycle 37 (n=7)	30.9	1.86	32.0	27	32	30.0	6	3.2	5.19	1.5	-1	13	40.0
	Pre-cycle 49 (n=3)	28.3	3.51	28.0	25	32	70.0	3	2.7	7.37	0.0	-3	11	70.0

[a] Parents/legal guardians of female children from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\reqlc2.sas Executed: 2023-03-17T09:56

Table 2.5.3.1.3 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [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=6)	35.58	3.294	36.00	30.7	39.6	0.0							
	Pre-cycle 3 (n=6)	37.48	4.815	37.60	29.9	44.3	0.0	6	1.90	3.300	2.15	-2.6	6.7	0.0
	Pre-cycle 5 (n=6)	36.85	5.913	36.35	28.7	44.1	0.0	6	1.27	4.719	2.15	-5.8	6.4	0.0
	Pre-cycle 9 (n=6)	36.95	3.375	38.50	31.1	40.2	0.0	6	1.37	3.499	1.75	-4.8	4.9	0.0
	Pre-cycle 13 (n=5)	35.46	3.110	35.70	30.8	38.3	16.7	5	0.68	2.078	0.70	-2.0	3.8	16.7
	Pre-cycle 25 (n=1)	NC	NC	NC	38.9	38.9	83.3	1	NC	NC	NC	4.5	4.5	83.3
	Pre-cycle 37 (n=1)	NC	NC	NC	38.9	38.9	83.3	1	NC	NC	NC	4.5	4.5	83.3
	Pre-cycle 49 (n=1)	NC	NC	NC	36.1	36.1	83.3	1	NC	NC	NC	1.7	1.7	83.3

[a] Parents/legal guardians of children with a progressive PN status at baseline from 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req1c3.sas Executed: 2023-03-17T09:56

Table 2.5.3.1.3 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [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]
Raw Score	Baseline (n=6)	21.0	4.10	20.0	16	28	0.0							
	Pre-cycle 3 (n=6)	23.5	4.59	25.0	15	28	0.0	6	2.5	3.99	3.0	-3	8	0.0
	Pre-cycle 5 (n=6)	22.7	6.77	23.0	12	30	0.0	6	1.7	6.38	2.5	-7	9	0.0
	Pre-cycle 9 (n=6)	23.2	4.22	25.5	16	26	0.0	6	2.2	5.53	4.5	-8	6	0.0
	Pre-cycle 13 (n=5)	21.0	3.39	21.0	16	25	16.7	5	1.4	2.70	1.0	-2	5	16.7
	Pre-cycle 25 (n=1)	NC	NC	NC	25	25	83.3	1	NC	NC	NC	5	5	83.3
	Pre-cycle 37 (n=1)	NC	NC	NC	25	25	83.3	1	NC	NC	NC	5	5	83.3
	Pre-cycle 49 (n=1)	NC	NC	NC	23	23	83.3	1	NC	NC	NC	3	3	83.3

[a] Parents/legal guardians of children with a progressive PN status at baseline from 8 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.

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Table 2.5.3.1.3 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [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=6)	37.78	13.705	33.30	23.6	54.8	0.0							
	Pre-cycle 3 (n=6)	32.52	7.002	34.30	21.4	41.3	0.0	6	-5.27	10.626	-4.10	-20.9	7.8	0.0
	Pre-cycle 5 (n=6)	36.80	10.387	34.90	24.9	54.8	0.0	6	-0.98	7.228	0.65	-13.5	8.2	0.0
	Pre-cycle 9 (n=6)	33.07	5.142	31.35	28.0	41.3	0.0	6	-4.72	12.457	0.00	-25.3	6.1	0.0
	Pre-cycle 13 (n=5)	36.46	6.472	37.40	29.3	45.9	16.7	5	2.08	11.098	4.70	-16.7	12.9	16.7
	Pre-cycle 25 (n=1)	NC	NC	NC	28.8	28.8	83.3	1	NC	NC	NC	5.2	5.2	83.3
	Pre-cycle 37 (n=1)	NC	NC	NC	29.7	29.7	83.3	1	NC	NC	NC	6.1	6.1	83.3
	Pre-cycle 49 (n=1)	NC	NC	NC	31.1	31.1	83.3	1	NC	NC	NC	7.5	7.5	83.3

[a] Parents/legal guardians of children with a progressive PN status at baseline from 8 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.

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Table 2.5.3.1.3 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [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]
Raw Score	Baseline (n=6)	23.0	9.38	25.5	11	32	0.0							
	Pre-cycle 3 (n=6)	20.8	8.57	22.0	7	31	0.0	6	-2.2	6.31	-2.5	-9	8	0.0
	Pre-cycle 5 (n=6)	24.5	7.34	25.0	12	32	0.0	6	1.5	4.89	0.5	-3	11	0.0
	Pre-cycle 9 (n=6)	21.7	6.38	19.5	15	31	0.0	6	-1.3	9.75	0.5	-17	8	0.0
	Pre-cycle 13 (n=5)	25.2	4.82	25.0	20	31	16.7	5	4.0	5.43	5.0	-3	10	16.7
	Pre-cycle 25 (n=1)	NC	NC	NC	21	21	83.3	1	NC	NC	NC	10	10	83.3
	Pre-cycle 37 (n=1)	NC	NC	NC	22	22	83.3	1	NC	NC	NC	11	11	83.3
	Pre-cycle 49 (n=1)	NC	NC	NC	23	23	83.3	1	NC	NC	NC	12	12	83.3

[a] Parents/legal guardians of children with a progressive PN status at baseline from 8 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.

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Table 2.5.3.1.4 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=8) [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=8)	40.43	7.761	38.05	33.2	56.5	0.0							
	Pre-cycle 3 (n=7)	39.96	5.304	40.20	32.7	48.6	12.5	7	1.83	3.408	1.50	-3.9	5.5	12.5
	Pre-cycle 5 (n=8)	39.31	4.788	38.70	32.7	46.8	0.0	8	-1.11	3.951	-0.25	-9.7	2.7	0.0
	Pre-cycle 9 (n=8)	42.64	7.081	40.25	34.6	56.5	0.0	8	2.21	8.023	2.45	-9.7	18.5	0.0
	Pre-cycle 13 (n=7)	45.16	8.563	42.30	34.6	56.5	12.5	7	3.70	5.291	2.70	-3.4	12.2	12.5
	Pre-cycle 25 (n=7)	46.96	7.097	46.80	39.4	56.5	12.5	7	5.50	5.175	3.40	0.0	13.5	12.5
	Pre-cycle 37 (n=6)	46.68	8.063	44.15	37.7	56.5	25.0	6	4.65	4.270	3.70	0.0	12.2	25.0
	Pre-cycle 49 (n=5)	50.00	6.016	46.80	44.1	56.5	37.5	5	7.18	5.455	10.20	0.0	12.2	37.5

[a] Parents/legal guardians of children with a non-progressive PN status at baseline from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 2.5.3.1.4 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=8) [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]
Raw Score	Baseline (n=8)	25.3	4.86	24.0	20	32	0.0							
	Pre-cycle 3 (n=7)	25.6	4.35	25.0	19	31	12.5	7	1.3	2.21	1.0	-2	4	12.5
	Pre-cycle 5 (n=8)	25.6	3.81	25.0	20	31	0.0	8	0.4	2.45	0.0	-3	4	0.0
	Pre-cycle 9 (n=8)	27.0	3.85	26.0	22	32	0.0	8	1.8	3.49	2.5	-5	6	0.0
	Pre-cycle 13 (n=7)	28.1	3.93	29.0	23	32	12.5	7	2.1	3.53	2.0	-3	8	12.5
	Pre-cycle 25 (n=7)	29.4	2.94	31.0	24	32	12.5	7	3.4	3.46	2.0	0	10	12.5
	Pre-cycle 37 (n=6)	28.7	2.80	28.0	25	32	25.0	6	2.7	3.78	3.0	-3	7	25.0
	Pre-cycle 49 (n=5)	30.4	2.07	31.0	27	32	37.5	5	3.6	3.78	2.0	0	9	37.5

[a] Parents/legal guardians of children with a non-progressive PN status at baseline from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 2.5.3.1.4 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=8) [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=7)	39.01	9.104	39.30	27.5	54.8	12.5							
	Pre-cycle 3 (n=7)	44.26	11.441	45.00	28.2	54.8	12.5	7	5.24	6.076	3.10	-1.5	15.5	12.5
	Pre-cycle 5 (n=8)	43.16	11.098	42.15	27.8	54.8	0.0	7	2.49	4.488	0.00	-1.9	10.5	12.5
	Pre-cycle 9 (n=8)	41.23	9.680	38.15	30.0	54.8	0.0	7	0.27	6.884	0.00	-12.9	7.7	12.5
	Pre-cycle 13 (n=7)	44.91	9.554	39.90	32.5	54.8	12.5	6	2.70	4.368	0.85	-1.0	10.5	25.0
	Pre-cycle 25 (n=7)	45.99	8.588	42.00	34.6	54.8	12.5	6	3.95	4.166	3.05	0.0	10.5	25.0
	Pre-cycle 37 (n=6)	49.42	9.517	54.80	31.4	54.8	25.0	5	7.52	5.963	7.70	0.0	15.5	37.5
	Pre-cycle 49 (n=4)	49.18	11.250	54.80	32.3	54.8	50.0	4	7.70	6.742	7.65	0.0	15.5	50.0

[a] Parents/legal guardians of children with a non-progressive PN status at baseline from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 2.5.3.1.4 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=8) [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]
Raw Score	Baseline (n=7)	26.4	6.58	30.0	16	32	12.5							
	Pre-cycle 3 (n=7)	28.0	5.86	31.0	19	32	12.5	7	1.6	1.27	1.0	0	4	12.5
	Pre-cycle 5 (n=8)	28.0	5.66	30.0	18	32	0.0	7	1.0	1.53	0.0	0	4	12.5
	Pre-cycle 9 (n=8)	27.9	4.82	29.5	19	32	0.0	7	0.9	5.70	0.0	-9	10	12.5
	Pre-cycle 13 (n=7)	29.7	2.93	30.0	24	32	12.5	6	1.5	3.21	0.0	0	8	25.0
	Pre-cycle 25 (n=7)	30.3	2.50	31.0	25	32	12.5	6	2.2	3.43	1.0	0	9	25.0
	Pre-cycle 37 (n=6)	30.3	3.61	32.0	23	32	25.0	5	2.6	2.70	2.0	0	7	37.5
	Pre-cycle 49 (n=4)	30.0	4.00	32.0	24	32	50.0	4	2.8	3.59	1.5	0	8	50.0

[a] Parents/legal guardians of children with a non-progressive PN status at baseline from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 2.5.3.1.5 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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)	37.18	9.656	38.30	19.8	56.5	0.0							
	Pre-cycle 3 (n=9)	38.94	8.335	40.20	27.5	56.5	10.0	9	2.33	2.474	2.20	-1.1	7.7	10.0
	Pre-cycle 5 (n=9)	38.23	10.866	38.80	17.5	56.5	10.0	9	1.62	6.528	1.10	-7.9	15.4	10.0
	Pre-cycle 9 (n=9)	37.71	9.037	42.30	17.5	46.8	10.0	9	1.10	4.839	2.80	-9.7	7.0	10.0
	Pre-cycle 13 (n=9)	39.71	11.418	37.60	21.1	56.5	10.0	9	3.10	4.922	2.30	-0.9	15.4	10.0
	Pre-cycle 25 (n=6)	43.27	7.828	42.75	32.0	56.5	40.0	6	5.92	5.982	4.00	1.8	17.9	40.0
	Pre-cycle 37 (n=5)	40.94	5.835	41.70	31.8	46.8	50.0	5	4.34	2.962	5.00	0.9	7.3	50.0
	Pre-cycle 49 (n=3)	37.87	5.953	40.20	31.1	42.3	70.0	3	2.90	1.778	3.50	0.9	4.3	70.0

[a] Parents/legal guardians of children with an unknown PN status at baseline from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 2.5.3.1.5 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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]
Raw Score	Baseline (n=10)	21.7	8.99	24.5	3	32	0.0							
	Pre-cycle 3 (n=9)	23.8	6.89	26.0	10	32	10.0	9	2.9	2.85	3.0	-2	7	10.0
	Pre-cycle 5 (n=9)	22.8	9.52	26.0	0	32	10.0	9	1.9	3.95	2.0	-4	7	10.0
	Pre-cycle 9 (n=9)	23.6	9.82	28.0	1	31	10.0	9	2.7	3.81	2.0	-2	11	10.0
	Pre-cycle 13 (n=9)	23.6	8.82	26.0	4	32	10.0	9	2.7	2.45	4.0	-1	6	10.0
	Pre-cycle 25 (n=6)	27.7	5.01	29.5	18	32	40.0	6	4.3	2.07	4.0	2	8	40.0
	Pre-cycle 37 (n=5)	26.4	5.22	28.0	18	31	50.0	5	4.0	2.12	4.0	1	6	50.0
	Pre-cycle 49 (n=3)	24.0	6.24	26.0	17	29	70.0	3	3.0	1.00	3.0	2	4	70.0

[a] Parents/legal guardians of children with an unknown PN status at baseline from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 2.5.3.1.5 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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)	40.09	14.402	40.60	18.2	54.8	0.0							
	Pre-cycle 3 (n=9)	36.90	14.052	33.20	21.0	54.8	10.0	9	-1.56	3.562	0.00	-9.2	2.8	10.0
	Pre-cycle 5 (n=9)	37.70	13.275	34.70	16.6	54.8	10.0	9	-0.76	3.450	0.00	-8.9	2.8	10.0
	Pre-cycle 9 (n=9)	38.43	14.491	37.50	15.8	54.8	10.0	9	-0.02	3.864	0.00	-6.8	7.4	10.0
	Pre-cycle 13 (n=9)	39.74	15.428	35.90	14.0	54.8	10.0	9	1.29	7.220	0.00	-8.4	17.9	10.0
	Pre-cycle 25 (n=6)	47.03	12.038	54.80	30.9	54.8	40.0	6	5.72	7.253	2.95	0.0	17.9	40.0
	Pre-cycle 37 (n=5)	43.52	10.395	38.30	34.6	54.8	50.0	5	4.90	8.948	4.80	-6.0	17.9	50.0
	Pre-cycle 49 (n=3)	34.20	1.700	34.20	32.5	35.9	70.0	3	0.40	7.674	3.90	-8.4	5.7	70.0

[a] Parents/legal guardians of children with an unknown PN status at baseline from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 2.5.3.1.5 PROMIS parent-report scores and change from baseline over time - Ages 8-18 - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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]
Raw Score	Baseline (n=10)	24.0	10.25	29.5	4	32	0.0							
	Pre-cycle 3 (n=9)	21.9	9.74	25.0	7	32	10.0	9	-1.2	2.77	0.0	-6	3	10.0
	Pre-cycle 5 (n=9)	23.4	10.33	27.0	1	32	10.0	9	0.3	2.35	0.0	-3	5	10.0
	Pre-cycle 9 (n=9)	23.3	10.69	29.0	1	32	10.0	9	0.2	2.64	0.0	-3	4	10.0
	Pre-cycle 13 (n=9)	24.0	10.69	28.0	0	32	10.0	9	0.9	3.41	0.0	-4	7	10.0
	Pre-cycle 25 (n=6)	28.8	4.92	32.0	22	32	40.0	6	2.3	3.61	0.5	0	9	40.0
	Pre-cycle 37 (n=5)	29.6	2.51	30.0	27	32	50.0	5	4.2	5.54	4.0	-1	13	50.0
	Pre-cycle 49 (n=3)	26.3	1.53	26.0	25	28	70.0	3	4.0	7.00	4.0	-3	11	70.0

[a] Parents/legal guardians of children with an unknown PN status at baseline from 8 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.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 5.3.1.3.1 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=13)	Categories of change [d]			
		Improvement	4	30.8	9.1, 61.4
		Deterioration	0	0	0, 24.7
		No improvement or deterioration	9	69.2	38.6, 90.9
	Pre-cycle 5 (n=13)	Categories of change [d]			
		Improvement	5	38.5	13.9, 68.4
		Deterioration	0	0	0, 24.7
		No improvement or deterioration	8	61.5	31.6, 86.1
	Pre-cycle 9 (n=13)	Categories of change [d]			
		Improvement	5	38.5	13.9, 68.4
		Deterioration	1	7.7	0.2, 36.0
		No improvement or deterioration	7	53.8	25.1, 80.8
	Pre-cycle 13 (n=12)	Categories of change [d]			
		Improvement	4	33.3	9.9, 65.1
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	8	66.7	34.9, 90.1

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.1 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Overall (n=13)	Categories of change [d]			
		Improvement	10	76.9	46.2, 95.0
		Deterioration	1	7.7	0.2, 36.0
		No improvement or deterioration	2	15.4	1.9, 45.4

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.1 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=13)	Categories of change [d]			
		Improvement	1	7.7	0.2, 36.0
		Deterioration	2	15.4	1.9, 45.4
		No improvement or deterioration	10	76.9	46.2, 95.0
	Pre-cycle 5 (n=13)	Categories of change [d]			
		Improvement	1	7.7	0.2, 36.0
		Deterioration	0	0	0, 24.7
		No improvement or deterioration	12	92.3	64.0, 99.8
	Pre-cycle 9 (n=13)	Categories of change [d]			
		Improvement	3	23.1	5.0, 53.8
		Deterioration	2	15.4	1.9, 45.4
		No improvement or deterioration	8	61.5	31.6, 86.1
	Pre-cycle 13 (n=12)	Categories of change [d]			
		Improvement	5	41.7	15.2, 72.3
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	7	58.3	27.7, 84.8

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.1 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=13) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Overall (n=13)	Categories of change [d]			
		Improvement	7	53.8	25.1, 80.8
		Deterioration	3	23.1	5.0, 53.8
		No improvement or deterioration	4	30.8	9.1, 61.4

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.2 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=9)	Categories of change [d]			
		Improvement	0	0	0, 33.6
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	9	100	66.4, 100
	Pre-cycle 5 (n=10)	Categories of change [d]			
		Improvement	1	10.0	0.3, 44.5
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 9 (n=10)	Categories of change [d]			
		Improvement	1	10.0	0.3, 44.5
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 13 (n=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	8	88.9	51.8, 99.7

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.2 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 37 (n=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 49 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Overall (n=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	5	50.0	18.7, 81.3

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.2 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=9)	Categories of change [d]			
		Improvement	0	0	0, 33.6
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	8	88.9	51.8, 99.7
	Pre-cycle 5 (n=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	8	88.9	51.8, 99.7
	Pre-cycle 9 (n=9)	Categories of change [d]			
		Improvement	0	0	0, 33.6
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	8	88.9	51.8, 99.7
	Pre-cycle 13 (n=8)	Categories of change [d]			
		Improvement	0	0	0, 36.9
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	8	100	63.1, 100

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.2 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=10) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Overall (n=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	7	77.8	40.0, 97.2

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.3 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 5 (n=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 9 (n=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 13 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.3.3 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.3.3 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 5 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 9 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 13 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.3.3 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=6) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	1	16.7	0.4, 64.1

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.
NC = not calculated.

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Table 5.3.1.3.4 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=7)	Categories of change [d]			
		Improvement	0	0	0, 41.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	7	100	59.0, 100
	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	0	0	0, 36.9
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	8	100	63.1, 100
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	5	62.5	24.5, 91.5
	Pre-cycle 13 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.4 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Overall (n=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	3	37.5	8.5, 75.5

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.4 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=7)	Categories of change [d]			
		Improvement	0	0	0, 41.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	7	100	59.0, 100
	Pre-cycle 5 (n=7)	Categories of change [d]			
		Improvement	0	0	0, 41.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	7	100	59.0, 100
	Pre-cycle 9 (n=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 13 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.4 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=8) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 49 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Overall (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	4	57.1	18.4, 90.1

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.5 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=9) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 3 (n=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	7	77.8	40.0, 97.2
	Pre-cycle 5 (n=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 9 (n=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	8	88.9	51.8, 99.7
	Pre-cycle 13 (n=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	7	77.8	40.0, 97.2

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.5 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=9) [a] Response category	n	% [b]	95% CI [c]
Mobility	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Overall (n=9)	Categories of change [d]			
		Improvement	6	66.7	29.9, 92.5
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	3	33.3	7.5, 70.1

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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Table 5.3.1.3.5 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=9) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 3 (n=9)	Categories of change [d]			
		Improvement	0	0	0, 33.6
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	8	88.9	51.8, 99.7
	Pre-cycle 5 (n=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	8	88.9	51.8, 99.7
	Pre-cycle 9 (n=9)	Categories of change [d]			
		Improvement	0	0	0, 33.6
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	9	100	66.4, 100
	Pre-cycle 13 (n=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	8	88.9	51.8, 99.7

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req25c5.sas Executed: 2023-05-19T08:23

Table 5.3.1.3.5 PROMIS Parent-report raw score categories of change over time - percentage of patients with Improvement and Deterioration - Ages 8-18 - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=9) [a] Response category	n	% [b]	95% CI [c]
Upper Extremity	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Overall (n=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	6	66.7	29.9, 92.5

[a] Children ages 8-18 years at enrolment, with a motor PN-related morbidity completed parent-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 and deterioration are defined using the following thresholds at 15% of the range:
Mobility parent report - 4.8; Upper extremity parent report - 4.8.

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1.7.3 PROMIS MMRM-Analysen

1.7.3.1 PROMIS MMRM-Analyse – Elternberichtet (5–18 Jahre)

Tabelle 5: Ergebnisse für PROMIS MMRM-Analyse – Elternberichtet (5–18 Jahre)

Studie	**Selumetinib 25 mg/m² BID**				
SPRINT Phase II, Stratum 1 **Datenschnitt: 31. März 2021**	**Alle Patienten im Alter von 5–18 Jahren (FAS) N = 33**				
	N*	**adjustierter Mittelwert der Veränderung gegenüber Baseline**	**SE**	**[95 %-KI]**	**p-Wert**
PROMIS – elternberichtet – Itembank Mobilität					
Zyklus 3	30	1,71	0,537	[0,60; 2,81]	0,004
Zyklus 5	30	1,88	1,014	[-0,20; 3,97]	0,075
Zyklus 9	31	2,23	0,988	[0,21; 4,25]	0,032
Zyklus 13	28	2,70	0,840	[0,97; 4,43]	0,004
Zyklus 25	19	4,08	1,268	[1,44; 6,72]	0,004
Zyklus 37	15	4,01	1,103	[1,54; 6,47]	0,005
Zyklus 49	11	3,95	1,426	[0,89; 7,01]	0,015
PROMIS – elternberichtet – Itembank obere Extremitäten					
Zyklus 3	30	-0,11	1,234	[-2,65; 2,42]	0,927
Zyklus 5	29	0,90	0,942	[-1,05; 2,84]	0,351
Zyklus 9	30	-0,19	1,217	[-2,69; 2,31]	0,879
Zyklus 13	27	1,58	1,301	[-1,10; 4,27]	0,235
Zyklus 25	18	4,61	1,309	[1,88; 7,34]	0,002
Zyklus 37	14	3,88	1,572	[0,59; 7,18]	0,023
Zyklus 49	10	3,84	1,711	[0,26; 7,43]	0,037

BID: Zweimal täglich; FAS: Full Analysis Set; KI: Konfidenzintervall; MMRM: Mixed Model Repeated Measures; PN: Plexiformes Neurofibrom; PROMIS: Patient-Reported Outcomes Measurement Information System; SE: Standardfehler

N*: in die Analyse eingeschlossene Patienten. Die Analyse wird bis zu dem Zyklus, zu dem noch für mindestens 10 Patienten beobachtete Werte vorliegen, durchgeführt

Das MMRM-Modell basiert auf den transformierten Werten.

Quelle: AstraZeneca. Studie SPRINT - Phase II: CSR all tables. Stand: 25.03.2022. 2022.

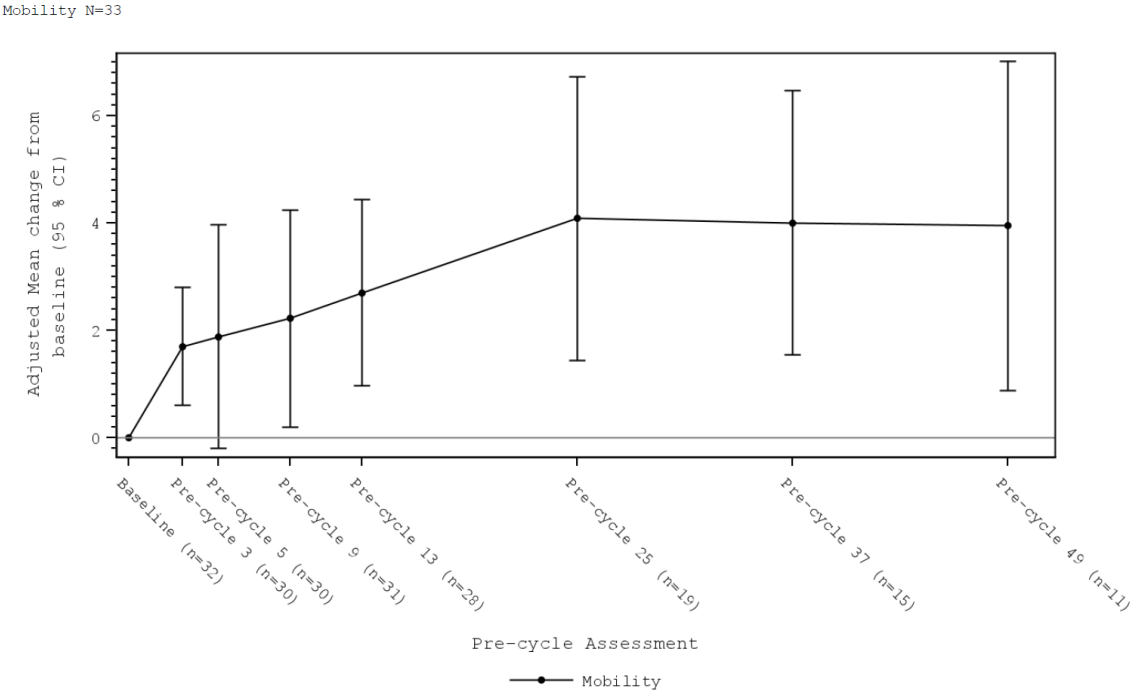

Abbildung 5: Elternberichteter (5 – 18 Jahre) PROMIS – Itembank Mobilität – Mittlere Veränderung gegenüber Baseline mittels MMRM
Quelle: AstraZeneca. Studie SPRINT - Phase II: CSR all figures. Stand: 25.03.2022. 2022.

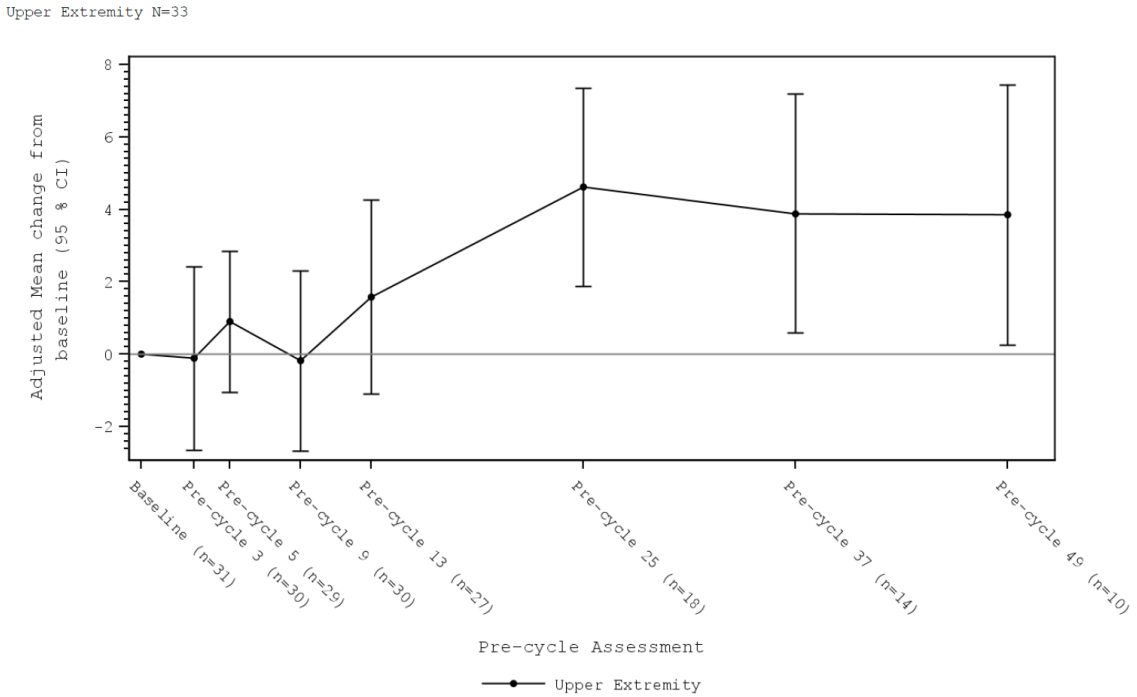

Abbildung 6: Elternberichteter (5 – 18 Jahre) PROMIS – Itembank obere Extremitäten – Mittlere Veränderung gegenüber Baseline mittels MMRM
Quelle: AstraZeneca. Studie SPRINT - Phase II: CSR all figures. Stand: 25.03.2022. 2022.

1.7.3.2 PROMIS MMRM-Analyse – Elternberichtet (8–18 Jahre)

Tabelle 6: Ergebnisse für PROMIS MMRM-Analyse – Elternberichtet (8–18 Jahre)

Studie	**Selumetinib 25 mg/m² BID**				
SPRINT Phase II, Stratum 1 **Datenschnitt: 31. März 2021**	**Alle Patienten im Alter von 8–18 Jahren (FAS)** **N = 33**				
	N*	**adjustierter Mittelwert der Veränderung gegenüber Baseline**	**SE**	**[95 %-KI]**	**p-Wert**
PROMIS – elternberichtet – Itembank Mobilität					
Zyklus 3	22	1,48	0,665	[0,02; 2,95]	0,048
Zyklus 5	23	0,43	0,990	[-1,63; 2,50]	0,667
Zyklus 9	23	1,40	1,102	[-0,91; 3,70]	0,220
Zyklus 13	21	2,59	0,968	[0,56; 4,61]	0,015
Zyklus 25	14	4,02	2,390	[-2,30; 10,35]	0,159
Zyklus 37	12	4,23	1,315	[0,91; 7,56]	0,022
Zyklus 49	9	–	–	–	–
PROMIS – elternberichtet – Itembank obere Extremitäten					
Zyklus 3	22	-0,45	1,550	[-3,70; 2,81]	0,777
Zyklus 5	22	0,17	1,087	[-2,11; 2,46]	0,874
Zyklus 9	22	-1,26	1,412	[-4,23; 1,72]	0,386
Zyklus 13	20	1,44	1,586	[-1,92; 4,80]	0,378
Zyklus 25	13	4,64	1,611	[1,17; 8,12]	0,013
Zyklus 37	11	4,16	1,926	[-0,11; 8,43]	0,055
Zyklus 49	8	–	–	–	–

BID: Zweimal täglich; FAS: Full Analysis Set; KI: Konfidenzintervall; MMRM: Mixed Model Repeated Measures; PN: Plexiformes Neurofibrom; PROMIS: Patient-Reported Outcomes Measurement Information System; SE: Standardfehler

N*: in die Analyse eingeschlossene Patienten. Die Analyse wird bis zu dem Zyklus, zu dem noch für mindestens 10 Patienten beobachtete Werte vorliegen, durchgeführt

Das MMRM-Modell basiert auf den transformierten Werten.

Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 5. Stand: 19.04.2023. 2023.

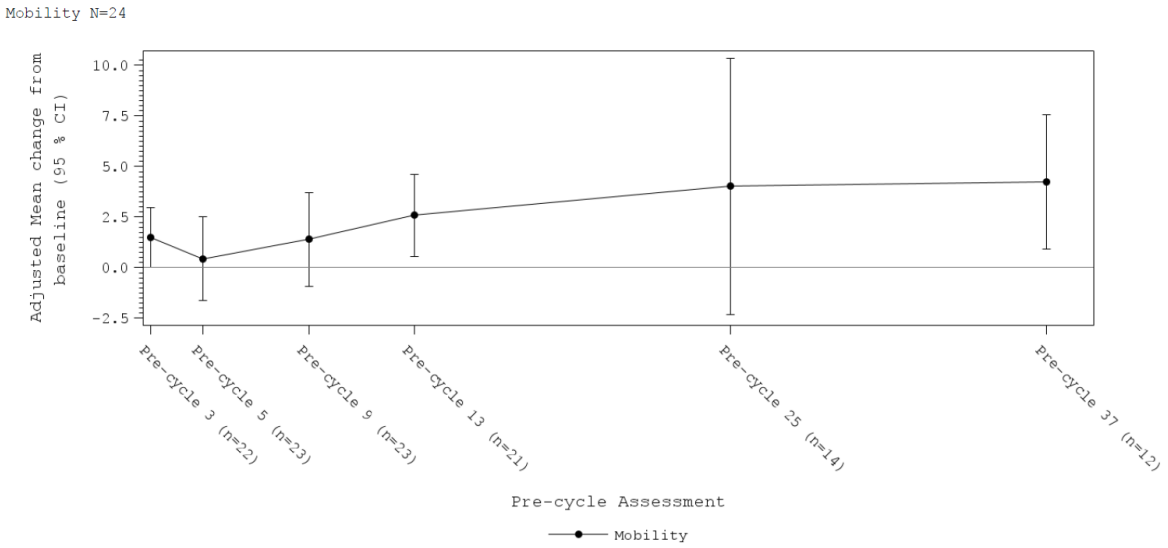

Abbildung 7: Elternberichteter (8–18 Jahre) PROMIS – Itembank Mobilität – Mittlere Veränderung gegenüber Baseline mittels MMRM
Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 5. Stand: 19.04.2023. 2023.

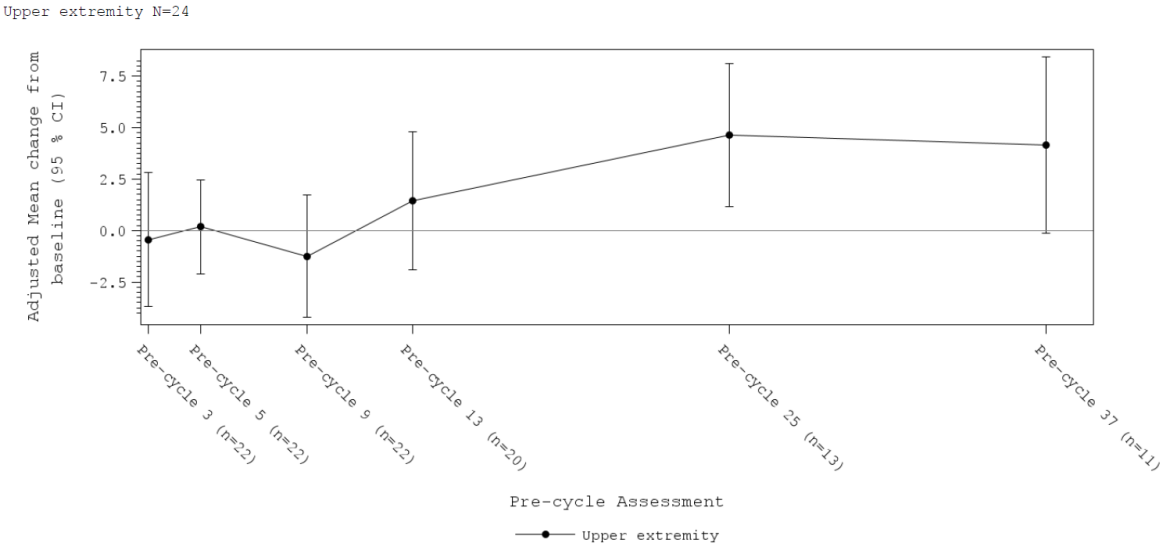

Abbildung 8: Elternberichteter (8–18 Jahre) PROMIS – Itembank obere Extremitäten – Mittlere Veränderung gegenüber Baseline mittels MMRM
Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 5. Stand: 19.04.2023. 2023.

1.7.4 PROMIS Responderanalysen

1.7.4.1 PROMIS Responderanalyse – Elternberichtet (8-18 Jahre)

Tabelle 7: Ergebnisse für den PROMIS Responderanalyse – Elternberichtet (8-18 Jahre)

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Verbesserung ≥ 4,8 Punkte n/N* (%[a]) [95 %-KI[b]]**	**Verschlechterung ≥ 4,8 Punkte n/N* (%[a]) [95 %-KI[b]]**
Itembank Mobilität		
Zyklus 3	4/22 (18,2) [5,2; 40,3]	0/22 (0,0) [0,0; 15,4]
Zyklus 5	6/23 (26,1) [10,2; 48,4]	1/23 (4,3) [0,1; 21,9]
Zyklus 9	6/23 (26,1) [10,2; 48,4]	2/23 (8,7) [1,1; 28,0]
Zyklus 13	5/21 (23,8) [8,2; 47,2]	0/21 (0,0) [0,0; 16,1]
Zyklus 25	5/14 (35,7) [12,8; 64,9]	0/14 (0,0) [0,0; 23,2]
Zyklus 37	5/12 (41,7) [15,2; 72,3]	0/12 (0,0) [0,0; 26,5]
Zyklus 49	2/9 (22,2) [2,8; 60,0]	0/9 (0,0) [0,0; 33,6]
Gesamt	14/23 (60,9) [38,5; 80,3]	2/23 (8,7) [1,1; 28,0]
Itembank obere Extremitäten		
Zyklus 3	1/22 (4,5) [0,1; 22,8]	3/22 (13,6) [2,9; 34,9]
Zyklus 5	2/22 (9,1) [1,1; 29,2]	0/22 (0,0) [0,0; 15,4]
Zyklus 9	3/22 (13,6) [2,9; 34,9]	3/22 (13,6) [2,9; 34,9]
Zyklus 13	5/20 (25,0) [8,7; 49,1]	0/20 (0,0) [0,0; 16,8]
Zyklus 25	3/13 (23,1) [5,0; 53,8]	0/13 (0,0) [0,0; 24,7]
Zyklus 37	4/11 (36,4) [10,9; 69,2]	0/11 (0,0) [0,0; 28,5]
Zyklus 49	3/8 (37,5) [8,5; 75,5]	0/8 (0,0) [0,0; 36,9]
Gesamt	8/22 (36,4) [17,2; 59,3]	4/22 (18,2) [5,2; 40,3]

BID: Zweimal täglich; KI: Konfidenzintervall; PROMIS: Patient-Reported Outcomes Measurement Information System

N*: in die Analyse eingeschlossene Patienten

a: Die Prozentsätze basieren auf der Anzahl der Patienten mit einem vorhandenen Wert zu dem jeweiligen Zeitpunkt

b: Konfidenzintervalle wurden mit der Clopper-Pearson-Methode für binomiale Verteilungen berechnet.

Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 8. Stand: 02.06.2023. 2023.

1.8 Endpunkt Motorfunktion: Manual Muscle Test (MMT)

1.8.1 Subgruppenanalysen zur Motorfunktion: MMT

1.8.1.1 Subgruppenanalysen MMT Veränderung gegenüber Baseline

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: 31 March 2021 (DC02)

		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=8)	4,34	0,923	4,76	2,4	5,0	57,9	8	0,36	0,417	0,28	0,0	1,2	57,9
	Pre-cycle 49 (n=6)	4,61	0,442	4,71	4,0	5,0	68,4	6	0,38	0,298	0,31	0,0	0,9	68,4
	Pre-cycle 61 (n=1)	NC	NC	NC	4,3	4,3	94,7	1	NC	NC	NC	0,7	0,7	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
	Pre-cycle 37 (n=2)	NC	NC	NC	3,7	4,8	89,5	2	NC	NC	NC	0,0	1,2	89,5
	Pre-cycle 49 (n=2)	NC	NC	NC	4,0	4,4	89,5	2	NC	NC	NC	0,3	0,9	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=4)	4,28	1,266	4,86	2,4	5,0	78,9	4	0,30	0,192	0,28	0,1	0,6	78,9
	Pre-cycle 49 (n=2)	NC	NC	NC	5,0	5,0	89,5	2	NC	NC	NC	0,3	0,3	89,5
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
	Pre-cycle 37 (n=2)	NC	NC	NC	4,2	5,0	89,5	2	NC	NC	NC	0,0	0,5	89,5
	Pre-cycle 49 (n=2)	NC	NC	NC	4,3	5,0	89,5	2	NC	NC	NC	0,0	0,6	89,5
	Pre-cycle 61 (n=1)	NC	NC	NC	4,3	4,3	94,7	1	NC	NC	NC	0,7	0,7	94,7

[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

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=8)	4,84	0,207	4,93	4,5	5,0	42,9	8	0,25	0,324	0,28	-0,3	0,8	42,9
	Pre-cycle 49 (n=4)	4,98	0,039	5,00	4,9	5,0	71,4	4	0,27	0,187	0,33	0,0	0,4	71,4
	Pre-cycle 61 (n=1)	NC	NC	NC	4,9	4,9	92,9	1	NC	NC	NC	0,4	0,4	92,9
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
	Pre-cycle 37 (n=3)	4,79	0,244	4,84	4,5	5,0	78,6	3	0,00	0,294	0,00	-0,3	0,3	78,6
	Pre-cycle 49 (n=2)	NC	NC	NC	4,9	5,0	85,7	2	NC	NC	NC	0,0	0,4	85,7
	Pre-cycle 61 (n=1)	NC	NC	NC	4,9	4,9	92,9	1	NC	NC	NC	0,4	0,4	92,9
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
	Pre-cycle 37 (n=4)	4,86	0,238	4,96	4,5	5,0	71,4	4	0,48	0,220	0,44	0,3	0,8	71,4
	Pre-cycle 49 (n=2)	NC	NC	NC	5,0	5,0	85,7	2	NC	NC	NC	0,3	0,4	85,7
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
	Pre-cycle 37 (n=1)	NC	NC	NC	4,9	4,9	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

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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: 31 March 2021 (DC02)

		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=4)	4,76	0,199	4,76	4,5	5,0	63,6	4	0,34	0,655	0,19	-0,3	1,2	63,6
	Pre-cycle 49 (n=2)	NC	NC	NC	4,4	5,0	81,8	2	NC	NC	NC	0,3	0,9	81,8
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
	Pre-cycle 37 (n=2)	NC	NC	NC	4,5	4,8	81,8	2	NC	NC	NC	-0,3	1,2	81,8
	Pre-cycle 49 (n=1)	NC	NC	NC	4,4	4,4	90,9	1	NC	NC	NC	0,9	0,9	90,9
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=2)	NC	NC	NC	4,7	5,0	81,8	2	NC	NC	NC	0,1	0,3	81,8
	Pre-cycle 49 (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

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=6)	4,53	1,053	4,98	2,4	5,0	45,5	6	0,23	0,207	0,25	0,0	0,6	45,5
	Pre-cycle 49 (n=5)	4,98	0,035	5,00	4,9	5,0	54,5	5	0,18	0,173	0,25	0,0	0,4	54,5
	Pre-cycle 61 (n=1)	NC	NC	NC	4,9	4,9	90,9	1	NC	NC	NC	0,4	0,4	90,9
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
	Pre-cycle 37 (n=2)	NC	NC	NC	4,8	5,0	81,8	2	NC	NC	NC	0,0	0,3	81,8
	Pre-cycle 49 (n=2)	NC	NC	NC	4,9	5,0	81,8	2	NC	NC	NC	0,0	0,4	81,8
	Pre-cycle 61 (n=1)	NC	NC	NC	4,9	4,9	90,9	1	NC	NC	NC	0,4	0,4	90,9
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
	Pre-cycle 37 (n=3)	4,12	1,498	4,96	2,4	5,0	72,7	3	0,35	0,173	0,25	0,3	0,6	72,7
	Pre-cycle 49 (n=2)	NC	NC	NC	5,0	5,0	81,8	2	NC	NC	NC	0,3	0,3	81,8
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
	Pre-cycle 37 (n=1)	NC	NC	NC	5,0	5,0	90,9	1	NC	NC	NC	0,0	0,0	90,9
	Pre-cycle 49 (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

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=6)	4,53	0,536	4,70	3,7	5,0	45,5	6	0,36	0,296	0,44	0,0	0,8	45,5
	Pre-cycle 49 (n=3)	4,42	0,516	4,25	4,0	5,0	72,7	3	0,43	0,136	0,41	0,3	0,6	72,7
	Pre-cycle 61 (n=1)	NC	NC	NC	4,3	4,3	90,9	1	NC	NC	NC	0,7	0,7	90,9
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
	Pre-cycle 37 (n=1)	NC	NC	NC	3,7	3,7	90,9	1	NC	NC	NC	0,0	0,0	90,9
	Pre-cycle 49 (n=1)	NC	NC	NC	4,0	4,0	90,9	1	NC	NC	NC	0,3	0,3	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
	Pre-cycle 37 (n=3)	4,82	0,278	4,96	4,5	5,0	72,7	3	0,55	0,196	0,46	0,4	0,8	72,7
	Pre-cycle 49 (n=1)	NC	NC	NC	5,0	5,0	90,9	1	NC	NC	NC	0,4	0,4	90,9
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
	Pre-cycle 37 (n=2)	NC	NC	NC	4,2	4,9	81,8	2	NC	NC	NC	0,1	0,5	81,8
	Pre-cycle 49 (n=1)	NC	NC	NC	4,3	4,3	90,9	1	NC	NC	NC	0,6	0,6	90,9
	Pre-cycle 61 (n=1)	NC	NC	NC	4,3	4,3	90,9	1	NC	NC	NC	0,7	0,7	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

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1.8.1.2 Subgruppenanalysen MMT MMRM-Analyse

Table 4.1.4.1 Change from baseline for Motor function, Range of Motion, MMRM - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
Strength MMT [a]	n	16	15	15
	Adjusted mean	0.17	0.04	0.24
	Standard Error	0.079	0.165	0.091
	95% CI	0.00, 0.34	-0.32, 0.40	0.04, 0.45
	p-value	0.050	0.826	0.026
Range of motion (degrees) [b]	n	15	15	15
	Adjusted mean	97.90	94.65	97.24
	Standard Error	30.848	32.444	28.933
	95% CI	31.00, 164.80	24.29, 165.01	34.11, 160.36
	p-value	0.008	0.012	0.006

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.

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Table 4.1.4.1 Change from baseline for Motor function, Range of Motion, MMRM - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
Strength MMT [a]	n	10	8	6
	Adjusted mean	0.27	NC	NC
	Standard Error	0.125	NC	NC
	95% CI	0.00, 0.54	NC	NC
	p-value	0.051	NC	NC
Range of motion (degrees) [b]	n	10	9	7
	Adjusted mean	97.44	NC	NC
	Standard Error	31.957	NC	NC
	95% CI	26.79, 168.09	NC	NC
	p-value	0.012	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.

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Table 4.1.4.2 Change from baseline for Motor function, Range of Motion, MMRM - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
Strength MMT [a]	n	14	14	12
	Adjusted mean	0.05	0.18	0.17
	Standard Error	0.049	0.055	0.040
	95% CI	-0.06, 0.15	0.06, 0.30	0.08, 0.27
	p-value	0.364	0.006	0.002
Range of motion (degrees) [b]	n	13	14	11
	Adjusted mean	33.26	26.27	21.84
	Standard Error	15.817	20.596	22.309
	95% CI	-2.69, 69.21	-19.33, 71.88	-28.09, 71.77
	p-value	0.066	0.230	0.351

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.

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Table 4.1.4.2 Change from baseline for Motor function, Range of Motion, MMRM - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
Strength MMT [a]	n	10	8	4
	Adjusted mean	0.14	NC	NC
	Standard Error	0.068	NC	NC
	95% CI	-0.01, 0.30	NC	NC
	p-value	0.069	NC	NC
Range of motion (degrees) [b]	n	10	8	4
	Adjusted mean	36.52	NC	NC
	Standard Error	18.067	NC	NC
	95% CI	-3.88, 76.93	NC	NC
	p-value	0.072	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.

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Table 4.1.4.3 Change from baseline for Motor function, Range of Motion, MMRM - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
Strength MMT [a]	n	11	11	10
	Adjusted mean	0.27	0.22	0.27
	Standard Error	0.083	0.075	0.074
	95% CI	0.05, 0.49	0.02, 0.41	0.07, 0.47
	p-value	0.028	0.037	0.019
Range of motion (degrees) [b]	n	11	11	10
	Adjusted mean	65.60	63.81	73.43
	Standard Error	33.576	34.527	33.699
	95% CI	-13.65, 144.84	-17.36, 144.98	-5.91, 152.76
	p-value	0.091	0.106	0.065

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.

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Table 4.1.4.3 Change from baseline for Motor function, Range of Motion, MMRM - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
Strength MMT [a]	n	5	4	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	5	4	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.

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Table 4.1.4.4 Change from baseline for Motor function, Range of Motion, MMRM - PN status = Non-progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
Strength MMT [a]	n	10	9	8
	Adjusted mean	0.03	NC	NC
	Standard Error	0.048	NC	NC
	95% CI	-0.08, 0.15	NC	NC
	p-value	0.529	NC	NC
Range of motion (degrees) [b]	n	9	8	8
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.

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Table 4.1.4.4 Change from baseline for Motor function, Range of Motion, MMRM - PN status = Non-progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
Strength MMT [a]	n	8	6	5
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	8	7	6
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.

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Table 4.1.4.5 Change from baseline for Motor function, Range of Motion, MMRM - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
Strength MMT [a]	n	9	9	9
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	8	10	8
	Adjusted mean	NC	65.50	NC
	Standard Error	NC	35.259	NC
	95% CI	NC	-20.77, 151.77	NC
	p-value	NC	0.113	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.

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Table 4.1.4.5 Change from baseline for Motor function, Range of Motion, MMRM - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
Strength MMT [a]	n	7	6	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	7	6	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (right upper, right lower, right bilateral, left upper, left lower, left bilateral) as the target PN.

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Table 4.1.5.1 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Unilateral Upper				
Strength MMT [a]	n	6	6	6
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	5	4	5
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.1 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Unilateral Upper				
Strength MMT [a]	n	5	4	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	4	4	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.1 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Unilateral Lower				
Strength MMT [a]	n	4	4	4
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	4	4	4
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.1 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Unilateral Lower				
Strength MMT [a]	n	2	2	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	2	2	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.1 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Bilateral Upper				
Strength MMT [a]	n	5	4	4
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	5	6	5
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.1 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Bilateral Upper				
Strength MMT [a]	n	3	2	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	4	3	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.1 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Bilateral Lower				
Strength MMT [a]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.1 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Male
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Bilateral Lower				
Strength MMT [a]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.2 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Unilateral Upper				
Strength MMT [a]	n	5	5	5
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	4	5	4
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.2 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Unilateral Upper				
Strength MMT [a]	n	4	4	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	4	4	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.2 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Unilateral Lower				
Strength MMT [a]	n	8	8	6
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	8	8	6
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.2 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Unilateral Lower				
Strength MMT [a]	n	5	3	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	5	3	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.2 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Bilateral Upper				
Strength MMT [a]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.2 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Bilateral Upper				
Strength MMT [a]	n	1	1	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	1	1	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.2 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Bilateral Lower				
Strength MMT [a]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.2 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - Gender = Female
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Bilateral Lower				
Strength MMT [a]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.3 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Unilateral Upper				
Strength MMT [a]	n	3	3	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	3	3	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.3 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Unilateral Upper				
Strength MMT [a]	n	2	2	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	2	2	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.3 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Unilateral Lower				
Strength MMT [a]	n	7	7	6
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	7	7	6
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.3 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Unilateral Lower				
Strength MMT [a]	n	3	2	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	3	2	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.3 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Bilateral Upper				
Strength MMT [a]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.3 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Bilateral Upper				
Strength MMT [a]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.3 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Bilateral Lower				
Strength MMT [a]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

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Table 4.1.5.3 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Progressive
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Bilateral Lower				
Strength MMT [a]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f3.sas Executed: 2023-05-17T16:07

Table 4.1.5.4 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Unilateral Upper				
Strength MMT [a]	n	4	4	4
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	3	2	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f4.sas Executed: 2023-05-17T16:08

Table 4.1.5.4 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Unilateral Upper				
Strength MMT [a]	n	4	3	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	3	3	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f4.sas Executed: 2023-05-17T16:08

Table 4.1.5.4 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Unilateral Lower				
Strength MMT [a]	n	4	4	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	4	4	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f4.sas Executed: 2023-05-17T16:08

Table 4.1.5.4 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Unilateral Lower				
Strength MMT [a]	n	3	2	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	3	2	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f4.sas Executed: 2023-05-17T16:08

Table 4.1.5.4 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Bilateral Upper				
Strength MMT [a]	n	2	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	2	2	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f4.sas Executed: 2023-05-17T16:08

Table 4.1.5.4 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Bilateral Upper				
Strength MMT [a]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	2	2	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f4.sas Executed: 2023-05-17T16:08

Table 4.1.5.4 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Bilateral Lower				
Strength MMT [a]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f4.sas Executed: 2023-05-17T16:08

Table 4.1.5.4 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Bilateral Lower				
Strength MMT [a]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f4.sas Executed: 2023-05-17T16:08

Table 4.1.5.5 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Unilateral Upper				
Strength MMT [a]	n	4	4	4
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	3	4	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f5.sas Executed: 2023-05-17T16:08

Table 4.1.5.5 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Unilateral Upper				
Strength MMT [a]	n	3	3	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	3	3	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f5.sas Executed: 2023-05-17T16:08

Table 4.1.5.5 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Unilateral Lower				
Strength MMT [a]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f5.sas Executed: 2023-05-17T16:08

Table 4.1.5.5 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Unilateral Lower				
Strength MMT [a]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	1	1	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f5.sas Executed: 2023-05-17T16:08

Table 4.1.5.5 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Bilateral Upper				
Strength MMT [a]	n	4	4	4
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	4	5	4
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f5.sas Executed: 2023-05-17T16:08

Table 4.1.5.5 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Bilateral Upper				
Strength MMT [a]	n	3	2	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	3	2	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f5.sas Executed: 2023-05-17T16:08

Table 4.1.5.5 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
PN Quadrant - Bilateral Lower				
Strength MMT [a]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f5.sas Executed: 2023-05-17T16:08

Table 4.1.5.5 Change from baseline for Motor function, Range of Motion, MMRM by PN Quadrant - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
PN Quadrant - Bilateral Lower				
Strength MMT [a]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC
Range of motion (degrees) [b]	n	0	0	0
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures. MMT = Manual Muscle Test.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.
[a] Average strength score from all muscles in the same body quadrant (upper, lower) as the target PN.
[b] Sum of all the degrees of movement for each of the joints in the same body quadrant (upper, lower) as the target PN.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req16f5.sas Executed: 2023-05-17T16:08

Table 5.5.1.1 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=19) [a] 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
		Deterioration	0	0	0.0, 20.6
		No improvement or deterioration	15	93.8	69.8, 99.8
	Pre-cycle 9 (N=15)	Categories of change [d]			
		Improvement	1	6.7	0.2, 31.9
		Deterioration	1	6.7	0.2, 31.9
		No improvement or deterioration	13	86.7	59.5, 98.3
	Pre-cycle 13 (N=15)	Categories of change [d]			
		Improvement	1	6.7	0.2, 31.9
		Deterioration	0	0	0.0, 21.8
		No improvement or deterioration	14	93.3	68.1, 99.8
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	1	10.0	0.3, 44.5
		Deterioration	0	0	0.0, 30.8
		No improvement or deterioration	9	90.0	55.5, 99.7

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = Not Calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req28a1.sas Executed: 2023-06-01T12:30

Table 5.5.1.1 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=19) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 37 (N=8)	Categories of change [d]			
		Improvement	1	12.5	0.3, 52.7
		Deterioration	0	0	0.0, 36.9
		No improvement or deterioration	7	87.5	47.3, 99.7
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0.0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Overall (N=16)	Categories of change [d]			
		Improvement	1	6.3	0.2, 30.2
		Deterioration	1	6.3	0.2, 30.2
		No improvement or deterioration	14	87.5	61.7, 98.4
Strength MMT - Unilateral upper	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	0	0	0.0, 45.9
		Deterioration	0	0	0.0, 45.9
		No improvement or deterioration	6	100	54.1, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = Not Calculated.

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Table 5.5.1.1 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=19) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral upper	Pre-cycle 9 (N=6)	Categories of change [d]			
		Improvement	0	0	0.0, 45.9
		Deterioration	0	0	0.0, 45.9
		No improvement or deterioration	6	100	54.1, 100
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	0	0	0.0, 45.9
		Deterioration	0	0	0.0, 45.9
		No improvement or deterioration	6	100	54.1, 100
	Pre-cycle 25 (N=5)	Categories of change [d]			
		Improvement	0	0	0.0, 52.2
		Deterioration	0	0	0.0, 52.2
		No improvement or deterioration	5	100	47.8, 100
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = Not Calculated.

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Table 5.5.1.1 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=19) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral upper	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Overall (N=6)	Categories of change [d]			
		Improvement	0	0	0.0, 45.9
		Deterioration	0	0	0.0, 45.9
		No improvement or deterioration	6	100	54.1, 100
Strength MMT - Unilateral lower	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = Not Calculated.

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Table 5.5.1.1 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=19) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral lower	Pre-cycle 13 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = Not Calculated.

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Table 5.5.1.1 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=19) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral lower	Overall (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
Strength MMT - Bilateral upper	Pre-cycle 5 (N=5)	Categories of change [d]			
		Improvement	0	0	0.0, 52.2
		Deterioration	0	0	0.0, 52.2
		No improvement or deterioration	5	100	47.8, 100
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 13 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = Not Calculated.

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Table 5.5.1.1 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=19) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral upper	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Overall (N=5)	Categories of change [d]			
		Improvement	0	0	0.0, 52.2
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	4	80.0	28.4, 99.5

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = Not Calculated.

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Table 5.5.1.1 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Male (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=19) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral lower	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = Not Calculated.

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Table 5.5.1.2 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=14) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 5 (N=14)	Categories of change [d]			
		Improvement	0	0	0.0, 23.2
		Deterioration	0	0	0.0, 23.2
		No improvement or deterioration	14	100	76.8, 100
	Pre-cycle 9 (N=14)	Categories of change [d]			
		Improvement	0	0	0.0, 23.2
		Deterioration	0	0	0.0, 23.2
		No improvement or deterioration	14	100	76.8, 100
	Pre-cycle 13 (N=12)	Categories of change [d]			
		Improvement	0	0	0.0, 26.5
		Deterioration	0	0	0.0, 26.5
		No improvement or deterioration	12	100	73.5, 100
	Pre-cycle 25 (N=10)	Categories of change [d]			
		Improvement	0	0	0.0, 30.8
		Deterioration	0	0	0.0, 30.8
		No improvement or deterioration	10	100	69.2, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.2 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=14) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 37 (N=8)	Categories of change [d]			
		Improvement	1	12.5	0.3, 52.7
		Deterioration	0	0	0.0, 36.9
		No improvement or deterioration	7	87.5	47.3, 99.7
	Pre-cycle 49 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Overall (N=14)	Categories of change [d]			
		Improvement	1	7.1	0.2, 33.9
		Deterioration	0	0	0.0, 23.2
		No improvement or deterioration	13	92.9	66.1, 99.8
Strength MMT - Unilateral upper	Pre-cycle 5 (N=5)	Categories of change [d]			
		Improvement	0	0	0.0, 52.2
		Deterioration	0	0	0.0, 52.2
		No improvement or deterioration	5	100	47.8, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.2 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=14) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral upper	Pre-cycle 9 (N=5)	Categories of change [d]			
		Improvement	0	0	0.0, 52.2
		Deterioration	0	0	0.0, 52.2
		No improvement or deterioration	5	100	47.8, 100
	Pre-cycle 13 (N=5)	Categories of change [d]			
		Improvement	0	0	0.0, 52.2
		Deterioration	0	0	0.0, 52.2
		No improvement or deterioration	5	100	47.8, 100
	Pre-cycle 25 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.2 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=14) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral upper	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Overall (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0.0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
Strength MMT - Unilateral lower	Pre-cycle 5 (N=8)	Categories of change [d]			
		Improvement	0	0	0.0, 36.9
		Deterioration	0	0	0.0, 36.9
		No improvement or deterioration	8	100	63.1, 100
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	0	0	0.0, 36.9
		Deterioration	0	0	0.0, 36.9
		No improvement or deterioration	8	100	63.1, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.2 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=14) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral lower	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	0	0	0.0, 45.9
		Deterioration	0	0	0.0, 45.9
		No improvement or deterioration	6	100	54.1, 100
	Pre-cycle 25 (N=5)	Categories of change [d]			
		Improvement	0	0	0.0, 52.2
		Deterioration	0	0	0.0, 52.2
		No improvement or deterioration	5	100	47.8, 100
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.2 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=14) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral lower	Overall (N=8)	Categories of change [d]			
		Improvement	0	0	0.0, 36.9
		Deterioration	0	0	0.0, 36.9
		No improvement or deterioration	8	100	63.1, 100
Strength MMT - Bilateral upper	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.2 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - Gender = Female (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=14) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral upper	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.3 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] 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
		Deterioration	0	0	0.0, 28.5
		No improvement or deterioration	10	90.9	58.7, 99.8
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	1	9.1	0.2, 41.3
		Deterioration	0	0	0.0, 28.5
		No improvement or deterioration	10	90.9	58.7, 99.8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	1	10.0	0.3, 44.5
		Deterioration	0	0	0.0, 30.8
		No improvement or deterioration	9	90.0	55.5, 99.7
	Pre-cycle 25 (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0.0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.3 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 37 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=11)	Categories of change [d]			
		Improvement	1	9.1	0.2, 41.3
		Deterioration	0	0	0.0, 28.5
		No improvement or deterioration	10	90.9	58.7, 99.8
Strength MMT - Unilateral upper	Pre-cycle 5 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.3 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral upper	Pre-cycle 9 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 13 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.3 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral upper	Pre-cycle 49 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100
Strength MMT - Unilateral lower	Pre-cycle 5 (N=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	0	0	0.0, 41.0
		No improvement or deterioration	6	85.7	42.1, 99.6
	Pre-cycle 9 (N=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	0	0	0.0, 41.0
		No improvement or deterioration	6	85.7	42.1, 99.6

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.3 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral lower	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0.0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.3 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral lower	Overall (N=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	0	0	0.0, 41.0
		No improvement or deterioration	6	85.7	42.1, 99.6
Strength MMT - Bilateral lower	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.3 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral lower	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.4 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	0	0	0.0, 30.8
		Deterioration	0	0	0.0, 30.8
		No improvement or deterioration	10	100	69.2, 100
	Pre-cycle 9 (N=9)	Categories of change [d]			
		Improvement	0	0	0.0, 33.6
		Deterioration	0	0	0.0, 33.6
		No improvement or deterioration	9	100	66.4, 100
	Pre-cycle 13 (N=8)	Categories of change [d]			
		Improvement	0	0	0.0, 36.9
		Deterioration	0	0	0.0, 36.9
		No improvement or deterioration	8	100	63.1, 100
	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	0	0	0.0, 36.9
		Deterioration	0	0	0.0, 36.9
		No improvement or deterioration	8	100	63.1, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.4 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	0	0	0.0, 45.9
		Deterioration	0	0	0.0, 45.9
		No improvement or deterioration	6	100	54.1, 100
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	0	0	0.0, 52.2
		Deterioration	0	0	0.0, 52.2
		No improvement or deterioration	5	100	47.8, 100
	Overall (N=10)	Categories of change [d]			
		Improvement	0	0	0.0, 30.8
		Deterioration	0	0	0.0, 30.8
		No improvement or deterioration	10	100	69.2, 100
Strength MMT - Unilateral upper	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.4 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral upper	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 13 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 25 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.4 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral upper	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Overall (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
Strength MMT - Unilateral lower	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.4 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral lower	Pre-cycle 13 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.4 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral lower	Overall (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
Strength MMT - Bilateral upper	Pre-cycle 5 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.4 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral upper	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.5 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	0	0	0.0, 33.6
		Deterioration	0	0	0.0, 33.6
		No improvement or deterioration	9	100	66.4, 100
	Pre-cycle 9 (N=9)	Categories of change [d]			
		Improvement	0	0	0.0, 33.6
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	8	88.9	51.8, 99.7
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	0	0	0.0, 33.6
		Deterioration	0	0	0.0, 33.6
		No improvement or deterioration	9	100	66.4, 100
	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	0	0	0.0, 41.0
		Deterioration	0	0	0.0, 41.0
		No improvement or deterioration	7	100	59.0, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.5 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Total	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0.0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 49 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Overall (N=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	7	77.8	40.0, 97.2
Strength MMT - Unilateral upper	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.5 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral upper	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 13 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.5 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral upper	Pre-cycle 49 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
Strength MMT - Unilateral lower	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.5 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral lower	Pre-cycle 13 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.5 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Unilateral lower	Overall (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
Strength MMT - Bilateral upper	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 13 (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	0	0	0.0, 60.2
		No improvement or deterioration	4	100	39.8, 100

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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Table 5.5.1.5 Motor function primary outcome categories of change over time - percentage of patients with Improvement and Deterioration - PN status = Unknown (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Selumetinib 25 mg/m² BID (N=11) [a] Response category	n	% [b]	95% CI [c]
Strength MMT - Bilateral upper	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	0	0	0.0, 70.8
		Deterioration	0	0	0.0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 49 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=4)	Categories of change [d]			
		Improvement	0	0	0.0, 60.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	3	75.0	19.4, 99.4

[a] Patients with a motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who 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] Confidence intervals (CI) are calculated using Clopper-Pearson exact method for binomial proportions.
[d] Improvement and deterioration are defined using a threshold of 0.75 points at any timepoint post-baseline
MMT - Manual muscle test. NC = not calculated.

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1.9 Endpunkt Motorfunktion: Range of Motion (ROM)

1.9.1 Subgruppenanalysen zur Motorfunktion: ROM Veränderung gegenüber Baseline

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: 31 March 2021 (DC02)

		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=9)	985,33	435,550	969,00	374,0	1653,0	52,6	9	66,78	211,109	14,00	-180,0	446,0	52,6
	Pre-cycle 49 (n=7)	1080,86	578,450	1012,00	311,0	1804,0	63,2	7	146,43	196,687	157,00	-49,0	422,0	63,2
	Pre-cycle 61 (n=1)	NC	NC	NC	1884,0	1884,0	94,7	1	NC	NC	NC	415,0	415,0	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
	Pre-cycle 37 (n=2)	NC	NC	NC	374,0	478,0	89,5	2	NC	NC	NC	7,0	14,0	89,5
	Pre-cycle 49 (n=2)	NC	NC	NC	311,0	426,0	89,5	2	NC	NC	NC	-49,0	-45,0	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=4)	894,50	159,008	944,00	665,0	1025,0	78,9	4	100,75	197,133	109,00	-135,0	320,0	78,9
	Pre-cycle 49 (n=2)	NC	NC	NC	957,0	1012,0	89,5	2	NC	NC	NC	157,0	363,0	89,5
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
	Pre-cycle 37 (n=3)	1479,33	150,918	1405,00	1380,0	1653,0	84,2	3	59,00	338,226	-89,00	-180,0	446,0	84,2
	Pre-cycle 49 (n=3)	1620,00	216,797	1675,00	1381,0	1804,0	84,2	3	199,67	225,567	206,00	-29,0	422,0	84,2
	Pre-cycle 61 (n=1)	NC	NC	NC	1884,0	1884,0	94,7	1	NC	NC	NC	415,0	415,0	94,7

[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 2.4.2.1.2 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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=8)	804,75	345,557	794,00	505,0	1556,0	42,9	8	53,50	88,135	38,50	-33,0	240,0	42,9
	Pre-cycle 49 (n=4)	684,50	206,211	668,50	502,0	899,0	71,4	4	12,50	40,764	24,50	-46,0	47,0	71,4
	Pre-cycle 61 (n=1)	NC	NC	NC	490,0	490,0	92,9	1	NC	NC	NC	35,0	35,0	92,9
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
	Pre-cycle 37 (n=3)	512,00	12,124	505,00	505,0	526,0	78,6	3	34,00	21,932	43,00	9,0	50,0	78,6
	Pre-cycle 49 (n=2)	NC	NC	NC	502,0	514,0	85,7	2	NC	NC	NC	31,0	47,0	85,7
	Pre-cycle 61 (n=1)	NC	NC	NC	490,0	490,0	92,9	1	NC	NC	NC	35,0	35,0	92,9
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
	Pre-cycle 37 (n=4)	836,50	57,905	824,00	783,0	915,0	71,4	4	53,75	127,756	4,00	-33,0	240,0	71,4
	Pre-cycle 49 (n=2)	NC	NC	NC	823,0	899,0	85,7	2	NC	NC	NC	-46,0	18,0	85,7
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
	Pre-cycle 37 (n=1)	NC	NC	NC	1556,0	1556,0	92,9	1	NC	NC	NC	111,0	111,0	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: 31 March 2021 (DC02)

		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=4)	717,75	262,279	712,00	478,0	969,0	63,6	4	91,25	152,823	19,00	7,0	320,0	63,6
	Pre-cycle 49 (n=2)	NC	NC	NC	426,0	1012,0	81,8	2	NC	NC	NC	-45,0	363,0	81,8
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
	Pre-cycle 37 (n=2)	NC	NC	NC	478,0	505,0	81,8	2	NC	NC	NC	7,0	9,0	81,8
	Pre-cycle 49 (n=1)	NC	NC	NC	426,0	426,0	90,9	1	NC	NC	NC	-45,0	-45,0	90,9
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=2)	NC	NC	NC	919,0	969,0	81,8	2	NC	NC	NC	29,0	320,0	81,8
	Pre-cycle 49 (n=1)	NC	NC	NC	1012,0	1012,0	90,9	1	NC	NC	NC	363,0	363,0	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

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	956,29	440,990	915,00	505,0	1653,0	36,4	7	63,86	209,055	43,00	-180,0	446,0	36,4
	Pre-cycle 49 (n=6)	1009,50	507,402	928,00	502,0	1804,0	45,5	6	107,67	165,840	39,00	-29,0	422,0	45,5
	Pre-cycle 61 (n=1)	NC	NC	NC	490,0	490,0	90,9	1	NC	NC	NC	35,0	35,0	90,9
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
	Pre-cycle 37 (n=2)	NC	NC	NC	505,0	526,0	81,8	2	NC	NC	NC	43,0	50,0	81,8
	Pre-cycle 49 (n=2)	NC	NC	NC	502,0	514,0	81,8	2	NC	NC	NC	31,0	47,0	81,8
	Pre-cycle 61 (n=1)	NC	NC	NC	490,0	490,0	90,9	1	NC	NC	NC	35,0	35,0	90,9
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
	Pre-cycle 37 (n=3)	868,33	184,481	915,00	665,0	1025,0	72,7	3	29,33	162,050	34,00	-135,0	189,0	72,7
	Pre-cycle 49 (n=2)	NC	NC	NC	899,0	957,0	81,8	2	NC	NC	NC	18,0	157,0	81,8
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
	Pre-cycle 37 (n=2)	NC	NC	NC	1405,0	1653,0	81,8	2	NC	NC	NC	-180,0	446,0	81,8
	Pre-cycle 49 (n=2)	NC	NC	NC	1381,0	1804,0	81,8	2	NC	NC	NC	-29,0	422,0	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

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=6)	956,83	434,510	824,00	374,0	1556,0	45,5	6	36,17	119,962	-6,00	-89,0	240,0	45,5
	Pre-cycle 49 (n=3)	936,33	689,026	823,00	311,0	1675,0	72,7	3	37,00	146,366	-46,00	-49,0	206,0	72,7
	Pre-cycle 61 (n=1)	NC	NC	NC	1884,0	1884,0	90,9	1	NC	NC	NC	415,0	415,0	90,9
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
	Pre-cycle 37 (n=1)	NC	NC	NC	374,0	374,0	90,9	1	NC	NC	NC	14,0	14,0	90,9
	Pre-cycle 49 (n=1)	NC	NC	NC	311,0	311,0	90,9	1	NC	NC	NC	-49,0	-49,0	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
	Pre-cycle 37 (n=3)	810,33	30,353	805,00	783,0	843,0	72,7	3	60,33	155,635	-26,00	-33,0	240,0	72,7
	Pre-cycle 49 (n=1)	NC	NC	NC	823,0	823,0	90,9	1	NC	NC	NC	-46,0	-46,0	90,9
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
	Pre-cycle 37 (n=2)	NC	NC	NC	1380,0	1556,0	81,8	2	NC	NC	NC	-89,0	111,0	81,8
	Pre-cycle 49 (n=1)	NC	NC	NC	1675,0	1675,0	90,9	1	NC	NC	NC	206,0	206,0	90,9
	Pre-cycle 61 (n=1)	NC	NC	NC	1884,0	1884,0	90,9	1	NC	NC	NC	415,0	415,0	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

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1.10 Endpunkt Motorfunktion: Grooved Pegboard-Test, Greifkraft und Schlüsselgriff sowie Beinlängendiskrepanz

1.10.1 Subgruppenanalysen zur Motorfunktion: Grooved Pegboard-Test, Greifkraft und Schlüsselgriff sowie Beinlängendiskrepanz – Veränderung gegenüber Baseline

Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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=9)	103.77	49.773	89.78	60.2	228.2	52.6	9	-0.92	44.114	-10.99	-59.8	63.5	52.6
	Pre-cycle 37 (n=7)	83.88	19.830	82.00	65.5	126.2	63.2	7	-10.80	35.825	-6.51	-84.1	22.0	63.2
	Pre-cycle 49 (n=5)	67.81	26.790	74.13	21.2	86.1	73.7	5	-26.62	46.751	-28.43	-75.5	25.0	73.7

[a] Male 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.

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Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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, 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
	Pre-cycle 37 (n=6)	103.97	34.131	91.43	82.8	172.1	68.4	6	3.65	25.543	-2.48	-20.9	42.0	68.4
	Pre-cycle 49 (n=5)	91.34	47.381	82.50	25.6	146.5	73.7	5	0.10	60.459	-3.95	-79.3	67.0	73.7

[a] Male 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.

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Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 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=9)	1.79	2.285	1.13	-0.1	7.3	52.6	9	-2.22	3.997	-2.14	-12.2	1.1	52.6
	Pre-cycle 37 (n=7)	0.41	1.028	0.04	-0.6	2.2	63.2	7	-2.72	4.747	-0.52	-13.0	0.4	63.2
	Pre-cycle 49 (n=5)	-0.29	1.162	0.05	-2.3	0.6	73.7	5	-4.30	4.725	-2.74	-12.5	-0.4	73.7

[a] Male 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.

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Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=6)	0.96	1.335	0.34	-0.1	3.4	68.4	6	-1.33	1.804	-1.13	-3.5	1.0	68.4
	Pre-cycle 49 (n=5)	0.43	1.263	0.41	-1.4	1.9	73.7	5	-1.82	1.642	-1.88	-3.2	0.9	73.7

[a] Male 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.

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Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 # 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=9)	1.00	1.000	1.00	0.0	2.0	52.6	9	0.00	1.000	0.00	-1.0	2.0	52.6
	Pre-cycle 37 (n=6)	1.50	1.761	1.00	0.0	4.0	68.4	6	0.50	2.510	0.50	-3.0	3.0	68.4
	Pre-cycle 49 (n=5)	0.40	0.548	0.00	0.0	1.0	73.7	5	-0.80	1.304	0.00	-3.0	0.0	73.7

[a] Male 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.

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Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=6)	1.83	1.472	1.50	0.0	4.0	68.4	6	0.00	2.098	0.00	-3.0	3.0	68.4
	Pre-cycle 49 (n=5)	1.40	1.140	1.00	0.0	3.0	73.7	5	-0.40	2.191	-1.00	-3.0	3.0	73.7

[a] Male 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.

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Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 (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
	Pre-cycle 37 (n=4)	14.33	11.385	14.00	1.3	28.0	78.9	3	6.63	8.187	10.00	-2.7	12.6	84.2
	Pre-cycle 49 (n=3)	20.40	12.345	17.30	9.9	34.0	84.2	2	NC	NC	NC	-0.7	28.6	89.5

[a] Male 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.

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Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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]
Right hand grip strength (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
	Pre-cycle 37 (n=4)	19.65	12.254	19.30	5.0	35.0	78.9	3	10.91	5.521	13.10	4.6	15.0	84.2
	Pre-cycle 49 (n=3)	23.30	13.552	23.00	9.9	37.0	84.2	2	NC	NC	NC	3.0	30.8	89.5

[a] Male 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.

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Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 Key-pinch strength (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
	Pre-cycle 37 (n=4)	4.77	2.129	4.95	2.2	7.0	78.9	3	1.35	0.450	1.50	0.8	1.7	84.2
	Pre-cycle 49 (n=2)	NC	NC	NC	5.5	7.8	89.5	1	NC	NC	NC	2.3	2.3	94.7

[a] Male 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.

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Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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]
Right hand Key-pinch strength (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
	Pre-cycle 37 (n=4)	5.99	1.415	6.40	4.0	7.2	78.9	3	2.22	1.111	2.50	1.0	3.2	84.2
	Pre-cycle 49 (n=2)	NC	NC	NC	4.6	7.5	89.5	1	NC	NC	NC	2.5	2.5	94.7

[a] Male 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.

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Table 4.2.1.1 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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]
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=7)	1.73	1.848	1.50	0.0	5.5	63.2	5	-1.42	0.952	-1.10	-3.0	-0.5	73.7
	Pre-cycle 49 (n=4)	2.20	1.651	1.65	1.0	4.5	78.9	3	-1.63	2.098	-0.90	-4.0	0.0	84.2

[a] Male 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=5)	78.98	11.611	72.00	69.9	94.8	64.3	5	-14.86	26.881	-11.00	-57.0	9.0	64.3
	Pre-cycle 49 (n=2)	NC	NC	NC	64.5	118.7	85.7	2	NC	NC	NC	-33.1	3.6	85.7

[a] Female 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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, 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
	Pre-cycle 37 (n=5)	84.10	16.259	77.39	68.0	104.0	64.3	5	-31.97	34.711	-25.56	-84.0	-1.2	64.3
	Pre-cycle 49 (n=2)	NC	NC	NC	74.9	76.3	85.7	2	NC	NC	NC	-44.4	-2.3	85.7

[a] Female 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=5)	0.42	0.092	0.40	0.3	0.6	64.3	5	-0.86	2.105	0.24	-4.0	0.9	64.3
	Pre-cycle 49 (n=2)	NC	NC	NC	-0.2	5.1	85.7	2	NC	NC	NC	0.4	0.8	85.7

[a] Female 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=5)	0.68	1.158	0.62	-0.3	2.6	64.3	5	-1.01	0.917	-1.03	-2.3	-0.1	64.3
	Pre-cycle 49 (n=2)	NC	NC	NC	0.4	0.5	85.7	2	NC	NC	NC	-0.7	-0.2	85.7

[a] Female 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 # 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
	Pre-cycle 37 (n=5)	0.80	1.095	0.00	0.0	2.0	64.3	5	-1.80	1.789	-2.00	-4.0	0.0	64.3
	Pre-cycle 49 (n=2)	NC	NC	NC	1.0	1.0	85.7	2	NC	NC	NC	-5.0	1.0	85.7

[a] Female 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=5)	1.00	1.414	0.00	0.0	3.0	64.3	5	-3.60	6.950	-1.00	-16.0	0.0	64.3
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	0.0	85.7	2	NC	NC	NC	-1.0	0.0	85.7

[a] Female 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 (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
	Pre-cycle 37 (n=3)	15.51	10.836	9.85	8.7	28.0	78.6	2	NC	NC	NC	-18.6	9.2	85.7
	Pre-cycle 49 (n=1)	NC	NC	NC	29.7	29.7	92.9	1	NC	NC	NC	2.4	2.4	92.9

[a] Female 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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]
Right hand grip strength (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
	Pre-cycle 37 (n=3)	11.39	3.465	10.00	8.8	15.3	78.6	2	NC	NC	NC	-15.5	4.7	85.7
	Pre-cycle 49 (n=1)	NC	NC	NC	29.7	29.7	92.9	1	NC	NC	NC	5.4	5.4	92.9

[a] Female 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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 Key-pinch strength (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
	Pre-cycle 37 (n=3)	13.94	12.759	6.82	6.3	28.7	78.6	2	NC	NC	NC	1.0	20.7	85.7
	Pre-cycle 49 (n=1)	NC	NC	NC	8.0	8.0	92.9	1	NC	NC	NC	0.0	0.0	92.9

[a] Female 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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]
Right hand Key-pinch strength (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
	Pre-cycle 37 (n=3)	13.06	13.254	6.36	4.5	28.3	78.6	2	NC	NC	NC	1.1	20.3	85.7
	Pre-cycle 49 (n=1)	NC	NC	NC	8.8	8.8	92.9	1	NC	NC	NC	0.8	0.8	92.9

[a] Female 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.

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Table 4.2.1.2 Motor function secondary outcome test 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: 31 March 2021 (DC02)

		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]
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
	Pre-cycle 37 (n=7)	0.74	0.973	0.20	0.0	2.5	50.0	6	-0.53	0.920	-0.75	-1.5	1.0	57.1
	Pre-cycle 49 (n=4)	0.75	0.645	0.75	0.0	1.5	71.4	4	-0.55	0.493	-0.50	-1.2	0.0	71.4

[a] Female 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=2)	NC	NC	NC	69.7	126.2	81.8	2	NC	NC	NC	-0.6	21.8	81.8
	Pre-cycle 49 (n=1)	NC	NC	NC	86.1	86.1	90.9	1	NC	NC	NC	15.9	15.9	90.9

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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, 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
	Pre-cycle 37 (n=2)	NC	NC	NC	93.9	172.1	81.8	2	NC	NC	NC	-1.3	26.4	81.8
	Pre-cycle 49 (n=1)	NC	NC	NC	146.5	146.5	90.9	1	NC	NC	NC	51.3	51.3	90.9

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=2)	NC	NC	NC	-0.4	2.2	81.8	2	NC	NC	NC	-3.9	0.4	81.8
	Pre-cycle 49 (n=1)	NC	NC	NC	0.3	0.3	90.9	1	NC	NC	NC	-3.3	-3.3	90.9

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.3	3.4	81.8	2	NC	NC	NC	-3.5	1.0	81.8
	Pre-cycle 49 (n=1)	NC	NC	NC	1.9	1.9	90.9	1	NC	NC	NC	-1.8	-1.8	90.9

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 # 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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.0	3.0	81.8	2	NC	NC	NC	-1.0	3.0	81.8
	Pre-cycle 49 (n=1)	NC	NC	NC	0.0	0.0	90.9	1	NC	NC	NC	-1.0	-1.0	90.9

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=2)	NC	NC	NC	2.0	3.0	81.8	2	NC	NC	NC	-3.0	1.0	81.8
	Pre-cycle 49 (n=1)	NC	NC	NC	2.0	2.0	90.9	1	NC	NC	NC	-3.0	-3.0	90.9

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 (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

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Right hand grip strength (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

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 Key-pinch strength (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

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Right hand Key-pinch strength (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

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.3 Motor function secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
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=4)	1.40	0.970	1.75	0.0	2.1	63.6	2	NC	NC	NC	-1.5	-1.1	81.8
	Pre-cycle 49 (n=2)	NC	NC	NC	1.0	2.3	81.8	1	NC	NC	NC	-0.9	-0.9	90.9

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=4)	116.08	74.809	80.49	75.2	228.2	63.6	4	5.31	39.369	-9.53	-23.3	63.5	63.6
	Pre-cycle 37 (n=4)	78.41	5.818	80.82	69.9	82.1	63.6	4	-6.42	11.562	-7.87	-18.9	9.0	63.6
	Pre-cycle 49 (n=3)	52.76	27.670	64.50	21.2	72.6	72.7	3	-31.63	36.949	-28.43	-70.1	3.6	72.7

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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, 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
	Pre-cycle 37 (n=3)	83.45	5.800	84.00	77.4	89.0	72.7	3	-14.28	11.299	-20.67	-20.9	-1.2	72.7
	Pre-cycle 49 (n=3)	59.01	28.929	75.07	25.6	76.3	72.7	3	-38.72	38.689	-34.55	-79.3	-2.3	72.7

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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=4)	2.14	3.497	0.67	-0.1	7.3	63.6	4	-1.16	1.207	-1.19	-2.2	0.0	63.6
	Pre-cycle 37 (n=4)	0.52	0.705	0.24	0.0	1.6	63.6	4	-0.28	1.121	-0.09	-1.8	0.9	63.6
	Pre-cycle 49 (n=3)	-0.61	1.517	-0.15	-2.3	0.6	72.7	3	-1.64	1.727	-2.53	-2.7	0.4	72.7

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=3)	0.80	0.781	0.62	0.1	1.7	72.7	3	-0.79	0.940	-0.39	-1.9	-0.1	72.7
	Pre-cycle 49 (n=3)	-0.14	1.058	0.41	-1.4	0.5	72.7	3	-1.73	1.461	-1.88	-3.1	-0.2	72.7

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 # 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=4)	1.25	0.957	1.50	0.0	2.0	63.6	4	0.00	0.816	0.00	-1.0	1.0	63.6
	Pre-cycle 37 (n=3)	1.33	2.309	0.00	0.0	4.0	72.7	3	0.67	2.082	0.00	-1.0	3.0	72.7
	Pre-cycle 49 (n=3)	1.00	0.000	1.00	1.0	1.0	72.7	3	0.33	0.577	0.00	0.0	1.0	72.7

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=3)	1.33	2.309	0.00	0.0	4.0	72.7	3	0.67	2.082	0.00	-1.0	3.0	72.7
	Pre-cycle 49 (n=3)	0.33	0.577	0.00	0.0	1.0	72.7	3	-0.33	0.577	0.00	-1.0	0.0	72.7

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 (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
	Pre-cycle 37 (n=4)	13.99	11.571	13.34	1.3	28.0	63.6	4	0.32	14.291	3.65	-18.6	12.6	63.6
	Pre-cycle 49 (n=3)	26.99	8.667	29.67	17.3	34.0	72.7	3	10.09	16.103	2.37	-0.7	28.6	72.7

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Right hand grip strength (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
	Pre-cycle 37 (n=4)	20.61	10.790	19.30	8.8	35.0	63.6	4	4.32	13.939	8.87	-15.5	15.0	63.6
	Pre-cycle 49 (n=3)	29.89	7.003	29.67	23.0	37.0	72.7	3	13.06	15.412	5.37	3.0	30.8	72.7

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 Key-pinch strength (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
	Pre-cycle 37 (n=4)	10.94	12.003	6.45	2.2	28.7	63.6	4	6.18	9.669	1.60	0.8	20.7	63.6
	Pre-cycle 49 (n=2)	NC	NC	NC	7.8	8.0	81.8	2	NC	NC	NC	0.0	2.3	81.8

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Right hand Key-pinch strength (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
	Pre-cycle 37 (n=4)	12.08	10.848	6.99	6.0	28.3	63.6	4	6.75	9.099	2.84	1.0	20.3	63.6
	Pre-cycle 49 (n=2)	NC	NC	NC	7.5	8.8	81.8	2	NC	NC	NC	0.8	2.5	81.8

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.4 Motor function secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
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
	Pre-cycle 37 (n=6)	0.75	0.935	0.50	0.0	2.5	45.5	6	-0.62	0.884	-0.75	-1.5	1.0	45.5
	Pre-cycle 49 (n=4)	0.88	0.629	1.00	0.0	1.5	63.6	4	-0.43	0.568	-0.25	-1.2	0.0	63.6

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=6)	78.75	11.378	77.00	65.5	94.8	45.5	6	-24.23	39.871	-16.63	-84.1	22.0	45.5
	Pre-cycle 49 (n=3)	92.62	23.250	85.00	74.1	118.7	72.7	3	-27.84	50.417	-33.05	-75.5	25.0	72.7

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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, 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
	Pre-cycle 37 (n=6)	87.99	15.773	90.83	68.0	104.0	45.5	6	-20.05	43.114	-14.60	-84.0	42.0	45.5
	Pre-cycle 49 (n=3)	94.81	28.130	82.50	74.9	127.0	72.7	3	6.21	56.386	-3.95	-44.4	67.0	72.7

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=6)	0.18	0.424	0.37	-0.6	0.6	45.5	6	-3.11	5.113	-1.33	-13.0	0.7	45.5
	Pre-cycle 49 (n=3)	1.65	2.955	0.05	-0.2	5.1	72.7	3	-4.06	7.358	-0.44	-12.5	0.8	72.7

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=6)	0.52	1.084	0.16	-0.3	2.6	45.5	6	-1.36	1.242	-1.23	-3.2	0.0	45.5
	Pre-cycle 49 (n=3)	0.53	0.690	0.40	-0.1	1.3	72.7	3	-1.01	2.047	-0.70	-3.2	0.9	72.7

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 # 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
	Pre-cycle 37 (n=6)	1.00	1.095	1.00	0.0	2.0	45.5	6	-1.67	2.251	-2.50	-4.0	2.0	45.5
	Pre-cycle 49 (n=3)	0.33	0.577	0.00	0.0	1.0	72.7	3	-2.67	2.517	-3.00	-5.0	0.0	72.7

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=6)	1.17	1.169	1.00	0.0	3.0	45.5	6	-3.00	6.419	-1.00	-16.0	1.0	45.5
	Pre-cycle 49 (n=3)	1.33	1.528	1.00	0.0	3.0	72.7	3	0.33	2.309	-1.00	-1.0	3.0	72.7

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 (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
	Pre-cycle 37 (n=3)	15.95	10.436	10.00	9.9	28.0	72.7	1	NC	NC	NC	9.2	9.2	90.9
	Pre-cycle 49 (n=1)	NC	NC	NC	9.9	9.9	90.9	0	NC	NC	NC	NC	NC	100.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Right hand grip strength (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
	Pre-cycle 37 (n=3)	10.11	5.166	10.00	5.0	15.3	72.7	1	NC	NC	NC	4.7	4.7	90.9
	Pre-cycle 49 (n=1)	NC	NC	NC	9.9	9.9	90.9	0	NC	NC	NC	NC	NC	100.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 Key-pinch strength (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
	Pre-cycle 37 (n=3)	5.72	1.507	6.33	4.0	6.8	72.7	1	NC	NC	NC	1.0	1.0	90.9
	Pre-cycle 49 (n=1)	NC	NC	NC	5.5	5.5	90.9	0	NC	NC	NC	NC	NC	100.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Right hand Key-pinch strength (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
	Pre-cycle 37 (n=3)	4.95	1.244	4.50	4.0	6.4	72.7	1	NC	NC	NC	1.1	1.1	90.9
	Pre-cycle 49 (n=1)	NC	NC	NC	4.6	4.6	90.9	0	NC	NC	NC	NC	NC	100.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.1.5 Motor function secondary outcome test scores and change from baseline over time - PN status = Unknown
(Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
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
	Pre-cycle 37 (n=4)	1.80	2.555	0.85	0.0	5.5	63.6	3	-1.33	1.528	-1.00	-3.0	0.0	72.7
	Pre-cycle 49 (n=2)	NC	NC	NC	0.5	4.5	81.8	2	NC	NC	NC	-4.0	-0.5	81.8

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	107.71	43.293	88.36	82.0	172.1	4	3.06	15.929	-2.48	-9.2	26.4
	Pre-cycle 49 (n=3)	83.39	62.685	82.50	21.2	146.5	3	-7.57	60.771	-3.95	-70.1	51.3

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=6)	107.38	61.662	84.30	60.2	228.2	6	-5.96	48.828	-18.56	-59.8	63.5
	Pre-cycle 37 (n=5)	85.01	24.202	79.63	65.5	126.2	5	-18.07	39.988	-6.51	-84.1	21.8
	Pre-cycle 49 (n=3)	61.96	32.048	74.13	25.6	86.1	3	-46.30	53.870	-75.45	-79.3	15.9

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	82.0	82.1	2	NC	NC	NC	-18.9	22.0
	Pre-cycle 49 (n=2)	NC	NC	NC	72.6	85.0	2	NC	NC	NC	-28.4	25.0

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	89.0	102.0	2	NC	NC	NC	-20.7	42.0
	Pre-cycle 49 (n=2)	NC	NC	NC	75.1	127.0	2	NC	NC	NC	-34.6	67.0

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	0.91	1.650	0.18	-0.1	3.4	4	-1.46	2.213	-1.67	-3.5	1.0
	Pre-cycle 49 (n=3)	-0.16	2.106	-0.08	-2.3	1.9	3	-2.51	0.695	-2.53	-3.2	-1.8

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=6)	1.74	2.903	0.50	-0.2	7.3	6	-2.89	4.723	-1.44	-12.2	0.7
	Pre-cycle 37 (n=5)	0.28	1.090	0.04	-0.6	2.2	5	-3.39	5.614	-0.39	-13.0	0.4
	Pre-cycle 49 (n=3)	-0.40	0.870	-0.16	-1.4	0.3	3	-5.89	5.794	-3.25	-12.5	-1.9

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.0	1.6	2	NC	NC	NC	-1.8	-0.5
	Pre-cycle 49 (n=2)	NC	NC	NC	0.1	0.6	2	NC	NC	NC	-2.7	-0.4

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.4	1.7	2	NC	NC	NC	-1.9	0.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.4	1.3	2	NC	NC	NC	-3.1	0.9

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	2.50	1.291	2.50	1.0	4.0	4	0.00	2.582	0.00	-3.0	3.0
	Pre-cycle 49 (n=3)	1.33	0.577	1.00	1.0	2.0	3	-1.33	1.528	-1.00	-3.0	0.0

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=6)	1.17	0.983	1.50	0.0	2.0	6	-0.17	1.169	-0.50	-1.0	2.0
	Pre-cycle 37 (n=4)	1.75	2.062	1.50	0.0	4.0	4	0.50	3.000	1.00	-3.0	3.0
	Pre-cycle 49 (n=3)	0.33	0.577	0.00	0.0	1.0	3	-1.33	1.528	-1.00	-3.0	0.0

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.0	2.0	2	NC	NC	NC	-1.0	2.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	1.0	2	NC	NC	NC	0.0	0.0

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.0	1.0	2	NC	NC	NC	-1.0	1.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	3.0	2	NC	NC	NC	-1.0	3.0

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	1.3	19.3	2	NC	NC	NC	-2.7	13.1
	Pre-cycle 49 (n=1)	NC	NC	NC	37.0	37.0	1	NC	NC	NC	30.8	30.8

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	18.0	19.3	2	NC	NC	NC	4.6	12.6
	Pre-cycle 49 (n=1)	NC	NC	NC	34.0	34.0	1	NC	NC	NC	28.6	28.6

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	10.0	35.0	1	NC	NC	NC	15.0	15.0
	Pre-cycle 49 (n=2)	NC	NC	NC	9.9	23.0	1	NC	NC	NC	3.0	3.0

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	5.0	28.0	1	NC	NC	NC	10.0	10.0
	Pre-cycle 49 (n=2)	NC	NC	NC	9.9	17.3	1	NC	NC	NC	-0.7	-0.7

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	2.2	6.8	2	NC	NC	NC	0.8	2.5

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	5.9	7.2	2	NC	NC	NC	1.7	3.2

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	4.0	6.0	1	NC	NC	NC	1.0	1.0
	Pre-cycle 49 (n=2)	NC	NC	NC	5.5	7.5	1	NC	NC	NC	2.5	2.5

[a] Male 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.

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Table 4.2.2.1 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Male (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	4.0	7.0	1	NC	NC	NC	1.5	1.5
	Pre-cycle 49 (n=2)	NC	NC	NC	4.6	7.8	1	NC	NC	NC	2.3	2.3

[a] Male 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	93.75	11.542	96.81	77.4	104.0	4	-41.95	36.153	-41.28	-84.0	-1.2
	Pre-cycle 49 (n=2)	NC	NC	NC	76.3	118.7	2	NC	NC	NC	-33.1	-2.3

[a] Female 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req17b2.sas Executed: 2023-05-18T13:18

Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	75.09	8.670	71.26	69.9	88.0	4	-17.84	23.377	-16.63	-47.1	9.0
	Pre-cycle 49 (n=2)	NC	NC	NC	64.5	74.9	2	NC	NC	NC	-44.4	3.6

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	72.0	72.0	1	NC	NC	NC	7.0	7.0

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	68.0	68.0	1	NC	NC	NC	-2.0	-2.0

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	1.07	1.003	0.71	0.3	2.6	4	-1.85	1.665	-1.67	-4.0	-0.1
	Pre-cycle 49 (n=2)	NC	NC	NC	0.5	5.1	2	NC	NC	NC	-0.2	0.8

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	0.21	0.362	0.39	-0.3	0.4	4	-0.62	1.405	-0.60	-2.1	0.9
	Pre-cycle 49 (n=2)	NC	NC	NC	-0.2	0.4	2	NC	NC	NC	-0.7	0.4

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	0.6	0.6	1	NC	NC	NC	0.7	0.7

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	-0.2	-0.2	1	NC	NC	NC	-0.2	-0.2

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	1.75	1.258	2.00	0.0	3.0	4	-5.00	7.572	-2.00	-16.0	0.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	1.0	2	NC	NC	NC	-5.0	0.0

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	0.50	1.000	0.00	0.0	2.0	4	-1.50	1.291	-1.50	-3.0	0.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	1.0	2	NC	NC	NC	-1.0	1.0

[a] Female 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.
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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	0.0	0.0	1	NC	NC	NC	0.0	0.0

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	0.0	0.0	1	NC	NC	NC	-1.0	-1.0

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	8.8	15.3	2	NC	NC	NC	-15.5	4.7
	Pre-cycle 49 (n=1)	NC	NC	NC	29.7	29.7	1	NC	NC	NC	5.4	5.4

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	8.7	28.0	2	NC	NC	NC	-18.6	9.2
	Pre-cycle 49 (n=1)	NC	NC	NC	29.7	29.7	1	NC	NC	NC	2.4	2.4

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	10.0	10.0	0	NC	NC	NC	NC	NC

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	9.9	9.9	0	NC	NC	NC	NC	NC

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	4.5	28.3	2	NC	NC	NC	1.1	20.3
	Pre-cycle 49 (n=1)	NC	NC	NC	8.8	8.8	1	NC	NC	NC	0.8	0.8

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	6.3	28.7	2	NC	NC	NC	1.0	20.7
	Pre-cycle 49 (n=1)	NC	NC	NC	8.0	8.0	1	NC	NC	NC	0.0	0.0

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	6.4	6.4	0	NC	NC	NC	NC	NC

[a] Female 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.

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Table 4.2.2.2 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - Gender = Female (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	6.8	6.8	0	NC	NC	NC	NC	NC

[a] Female 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	93.9	172.1	2	NC	NC	NC	-1.3	26.4
	Pre-cycle 49 (n=1)	NC	NC	NC	146.5	146.5	1	NC	NC	NC	51.3	51.3

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	69.7	126.2	2	NC	NC	NC	-0.6	21.8
	Pre-cycle 49 (n=1)	NC	NC	NC	86.1	86.1	1	NC	NC	NC	15.9	15.9

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.3	3.4	2	NC	NC	NC	-3.5	1.0
	Pre-cycle 49 (n=1)	NC	NC	NC	1.9	1.9	1	NC	NC	NC	-1.8	-1.8

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	-0.4	2.2	2	NC	NC	NC	-3.9	0.4
	Pre-cycle 49 (n=1)	NC	NC	NC	0.3	0.3	1	NC	NC	NC	-3.3	-3.3

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	2.0	3.0	2	NC	NC	NC	-3.0	1.0
	Pre-cycle 49 (n=1)	NC	NC	NC	2.0	2.0	1	NC	NC	NC	-3.0	-3.0

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.0	3.0	2	NC	NC	NC	-1.0	3.0
	Pre-cycle 49 (n=1)	NC	NC	NC	0.0	0.0	1	NC	NC	NC	-1.0	-1.0

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.3 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	77.4	82.0	2	NC	NC	NC	-9.2	-1.2
	Pre-cycle 49 (n=2)	NC	NC	NC	21.2	76.3	2	NC	NC	NC	-70.1	-2.3

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=3)	127.38	87.315	78.81	75.2	228.2	3	8.81	47.992	-10.99	-26.1	63.5
	Pre-cycle 37 (n=3)	77.83	7.245	79.63	69.9	84.0	3	-6.16	14.953	-6.51	-20.9	9.0
	Pre-cycle 49 (n=2)	NC	NC	NC	25.6	64.5	2	NC	NC	NC	-79.3	3.6

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	82.1	82.1	1	NC	NC	NC	-18.9	-18.9
	Pre-cycle 49 (n=1)	NC	NC	NC	72.6	72.6	1	NC	NC	NC	-28.4	-28.4

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	89.0	89.0	1	NC	NC	NC	-20.7	-20.7
	Pre-cycle 49 (n=1)	NC	NC	NC	75.1	75.1	1	NC	NC	NC	-34.6	-34.6

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.1	0.6	2	NC	NC	NC	-0.1	-0.1
	Pre-cycle 49 (n=2)	NC	NC	NC	-2.3	0.5	2	NC	NC	NC	-2.5	-0.2

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=3)	2.34	4.316	-0.12	-0.2	7.3	3	-1.03	1.013	-0.71	-2.2	-0.2
	Pre-cycle 37 (n=3)	0.18	0.171	0.13	0.0	0.4	3	0.14	0.652	-0.05	-0.4	0.9
	Pre-cycle 49 (n=2)	NC	NC	NC	-1.4	-0.2	2	NC	NC	NC	-1.9	0.4

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	1.6	1.6	1	NC	NC	NC	-1.8	-1.8
	Pre-cycle 49 (n=1)	NC	NC	NC	0.6	0.6	1	NC	NC	NC	-2.7	-2.7

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	1.7	1.7	1	NC	NC	NC	-1.9	-1.9
	Pre-cycle 49 (n=1)	NC	NC	NC	0.4	0.4	1	NC	NC	NC	-3.1	-3.1

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.0	4.0	2	NC	NC	NC	0.0	3.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	1.0	2	NC	NC	NC	0.0	0.0

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=3)	1.00	1.000	1.00	0.0	2.0	3	-0.33	0.577	0.00	-1.0	0.0
	Pre-cycle 37 (n=2)	NC	NC	NC	0.0	4.0	2	NC	NC	NC	0.0	3.0
	Pre-cycle 49 (n=2)	NC	NC	NC	1.0	1.0	2	NC	NC	NC	0.0	1.0

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	0.0	0.0	1	NC	NC	NC	-1.0	-1.0
	Pre-cycle 49 (n=1)	NC	NC	NC	1.0	1.0	1	NC	NC	NC	0.0	0.0

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	0.0	0.0	1	NC	NC	NC	-1.0	-1.0
	Pre-cycle 49 (n=1)	NC	NC	NC	0.0	0.0	1	NC	NC	NC	-1.0	-1.0

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=3)	9.81	9.040	8.83	1.3	19.3	3	-1.69	14.312	-2.70	-15.5	13.1
	Pre-cycle 49 (n=2)	NC	NC	NC	29.7	37.0	2	NC	NC	NC	5.4	30.8

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=3)	15.32	5.799	18.00	8.7	19.3	3	-0.47	16.227	4.63	-18.6	12.6
	Pre-cycle 49 (n=2)	NC	NC	NC	29.7	34.0	2	NC	NC	NC	2.4	28.6

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	35.0	35.0	1	NC	NC	NC	15.0	15.0
	Pre-cycle 49 (n=1)	NC	NC	NC	23.0	23.0	1	NC	NC	NC	3.0	3.0

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	28.0	28.0	1	NC	NC	NC	10.0	10.0
	Pre-cycle 49 (n=1)	NC	NC	NC	17.3	17.3	1	NC	NC	NC	-0.7	-0.7

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=3)	12.43	13.960	6.80	2.2	28.3	3	7.89	10.805	2.50	0.8	20.3
	Pre-cycle 49 (n=1)	NC	NC	NC	8.8	8.8	1	NC	NC	NC	0.8	0.8

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=3)	13.91	12.795	7.17	5.9	28.7	3	8.51	10.554	3.17	1.7	20.7
	Pre-cycle 49 (n=1)	NC	NC	NC	8.0	8.0	1	NC	NC	NC	0.0	0.0

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	6.0	6.0	1	NC	NC	NC	1.0	1.0
	Pre-cycle 49 (n=1)	NC	NC	NC	7.5	7.5	1	NC	NC	NC	2.5	2.5

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.4 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Non-progressive (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	7.0	7.0	1	NC	NC	NC	1.5	1.5
	Pre-cycle 49 (n=1)	NC	NC	NC	7.8	7.8	1	NC	NC	NC	2.3	2.3

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	95.11	9.025	96.81	82.8	104.0	4	-42.55	35.257	-41.28	-84.0	-3.6
	Pre-cycle 49 (n=2)	NC	NC	NC	82.5	118.7	2	NC	NC	NC	-33.1	-4.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	74.00	9.761	71.26	65.5	88.0	4	-41.11	32.385	-34.67	-84.1	-11.0
	Pre-cycle 49 (n=2)	NC	NC	NC	74.1	74.9	2	NC	NC	NC	-75.5	-44.4

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	72.0	82.0	2	NC	NC	NC	7.0	22.0
	Pre-cycle 49 (n=1)	NC	NC	NC	85.0	85.0	1	NC	NC	NC	25.0	25.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	68.0	102.0	2	NC	NC	NC	-2.0	42.0
	Pre-cycle 49 (n=1)	NC	NC	NC	127.0	127.0	1	NC	NC	NC	67.0	67.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	0.89	1.163	0.56	-0.1	2.6	4	-2.63	1.257	-2.76	-4.0	-1.0
	Pre-cycle 49 (n=2)	NC	NC	NC	-0.1	5.1	2	NC	NC	NC	-3.2	0.8

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	-0.03	0.507	0.04	-0.6	0.4	4	-4.07	6.003	-1.79	-13.0	0.2
	Pre-cycle 49 (n=2)	NC	NC	NC	-0.2	0.4	2	NC	NC	NC	-12.5	-0.7

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.0	0.6	2	NC	NC	NC	-0.5	0.7
	Pre-cycle 49 (n=1)	NC	NC	NC	0.1	0.1	1	NC	NC	NC	-0.4	-0.4

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	-0.2	0.4	2	NC	NC	NC	-0.2	0.0
	Pre-cycle 49 (n=1)	NC	NC	NC	1.3	1.3	1	NC	NC	NC	0.9	0.9

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	2.00	0.816	2.00	1.0	3.0	4	-5.25	7.365	-2.50	-16.0	0.0
	Pre-cycle 49 (n=2)	NC	NC	NC	1.0	1.0	2	NC	NC	NC	-5.0	-1.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=4)	0.50	1.000	0.00	0.0	2.0	4	-2.25	0.957	-2.50	-3.0	-1.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	0.0	2	NC	NC	NC	-3.0	-1.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.0	2.0	2	NC	NC	NC	0.0	2.0
	Pre-cycle 49 (n=1)	NC	NC	NC	0.0	0.0	1	NC	NC	NC	0.0	0.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.0	1.0	2	NC	NC	NC	-1.0	1.0
	Pre-cycle 49 (n=1)	NC	NC	NC	3.0	3.0	1	NC	NC	NC	3.0	3.0

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	15.3	15.3	1	NC	NC	NC	4.7	4.7

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	28.0	28.0	1	NC	NC	NC	9.2	9.2

[a] Patients with an unknown PN status at baseline, 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req17b5.sas Executed: 2023-05-18T13:21

Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	10.0	10.0	0	NC	NC	NC	NC	NC
	Pre-cycle 49 (n=1)	NC	NC	NC	9.9	9.9	0	NC	NC	NC	NC	NC

[a] Patients with an unknown PN status at baseline, 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req17b5.sas Executed: 2023-05-18T13:21

Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	5.0	9.9	0	NC	NC	NC	NC	NC
	Pre-cycle 49 (n=1)	NC	NC	NC	9.9	9.9	0	NC	NC	NC	NC	NC

[a] Patients with an unknown PN status at baseline, 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req17b5.sas Executed: 2023-05-18T13:21

Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	4.5	4.5	1	NC	NC	NC	1.1	1.1

[a] Patients with an unknown PN status at baseline, 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req17b5.sas Executed: 2023-05-18T13:21

Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=1)	NC	NC	NC	6.3	6.3	1	NC	NC	NC	1.0	1.0

[a] Patients with an unknown PN status at baseline, 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req17b5.sas Executed: 2023-05-18T13:21

Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	4.0	6.4	0	NC	NC	NC	NC	NC
	Pre-cycle 49 (n=1)	NC	NC	NC	5.5	5.5	0	NC	NC	NC	NC	NC

[a] Patients with an unknown PN status at baseline, 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req17b5.sas Executed: 2023-05-18T13:21

Table 4.2.2.5 Motor function secondary outcome test scores and change from baseline over time by PN-affected laterality - PN status = Unknown (Full analysis set with a motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=2)	NC	NC	NC	4.0	6.8	0	NC	NC	NC	NC	NC
	Pre-cycle 49 (n=1)	NC	NC	NC	4.6	4.6	0	NC	NC	NC	NC	NC

[a] Patients with an unknown PN status at baseline, 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.

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1.11 Endpunkt Sehfähigkeit

1.11.1 Subgruppenanalysen zur Sehfähigkeit

1.11.1.1 Subgruppenanalyse zur Sehfertigkeit: Veränderung gegenüber Baseline

Table 4.3.1.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=3)	6.6	5.74	9.0	0	11	25.0	3	-10.4	19.53	0.7	-33	1	25.0
	Pre-cycle 49 (n=3)	19.3	6.56	17.7	14	27	25.0	3	2.3	8.17	3.7	-7	10	25.0

[a] Male 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req18a1.sas Executed: 2023-06-19T12:04

Table 4.3.1.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=3)	6.0	6.98	4.3	0	14	25.0	3	-7.7	4.33	-10.0	-10	-3	25.0
	Pre-cycle 49 (n=3)	5.7	9.81	0.0	0	17	25.0	3	-8.0	17.09	-10.0	-24	10	25.0

[a] Male 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req18a1.sas Executed: 2023-06-19T12:04

Table 4.3.1.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
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=2)	NC	NC	NC	-0.1	0.0	50.0	2	NC	NC	NC	-0.1	-0.1	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.1	0.1	50.0	2	NC	NC	NC	0.0	0.1	50.0

[a] Male 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\reql8a1.sas Executed: 2023-06-19T12:04

Table 4.3.1.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
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
	Pre-cycle 37 (n=1)	NC	NC	NC	1.0	1.0	75.0	1	NC	NC	NC	0.7	0.7	75.0
	Pre-cycle 49 (n=1)	NC	NC	NC	1.0	1.0	75.0	1	NC	NC	NC	0.7	0.7	75.0

[a] Male 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req18a1.sas Executed: 2023-06-19T12:04

Table 4.3.1.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - OS	Baseline (n=1)	NC	NC	NC	0.7	0.7	75.0							
	Pre-cycle 5 (n=1)	NC	NC	NC	0.8	0.8	75.0	1	NC	NC	NC	0.1	0.1	75.0
	Pre-cycle 9 (n=1)	NC	NC	NC	0.7	0.7	75.0	1	NC	NC	NC	0.0	0.0	75.0
	Pre-cycle 13 (n=1)	NC	NC	NC	1.1	1.1	75.0	1	NC	NC	NC	0.4	0.4	75.0
	Pre-cycle 25 (n=1)	NC	NC	NC	0.5	0.5	75.0	1	NC	NC	NC	-0.2	-0.2	75.0
	Pre-cycle 37 (n=1)	NC	NC	NC	0.7	0.7	75.0	1	NC	NC	NC	0.0	0.0	75.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.5	1.0	50.0	1	NC	NC	NC	-0.2	-0.2	75.0

[a] Male 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req18a1.sas Executed: 2023-06-19T12:04

Table 4.3.1.2 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=3)	10.4	9.34	13.3	0	18	50.0	3	0.3	1.53	0.0	-1	2	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0	20	66.7	2	NC	NC	NC	-16	20	66.7

[a] Female 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req18a2.sas Executed: 2023-06-19T12:04

Table 4.3.1.2 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=3)	9.6	8.44	12.7	0	16	50.0	3	1.0	2.96	0.0	-1	4	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0	17	66.7	2	NC	NC	NC	-12	17	66.7

[a] Female 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req18a2.sas Executed: 2023-06-19T12:04

Table 4.3.1.2 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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=3)	0.67	0.551	0.40	0.3	1.3	50.0	3	0.03	0.115	0.10	-0.1	0.1	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.3	1.2	66.7	2	NC	NC	NC	-0.1	0.0	66.7

[a] Female 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 4.3.1.2 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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=3)	0.00	0.100	0.00	-0.1	0.1	50.0	3	0.00	0.100	0.00	-0.1	0.1	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	0.0	66.7	2	NC	NC	NC	-0.1	0.2	66.7

[a] Female 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 4.3.1.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=2)	NC	NC	NC	9	13	33.3	2	NC	NC	NC	-1	1	33.3
	Pre-cycle 49 (n=1)	NC	NC	NC	18	18	66.7	1	NC	NC	NC	10	10	66.7

[a] Patients with a progressive PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 4.3.1.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=2)	NC	NC	NC	4	13	33.3	2	NC	NC	NC	-3	-1	33.3
	Pre-cycle 49 (n=1)	NC	NC	NC	17	17	66.7	1	NC	NC	NC	10	10	66.7

[a] Patients with a progressive PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req18a3.sas Executed: 2023-06-19T12:05

Table 4.3.1.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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=2)	NC	NC	NC	0.0	0.4	33.3	2	NC	NC	NC	-0.1	0.1	33.3
	Pre-cycle 49 (n=1)	NC	NC	NC	0.1	0.1	66.7	1	NC	NC	NC	0.0	0.0	66.7

[a] Patients with a progressive PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 4.3.1.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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=2)	NC	NC	NC	0.1	1.0	33.3	2	NC	NC	NC	0.0	0.7	33.3
	Pre-cycle 49 (n=1)	NC	NC	NC	1.0	1.0	66.7	1	NC	NC	NC	0.7	0.7	66.7

[a] Patients with a progressive PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 4.3.1.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Teller Acuity Cards (logMAR) - OS	Pre-cycle 49 (n=1)	NC	NC	NC	1.0	1.0	66.7	0	NC	NC	NC	NC	NC	100.0

[a] Patients with a progressive PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 4.3.1.4 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=2)	NC	NC	NC	0	11	50.0	2	NC	NC	NC	-33	1	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	14	27	50.0	2	NC	NC	NC	-7	4	50.0

[a] Patients with a non-progressive PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req18a4.sas Executed: 2023-06-19T12:05

Table 4.3.1.4 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=2)	NC	NC	NC	0	14	50.0	2	NC	NC	NC	-10	-10	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0	0	50.0	2	NC	NC	NC	-24	-10	50.0

[a] Patients with a non-progressive PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\reql8a4.sas Executed: 2023-06-19T12:05

Table 4.3.1.4 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
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
	Pre-cycle 49 (n=1)	NC	NC	NC	0.1	0.1	75.0	1	NC	NC	NC	0.1	0.1	75.0

[a] Patients with a non-progressive PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\reql8a4.sas Executed: 2023-06-19T12:05

Table 4.3.1.4 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
HOTV (logMAR) - OS	Baseline (n=1)	NC	NC	NC	0.5	0.5	75.0							

[a] Patients with a non-progressive PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 4.3.1.4 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - OS	Baseline (n=1)	NC	NC	NC	0.7	0.7	75.0							
	Pre-cycle 5 (n=1)	NC	NC	NC	0.8	0.8	75.0	1	NC	NC	NC	0.1	0.1	75.0
	Pre-cycle 9 (n=1)	NC	NC	NC	0.7	0.7	75.0	1	NC	NC	NC	0.0	0.0	75.0
	Pre-cycle 13 (n=1)	NC	NC	NC	1.1	1.1	75.0	1	NC	NC	NC	0.4	0.4	75.0
	Pre-cycle 25 (n=1)	NC	NC	NC	0.5	0.5	75.0	1	NC	NC	NC	-0.2	-0.2	75.0
	Pre-cycle 37 (n=1)	NC	NC	NC	0.7	0.7	75.0	1	NC	NC	NC	0.0	0.0	75.0
	Pre-cycle 49 (n=1)	NC	NC	NC	0.5	0.5	75.0	1	NC	NC	NC	-0.2	-0.2	75.0

[a] Patients with a non-progressive PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req18a4.sas Executed: 2023-06-19T12:05

Table 4.3.1.5 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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
	Pre-cycle 37 (n=2)	NC	NC	NC	0	18	33.3	2	NC	NC	NC	0	2	33.3
	Pre-cycle 49 (n=2)	NC	NC	NC	0	20	33.3	2	NC	NC	NC	-16	20	33.3

[a] Patients with an unknown PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 4.3.1.5 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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
	Pre-cycle 37 (n=2)	NC	NC	NC	0	16	33.3	2	NC	NC	NC	0	4	33.3
	Pre-cycle 49 (n=2)	NC	NC	NC	0	17	33.3	2	NC	NC	NC	-12	17	33.3

[a] Patients with an unknown PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 4.3.1.5 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.3	1.3	33.3	2	NC	NC	NC	-0.1	0.1	33.3
	Pre-cycle 49 (n=2)	NC	NC	NC	0.3	1.2	33.3	2	NC	NC	NC	-0.1	0.0	33.3

[a] Patients with an unknown PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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Table 4.3.1.5 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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
	Pre-cycle 37 (n=2)	NC	NC	NC	-0.1	0.0	33.3	2	NC	NC	NC	-0.1	0.1	33.3
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	0.0	33.3	2	NC	NC	NC	-0.1	0.2	33.3

[a] Patients with an unknown PN status at baseline, 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. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.
Max = Maximum. Min = Minimum. SD = Standard deviation.

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1.11.1.2 Subgruppenanalyse zur Sehfertigkeit nach Lokalisation des PN: Veränderung gegenüber Baseline

Table 4.3.2.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=3)	6.0	6.98	4.3	0	14	25.0	3	-15.3	15.77	-10.3	-33	-3	25.0
	Pre-cycle 49 (n=3)	14.5	13.43	17.0	0	27	25.0	3	-6.8	17.00	-6.5	-24	10	25.0

[a] Male 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.

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Table 4.3.2.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (mm) - non PN-affected side	Baseline (n=4)	7.0	4.76	9.0	0	10	0.0							
	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=3)	6.6	5.74	9.0	0	11	25.0	3	-2.8	6.26	0.7	-10	1	25.0
	Pre-cycle 49 (n=3)	10.4	9.27	13.7	0	18	25.0	3	1.1	10.08	3.7	-10	10	25.0

[a] Male 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.

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Table 4.3.2.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
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
	Pre-cycle 37 (n=1)	NC	NC	NC	1.0	1.0	75.0	1	NC	NC	NC	0.7	0.7	75.0
	Pre-cycle 49 (n=1)	NC	NC	NC	1.0	1.0	75.0	1	NC	NC	NC	0.7	0.7	75.0

[a] Male 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.

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Table 4.3.2.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
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=2)	NC	NC	NC	-0.1	0.0	50.0	2	NC	NC	NC	-0.1	-0.1	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.1	0.1	50.0	2	NC	NC	NC	0.0	0.1	50.0

[a] Male 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.

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Table 4.3.2.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - PN-affected side	Pre-cycle 49 (n=1)	NC	NC	NC	1.0	1.0	75.0	0	NC	NC	NC	NC	NC	100.0

[a] Male 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.

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Table 4.3.2.1 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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	0.7	0.7	75.0							
	Pre-cycle 5 (n=1)	NC	NC	NC	0.8	0.8	75.0	1	NC	NC	NC	0.1	0.1	75.0
	Pre-cycle 9 (n=1)	NC	NC	NC	0.7	0.7	75.0	1	NC	NC	NC	0.0	0.0	75.0
	Pre-cycle 13 (n=1)	NC	NC	NC	1.1	1.1	75.0	1	NC	NC	NC	0.4	0.4	75.0
	Pre-cycle 25 (n=1)	NC	NC	NC	0.5	0.5	75.0	1	NC	NC	NC	-0.2	-0.2	75.0
	Pre-cycle 37 (n=1)	NC	NC	NC	0.7	0.7	75.0	1	NC	NC	NC	0.0	0.0	75.0
	Pre-cycle 49 (n=3)	0.23	0.231	0.10	0.1	0.5	25.0	1	NC	NC	NC	-0.2	-0.2	75.0

[a] Male 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.

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Table 4.3.2.2 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=3)	10.4	9.34	13.3	0	18	50.0	3	0.3	1.53	0.0	-1	2	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0	20	66.7	2	NC	NC	NC	-16	20	66.7

[a] Female 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.

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Table 4.3.2.2 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=3)	9.6	8.44	12.7	0	16	50.0	3	1.0	2.96	0.0	-1	4	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0	17	66.7	2	NC	NC	NC	-12	17	66.7

[a] Female 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.

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Table 4.3.2.2 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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=3)	0.67	0.551	0.40	0.3	1.3	50.0	3	0.03	0.115	0.10	-0.1	0.1	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.3	1.2	66.7	2	NC	NC	NC	-0.1	0.0	66.7

[a] Female 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.

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Table 4.3.2.2 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=3)	0.00	0.100	0.00	-0.1	0.1	50.0	3	0.00	0.100	0.00	-0.1	0.1	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	0.0	66.7	2	NC	NC	NC	-0.1	0.2	66.7

[a] Female 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.

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Table 4.3.2.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=2)	NC	NC	NC	4	13	33.3	2	NC	NC	NC	-3	-1	33.3
	Pre-cycle 49 (n=1)	NC	NC	NC	17	17	66.7	1	NC	NC	NC	10	10	66.7

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.3.2.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=2)	NC	NC	NC	9	13	33.3	2	NC	NC	NC	-1	1	33.3
	Pre-cycle 49 (n=1)	NC	NC	NC	18	18	66.7	1	NC	NC	NC	10	10	66.7

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.3.2.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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=2)	NC	NC	NC	0.4	1.0	33.3	2	NC	NC	NC	0.1	0.7	33.3
	Pre-cycle 49 (n=1)	NC	NC	NC	1.0	1.0	66.7	1	NC	NC	NC	0.7	0.7	66.7

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.3.2.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=2)	NC	NC	NC	0.0	0.1	33.3	2	NC	NC	NC	-0.1	0.0	33.3
	Pre-cycle 49 (n=1)	NC	NC	NC	0.1	0.1	66.7	1	NC	NC	NC	0.0	0.0	66.7

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.3.2.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Teller Acuity Cards (logMAR) - PN-affected side	Pre-cycle 49 (n=1)	NC	NC	NC	1.0	1.0	66.7	0	NC	NC	NC	NC	NC	100.0

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.3.2.3 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Teller Acuity Cards (logMAR) - non PN-affected side	Pre-cycle 49 (n=1)	NC	NC	NC	0.1	0.1	66.7	0	NC	NC	NC	NC	NC	100.0

[a] Patients with a progressive PN status at baseline, 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.

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Table 4.3.2.4 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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=2)	NC	NC	NC	0	14	50.0	2	NC	NC	NC	-33	-10	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0	27	50.0	2	NC	NC	NC	-24	-7	50.0

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.3.2.4 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (mm) - non PN-affected side	Baseline (n=4)	8.5	5.97	10.0	0	14	0.0							
	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=2)	NC	NC	NC	0	11	50.0	2	NC	NC	NC	-10	1	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0	14	50.0	2	NC	NC	NC	-10	4	50.0

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.3.2.4 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
HOTV (logMAR) - PN-affected side	Baseline (n=1)	NC	NC	NC	0.5	0.5	75.0							

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.3.2.4 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
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
	Pre-cycle 49 (n=1)	NC	NC	NC	0.1	0.1	75.0	1	NC	NC	NC	0.1	0.1	75.0

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.3.2.4 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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	0.7	0.7	75.0							
	Pre-cycle 5 (n=1)	NC	NC	NC	0.8	0.8	75.0	1	NC	NC	NC	0.1	0.1	75.0
	Pre-cycle 9 (n=1)	NC	NC	NC	0.7	0.7	75.0	1	NC	NC	NC	0.0	0.0	75.0
	Pre-cycle 13 (n=1)	NC	NC	NC	1.1	1.1	75.0	1	NC	NC	NC	0.4	0.4	75.0
	Pre-cycle 25 (n=1)	NC	NC	NC	0.5	0.5	75.0	1	NC	NC	NC	-0.2	-0.2	75.0
	Pre-cycle 37 (n=1)	NC	NC	NC	0.7	0.7	75.0	1	NC	NC	NC	0.0	0.0	75.0
	Pre-cycle 49 (n=2)	NC	NC	NC	0.1	0.5	50.0	1	NC	NC	NC	-0.2	-0.2	75.0

[a] Patients with a non-progressive PN status at baseline, 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.

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Table 4.3.2.5 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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
	Pre-cycle 37 (n=2)	NC	NC	NC	0	18	33.3	2	NC	NC	NC	0	2	33.3
	Pre-cycle 49 (n=2)	NC	NC	NC	0	20	33.3	2	NC	NC	NC	-16	20	33.3

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.3.2.5 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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]
Exophthalmometry (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
	Pre-cycle 37 (n=2)	NC	NC	NC	0	16	33.3	2	NC	NC	NC	0	4	33.3
	Pre-cycle 49 (n=2)	NC	NC	NC	0	17	33.3	2	NC	NC	NC	-12	17	33.3

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.3.2.5 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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
	Pre-cycle 37 (n=2)	NC	NC	NC	0.3	1.3	33.3	2	NC	NC	NC	-0.1	0.1	33.3
	Pre-cycle 49 (n=2)	NC	NC	NC	0.3	1.2	33.3	2	NC	NC	NC	-0.1	0.0	33.3

[a] Patients with an unknown PN status at baseline, 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.

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Table 4.3.2.5 Teller Acuity Cards, HOTV, and Exophthalmometry test scores and change from baseline over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=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
	Pre-cycle 37 (n=2)	NC	NC	NC	-0.1	0.0	33.3	2	NC	NC	NC	-0.1	0.1	33.3
	Pre-cycle 49 (n=2)	NC	NC	NC	0.0	0.0	33.3	2	NC	NC	NC	-0.1	0.2	33.3

[a] Patients with an unknown PN status at baseline, 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.

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1.11.1.3 Sugruppenanalyse zur Sehfehrtigkeit: Responderanalysen

Table 4.3.3.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
	Overall (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	3	100	29.2, 100
Exophthalmometry (mm) - OS	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OS	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	0	0	0, 70.8

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OS	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	1	33.3	0.8, 90.6
	Overall (n=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
HOTV (logMAR) - OD	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OD	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OD	Overall (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
HOTV (logMAR) - OS	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OS	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
Teller Acuity Cards (logMAR) - OS	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Teller Acuity Cards (logMAR) - OS	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Teller Acuity Cards (logMAR) - OS	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100
		Deterioration	0	0	0, 60.2

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
Exophthalmometry (mm) - OS	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	2	50.0	6.8, 93.2

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OS	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	3	75.0	19.4, 99.4
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	3	75.0	19.4, 99.4
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OS	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	3	75.0	19.4, 99.4
HOTV (logMAR) - OD	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OD	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OD	Overall (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
HOTV (logMAR) - OS	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
		Deterioration	1	25.0	0.6, 80.6

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OS	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	2	50.0	6.8, 93.2

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	2	66.7	9.4, 99.2
Exophthalmometry (mm) - OS	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	2	66.7	9.4, 99.2

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OS	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OS	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
HOTV (logMAR) - OD	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OD	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OD	Overall (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
HOTV (logMAR) - OS	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	2	66.7	9.4, 99.2

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OS	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	2	66.7	9.4, 99.2

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time – PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
Exophthalmometry (mm) - OS	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OS	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OS	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
HOTV (logMAR) - OD	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OD	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OD	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
Teller Acuity Cards (logMAR) - OS	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Teller Acuity Cards (logMAR) - OS	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OD	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
Exophthalmometry (mm) - OS	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OS	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - OS	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
HOTV (logMAR) - OD	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OD	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OD	Overall (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
HOTV (logMAR) - OS	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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Table 4.3.3.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - OS	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated. OS = 'oculus sinister' - left eye. OD = 'oculus dexter' - right eye.

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1.11.1.4 Subgruppenanalyse zur Sehfertigkeit nach Lokalisation des PN: Responderanalyse

Table 4.3.4.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	1	33.3	0.8, 90.6
	Overall (n=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	2	66.7	9.4, 99.2

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
	Overall (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	3	100	29.2, 100
HOTV (logMAR) - PN-affected side	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - PN-affected side	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - non PN-affected side	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - non PN-affected side	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
Teller Acuity Cards (logMAR) - non PN-affected side	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Teller Acuity Cards (logMAR) - non PN-affected side	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.1 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Male (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Teller Acuity Cards (logMAR) - non PN-affected side	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Male 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100
		Deterioration	0	0	0, 60.2

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	2	50.0	6.8, 93.2

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	3	75.0	19.4, 99.4
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	3	75.0	19.4, 99.4
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	3	75.0	19.4, 99.4
HOTV (logMAR) - PN-affected side	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - PN-affected side	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - PN-affected side	Overall (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
HOTV (logMAR) - non PN-affected side	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
		Deterioration	1	25.0	0.6, 80.6

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.2 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - Gender = Female (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - non PN-affected side	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	2	50.0	6.8, 93.2

[a] Female 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	2	66.7	9.4, 99.2
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	2	66.7	9.4, 99.2
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
HOTV (logMAR) - PN-affected side	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - PN-affected side	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - PN-affected side	Overall (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
HOTV (logMAR) - non PN-affected side	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.3 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - non PN-affected side	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6

[a] Patients with a progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
HOTV (logMAR) - non PN-affected side	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - non PN-affected side	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - non PN-affected side	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
Teller Acuity Cards (logMAR) - non PN-affected side	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.4 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Non-progressive (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Teller Acuity Cards (logMAR) - non PN-affected side	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC

[a] Patients with a non-progressive PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - PN-affected side	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
Exophthalmometry (mm) - non PN-affected side	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
HOTV (logMAR) - PN-affected side	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - PN-affected side	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - PN-affected side	Overall (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
HOTV (logMAR) - non PN-affected side	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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Table 4.3.4.5 Teller Acuity Cards, HOTV, and Exophthalmometry test score categories of change over time by orbital PN location - PN status = Unknown (Full analysis set with orbit PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=3) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
HOTV (logMAR) - non PN-affected side	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC

[a] Patients with an unknown PN status at baseline, 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 change/deterioration are defined using a threshold of 2 mm for Exophthalmometry and 0.2 logMAR for HOTV and Teller Acuity Cards.
NC = Not Calculated.

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1.12 Endpunkt Atemfunktion

1.12.1 Subgruppenanalysen zur Atemfunktion

1.12.1.1 Subgruppenanalyse zur Atemfunktion: Veränderung gegenüber Baseline

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: 31 March 2021 (DC02)

		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=6)	2,197	1,2190	1,780	0,99	4,26	40,0	6	0,437	0,3795	0,375	-0,07	0,97	40,0
	Pre-cycle 37 (n=6)	2,402	1,0985	1,940	1,39	4,22	40,0	6	0,642	0,3952	0,425	0,33	1,23	40,0
	Pre-cycle 49 (n=4)	2,973	1,0329	2,930	1,79	4,24	60,0	4	0,758	0,3880	0,690	0,40	1,25	60,0
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=5)	3,660	0,7785	3,730	2,51	4,62	50,0	5	-0,208	0,5209	-0,030	-1,12	0,19	50,0
	Pre-cycle 37 (n=4)	2,955	0,8269	3,055	1,86	3,85	60,0	4	-0,883	0,5268	-0,640	-1,67	-0,58	60,0
	Pre-cycle 49 (n=3)	2,453	0,5014	2,670	1,88	2,81	70,0	3	-1,187	0,7457	-0,860	-2,04	-0,66	70,0
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=4)	1,900	1,3441	2,050	0,30	3,20	60,0	4	-0,075	1,7154	0,400	-2,50	1,40	60,0
	Pre-cycle 37 (n=5)	2,660	1,9870	2,300	0,50	5,70	50,0	5	1,040	2,8893	0,100	-2,30	5,50	50,0
	Pre-cycle 49 (n=1)	NC	NC	NC	1,50	1,50	90,0	1	NC	NC	NC	1,00	1,00	90,0

[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.

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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: 31 March 2021 (DC02)

		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=5)	1,904	0,8667	1,420	1,02	2,91	16,7	5	0,318	0,3833	0,320	-0,20	0,72	16,7
	Pre-cycle 37 (n=5)	2,096	1,1301	1,450	1,05	3,50	16,7	5	0,510	0,2842	0,540	0,13	0,87	16,7
	Pre-cycle 49 (n=2)	NC	NC	NC	1,07	3,13	66,7	2	NC	NC	NC	0,17	0,37	66,7
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=5)	3,922	1,2005	3,440	2,88	5,97	16,7	5	0,058	0,5786	0,160	-0,76	0,64	16,7
	Pre-cycle 37 (n=5)	3,562	0,7064	3,450	2,87	4,69	16,7	5	-0,302	0,8720	-0,050	-1,31	0,65	16,7
	Pre-cycle 49 (n=2)	NC	NC	NC	2,93	4,28	66,7	2	NC	NC	NC	-1,53	-0,22	66,7
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=4)	2,050	1,9399	1,950	0,20	4,10	33,3	4	0,025	1,0905	-0,300	-0,80	1,50	33,3
	Pre-cycle 37 (n=3)	2,533	0,8737	2,300	1,80	3,50	50,0	3	0,033	1,6921	-0,400	-1,40	1,90	50,0
	Pre-cycle 49 (n=3)	1,900	1,7349	1,000	0,80	3,90	50,0	3	0,433	1,7559	0,600	-1,40	2,10	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.

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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: 31 March 2021 (DC02)

		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=4)	1,490	0,4445	1,450	0,99	2,07	0,0	4	0,295	0,3287	0,265	-0,07	0,72	0,0
	Pre-cycle 37 (n=4)	1,655	0,3834	1,545	1,35	2,18	0,0	4	0,460	0,1412	0,425	0,33	0,66	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	1,79	2,62	50,0	2	NC	NC	NC	0,50	0,88	50,0
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=4)	3,653	0,2760	3,585	3,43	4,01	0,0	4	-0,140	0,7294	-0,040	-1,12	0,64	0,0
	Pre-cycle 37 (n=3)	3,187	0,2601	3,180	2,93	3,45	25,0	3	-0,540	1,1612	-0,600	-1,67	0,65	25,0
	Pre-cycle 49 (n=2)	NC	NC	NC	2,67	2,81	50,0	2	NC	NC	NC	-2,04	-0,86	50,0
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
	Pre-cycle 37 (n=2)	NC	NC	NC	0,50	2,30	50,0	2	NC	NC	NC	-2,30	1,80	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	1,50	3,90	50,0	2	NC	NC	NC	1,00	2,10	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=4)	3,160	1,0606	3,360	1,70	4,22	20,0	4	0,803	0,4068	0,800	0,38	1,23	20,0
	Pre-cycle 49 (n=3)	3,537	0,6116	3,240	3,13	4,24	40,0	3	0,607	0,5689	0,400	0,17	1,25	40,0
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
	Pre-cycle 37 (n=3)	2,937	1,0050	3,100	1,86	3,85	40,0	3	-0,437	0,3386	-0,580	-0,68	-0,05	40,0
	Pre-cycle 49 (n=2)	NC	NC	NC	1,88	2,93	60,0	2	NC	NC	NC	-0,66	-0,22	60,0
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=2)	NC	NC	NC	2,80	3,20	60,0	2	NC	NC	NC	0,00	1,40	60,0
	Pre-cycle 37 (n=4)	3,075	1,9190	2,550	1,50	5,70	20,0	4	1,325	2,7933	0,100	-0,40	5,50	20,0
	Pre-cycle 49 (n=1)	NC	NC	NC	0,80	0,80	80,0	1	NC	NC	NC	-1,40	-1,40	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.

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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: 31 March 2021 (DC02)

		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=3)	1,783	0,9960	1,420	1,02	2,91	57,1	3	0,357	0,2768	0,320	0,10	0,65	57,1
	Pre-cycle 37 (n=3)	1,877	1,1037	1,450	1,05	3,13	57,1	3	0,450	0,3800	0,350	0,13	0,87	57,1
	Pre-cycle 49 (n=1)	NC	NC	NC	1,07	1,07	85,7	1	NC	NC	NC	0,37	0,37	85,7
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=3)	4,430	1,3551	3,900	3,42	5,97	57,1	3	-0,027	0,6601	0,160	-0,76	0,52	57,1
	Pre-cycle 37 (n=3)	3,753	0,9112	3,700	2,87	4,69	57,1	3	-0,703	0,8913	-1,120	-1,31	0,32	57,1
	Pre-cycle 49 (n=1)	NC	NC	NC	4,28	4,28	85,7	1	NC	NC	NC	-1,53	-1,53	85,7
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=3)	1,633	2,1455	0,600	0,20	4,10	57,1	3	-0,467	0,5774	-0,800	-0,80	0,20	57,1
	Pre-cycle 37 (n=2)	NC	NC	NC	2,30	3,50	71,4	2	NC	NC	NC	-1,40	1,90	71,4
	Pre-cycle 49 (n=1)	NC	NC	NC	1,00	1,00	85,7	1	NC	NC	NC	0,60	0,60	85,7

[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.

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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: 31 March 2021 (DC02)

		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	6	34,64	45,636	17,23	-7	120	40,0
	Pre-cycle 37	6	54,26	57,108	31,46	10	166	40,0
	Pre-cycle 49	4	40,64	22,416	44,67	10	63	60,0
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	5	-4,46	10,744	-1,18	-23	4	50,0
	Pre-cycle 37	4	-22,82	9,644	-21,88	-34	-13	60,0
	Pre-cycle 49	3	-30,80	9,784	-25,98	-42	-24	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.

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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: 31 March 2021 (DC02)

		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	5	35,93	43,169	28,76	-7	104	16,7
	Pre-cycle 37	5	42,45	33,734	38,50	10	96	16,7
	Pre-cycle 49	2	NC	NC	NC	6	53	66,7
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	5	2,85	16,809	2,75	-18	23	16,7
	Pre-cycle 37	5	-3,90	21,844	-1,59	-31	23	16,7
	Pre-cycle 49	2	NC	NC	NC	-26	-7	66,7

[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.

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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: 31 March 2021 (DC02)

		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	4	33,05	48,860	17,23	-7	104	0,0
	Pre-cycle 37	4	45,96	33,254	31,46	25	96	0,0
	Pre-cycle 49	2	NC	NC	NC	39	51	50,0
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	4	-0,64	18,818	-1,17	-23	23	0,0
	Pre-cycle 37	3	-9,41	29,564	-17,00	-34	23	25,0
	Pre-cycle 49	2	NC	NC	NC	-42	-24	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37	4	63,89	71,539	40,03	10	166	20,0
	Pre-cycle 49	3	26,32	31,687	10,42	6	63	40,0
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
	Pre-cycle 37	3	-13,82	12,608	-13,09	-27	-2	40,0
	Pre-cycle 49	2	NC	NC	NC	-26	-7	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.

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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: 31 March 2021 (DC02)

		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	3	27,35	19,108	28,76	8	46	57,1
	Pre-cycle 37	3	32,78	20,677	38,50	10	50	57,1
	Pre-cycle 49	1	NC	NC	NC	53	53	85,7
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	3	-0,01	16,954	2,75	-18	15	57,1
	Pre-cycle 37	3	-13,72	20,964	-19,28	-31	9	57,1
	Pre-cycle 49	1	NC	NC	NC	-26	-26	85,7

[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.

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1.12.2 Subgruppenanalyse zur Atemfunktion: Responderanalysen

Table 5.4.1.1 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - Gender = Male
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 5 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 9 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 13 (n=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.1 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - Gender = Male
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	5	83.3	35.9, 99.6
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 49 (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Overall (n=6)	Categories of change [d]			
		Improvement	5	83.3	35.9, 99.6
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.1 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - Gender = Male
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 5 (n=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	2	40.0	5.3, 85.3
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 9 (n=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 13 (n=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	5	100	47.8, 100
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.1 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - Gender = Male
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
	Overall (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	2	40.0	5.3, 85.3
		No improvement or deterioration	1	20.0	0.5, 71.6

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.2 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - Gender = Female
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 5 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 9 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 13 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.2 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - Gender = Female
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	4	80.0	28.4, 99.5
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	1	20.0	0.5, 71.6
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=5)	Categories of change [d]			
		Improvement	4	80.0	28.4, 99.5
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	1	20.0	0.5, 71.6

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.2 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - Gender = Female
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 5 (n=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 9 (n=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	2	40.0	5.3, 85.3
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 13 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.2 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - Gender = Female
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	2	40.0	5.3, 85.3
		No improvement or deterioration	2	40.0	5.3, 85.3

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.3 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Progressive
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.3 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Progressive
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	4	100	39.8, 100
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	0	0	0, 60.2
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	4	100	39.8, 100
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	0	0	0, 60.2

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.3 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Progressive
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.3 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Progressive
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.4 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Non-progressive
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.4 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Non-progressive
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Overall (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.4 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Non-progressive
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.4 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Non-progressive
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	2	66.7	9.4, 99.2
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.5 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Unknown
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.5 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Unknown
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.5 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Unknown
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	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 change/deterioration 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).
NC = not calculated.

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Table 5.4.1.5 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on REiNS literature (Plotkin et al., 2016) - PN status = Unknown
(Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration 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).
NC = not calculated.

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Table 5.4.2.1 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - Gender = Male (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 5 (n=6)	Categories of change [d]			
		Improvement	0	0	0, 45.9
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 9 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 13 (n=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.1 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - Gender = Male (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	5	83.3	35.9, 99.6
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 49 (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Overall (n=6)	Categories of change [d]			
		Improvement	5	83.3	35.9, 99.6
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.1 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - Gender = Male (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 5 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 9 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 13 (n=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.1 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - Gender = Male (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	3	75.0	19.4, 99.4
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	3	100	29.2, 100
		No improvement or deterioration	0	0	0, 70.8
	Overall (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	3	60.0	14.7, 94.7
		No improvement or deterioration	1	20.0	0.5, 71.6

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.2 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - Gender = Female (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 5 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 9 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 13 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.2 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - Gender = Female (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	4	80.0	28.4, 99.5
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	1	20.0	0.5, 71.6
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=5)	Categories of change [d]			
		Improvement	4	80.0	28.4, 99.5
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	1	20.0	0.5, 71.6

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.2 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - Gender = Female (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 5 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 9 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 13 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.2 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - Gender = Female (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	2	40.0	5.3, 85.3
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	2	40.0	5.3, 85.3
		No improvement or deterioration	1	20.0	0.5, 71.6

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.3 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Progressive (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.3 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Progressive (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	4	100	39.8, 100
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	0	0	0, 60.2
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	4	100	39.8, 100
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	0	0	0, 60.2

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.3 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Progressive (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.3 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Progressive (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	2	66.7	9.4, 99.2
		No improvement or deterioration	0	0	0, 70.8
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	2	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.4 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Non-progressive (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.4 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Non-progressive (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Overall (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.4 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Non-progressive (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.4 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Non-progressive (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.5 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Unknown (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.5 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Unknown (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
FEV1 (Liters)	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.5 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Unknown (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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Table 5.4.2.5 FEV1 and R20 test score categories of change over time - percentage of patients with Improvement and Deterioration based on a threshold of 15% - PN status = Unknown (Full analysis set with airway PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
R20 (Resistance)	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	2	66.7	9.4, 99.2
		No improvement or deterioration	0	0	0, 70.8

[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 change/deterioration are defined using a threshold of 15 % for FEV1 (FEV0.75 for pre-school children), 15% for R20 (Resistance).
NC = not calculated.

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1.13 Endpunkt Darm- und Blasenfunktion: Dysfunction Voiding Questionnaires (DVQ)

1.13.1 Subgruppenanalysen zur Darm- und Blasenfunktion: DVQ

1.13.1.1 Subgruppenanalyse zur DVQ: Veränderung gegenüber Baseline – Selbstberichtet

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: 31 March 2021 (DC02)

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.

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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: 31 March 2021 (DC02)

		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.

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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: 31 March 2021 (DC02)

		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.

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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: 31 March 2021 (DC02)

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.

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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: 31 March 2021 (DC02)

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.

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1.13.1.2 Subgruppenanalyse zur DVQ: Veränderung gegenüber Baseline – Elternberichtet

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: 31 March 2021 (DC02)

		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=3)	7,3	3,06	8,0	4	10	40,0	3	-5,7	5,03	-5,0	-11	-1	40,0
	Pre-cycle 37 (n=3)	10,7	6,66	9,0	5	18	40,0	3	-2,3	2,08	-3,0	-4	0	40,0
	Pre-cycle 49 (n=3)	9,0	5,20	12,0	3	12	40,0	3	-4,0	4,36	-2,0	-9	-1	40,0
	Pre-cycle 61 (n=1)	NC	NC	NC	4	4	80,0	1	NC	NC	NC	-1	-1	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=1)	NC	NC	NC	7	7	80,0	1	NC	NC	NC	-11	-11	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.

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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: 31 March 2021 (DC02)

		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=2)	NC	NC	NC	3	10	60,0	1	NC	NC	NC	-11	-11	80,0
	Pre-cycle 37 (n=2)	NC	NC	NC	7	18	60,0	2	NC	NC	NC	-11	-3	60,0
	Pre-cycle 49 (n=1)	NC	NC	NC	12	12	80,0	1	NC	NC	NC	-9	-9	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=1)	NC	NC	NC	5	5	66,7	1	NC	NC	NC	0	0	66,7
	Pre-cycle 49 (n=1)	NC	NC	NC	3	3	66,7	1	NC	NC	NC	-2	-2	66,7
	Pre-cycle 61 (n=1)	NC	NC	NC	4	4	66,7	1	NC	NC	NC	-1	-1	66,7

[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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=1)	NC	NC	NC	9	9	50,0	1	NC	NC	NC	-4	-4	50,0
	Pre-cycle 49 (n=1)	NC	NC	NC	12	12	50,0	1	NC	NC	NC	-1	-1	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.

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1.13.1.3 Subgruppenanalyse zur DVQ: Responderanalyse – Selbstberichtet

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: 31 March 2021 (DC02)

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.

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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: 31 March 2021 (DC02)

			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.

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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: 31 March 2021 (DC02)

			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.

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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: 31 March 2021 (DC02)

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.

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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: 31 March 2021 (DC02)

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.

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Table 2.8.1.4.1 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Deterioration - Gender = Male (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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] Deterioration/No deterioration are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

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Table 2.8.1.4.2 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Deterioration - Gender = Female (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	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] Deterioration/No deterioration are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

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Table 2.8.1.4.3 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Deterioration - PN status at enrol. = Progressive (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	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] Deterioration/No deterioration are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

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Table 2.8.1.4.4 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Deterioration - 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: 31 March 2021 (DC02)

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] Deterioration/No deterioration are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

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Table 2.8.1.4.5 Bowel and Bladder function self-report score categories of change over time - percentage of patients with Deterioration - PN status at enrol. = Unknown (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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] Deterioration/No deterioration are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

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1.13.1.4 Subgruppenanalyse zur DVQ: Responderanalyse – Elternberichtet

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: 31 March 2021 (DC02)

			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=3)	Categories of change [d]			
		Improvement	1	33,3	0,8, 90,6
		No improvement	2	66,7	9,4, 99,2
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70,8
		No improvement	3	100	29,2, 100
	Pre-cycle 49 (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 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Overall (N=5)	Categories of change [d]			
		Improvement	2	40,0	5,3, 85,3
		No improvement	3	60,0	14,7, 94,7

[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.

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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: 31 March 2021 (DC02)

			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
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	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.

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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: 31 March 2021 (DC02)

			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
	Pre-cycle 25 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 49 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement	0	NC	NC
	Overall (N=3)	Categories of change [d]			
		Improvement	2	66,7	9,4, 99,2
		No improvement	1	33,3	0,8, 90,6

[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.

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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: 31 March 2021 (DC02)

			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
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 49 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 61 (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

[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.

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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: 31 March 2021 (DC02)

			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
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement	1	NC	NC
	Pre-cycle 49 (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.

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Table 2.8.2.4.1 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Deterioration - Gender = Male (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	4	80,0	28,4, 99,5
		Deterioration	1	20,0	0,5, 71,6
	Pre-cycle 9 (N=5)	Categories of change [d]			
		No deterioration	4	80,0	28,4, 99,5
		Deterioration	1	20,0	0,5, 71,6
	Pre-cycle 13 (N=5)	Categories of change [d]			
		No deterioration	4	80,0	28,4, 99,5
		Deterioration	1	20,0	0,5, 71,6
	Pre-cycle 25 (N=3)	Categories of change [d]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8
	Pre-cycle 37 (N=3)	Categories of change [d]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8
	Pre-cycle 49 (N=3)	Categories of change [d]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8
	Pre-cycle 61 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (N=5)	Categories of change [d]			
		No deterioration	4	80,0	28,4, 99,5
		Deterioration	1	20,0	0,5, 71,6

[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] Deterioration/No deterioration are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

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Table 2.8.2.4.2 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Deterioration - Gender = Female (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8
	Pre-cycle 9 (N=3)	Categories of change [d]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8
	Pre-cycle 13 (N=2)	Categories of change [d]			
		No deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 25 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (N=3)	Categories of change [d]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8

[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] Deterioration/No deterioration are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/smptbwlsub_det.sas smptbwlsubg_det.rtf 08MAR2023:17:12 icesas79PD

Table 2.8.2.4.3 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Deterioration - PN status at enrol. = Progressive (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8
	Pre-cycle 9 (N=3)	Categories of change [d]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8
	Pre-cycle 13 (N=3)	Categories of change [d]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8
	Pre-cycle 25 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (N=2)	Categories of change [d]			
		No deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (N=3)	Categories of change [d]			
		No deterioration	3	100	29,2, 100
		Deterioration	0	0	0, 70,8

[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] Deterioration/No deterioration are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

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Table 2.8.2.4.4 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Deterioration - 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: 31 March 2021 (DC02)

			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]			
		No deterioration	2	66,7	9,4, 99,2
		Deterioration	1	33,3	0,8, 90,6
	Pre-cycle 9 (N=3)	Categories of change [d]			
		No deterioration	2	66,7	9,4, 99,2
		Deterioration	1	33,3	0,8, 90,6
	Pre-cycle 13 (N=2)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (N=2)	Categories of change [d]			
		No deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 61 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (N=3)	Categories of change [d]			
		No deterioration	2	66,7	9,4, 99,2
		Deterioration	1	33,3	0,8, 90,6

[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] Deterioration/No deterioration are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

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Table 2.8.2.4.5 Bowel and Bladder function parent-report score categories of change over time - percentage of patients with Deterioration - PN status at enrol. = Unknown (Full analysis set with a bowel and/or bladder PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

			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]			
		No deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (N=2)	Categories of change [d]			
		No deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (N=2)	Categories of change [d]			
		No deterioration	2	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 25 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (N=1)	Categories of change [d]			
		No deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (N=2)	Categories of change [d]			
		No deterioration	2	NC	NC
		Deterioration	0	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] Deterioration/No deterioration are defined using a threshold of 7.8 for Total score.
NC = Not Calculated.

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1.14 Endpunkt Allgemeiner Gesundheitszustand: Symptomcheckliste

1.14.1 Subgruppenanalysen zur Symptomcheckliste

1.14.1.1 Subgruppenanalyse zur Symptomcheckliste: Verteilung der Antwortkategorien

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	11 (55,0)
		A little	4 (20,0)
		Some	5 (25,0)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (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 49 (n=18)	Not at all	12 (66,7)
		A little	4 (22,2)
		Some	2 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	8 (72,7)
		A little	2 (18,2)
		Some	1 (9,1)
		Pretty much	0
		A lot	0

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

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Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	17 (85,0)
		A little	2 (10,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	14 (73,7)
		A little	3 (15,8)
		Some	1 (5,3)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	13 (72,2)
		A little	3 (16,7)
		Some	1 (5,6)
		Pretty much	1 (5,6)
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	7 (63,6)
		A little	3 (27,3)
		Some	0
		Pretty much	0
		A lot	1 (9,1)

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	16 (80,0)
		A little	3 (15,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	15 (83,3)
		A little	3 (16,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	9 (81,8)
		A little	2 (18,2)
		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.

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Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	11 (55,0)
		A little	6 (30,0)
		Some	1 (5,0)
		Pretty much	2 (10,0)
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	13 (68,4)
		A little	2 (10,5)
		Some	3 (15,8)
		Pretty much	1 (5,3)
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	12 (66,7)
		A little	1 (5,6)
		Some	3 (16,7)
		Pretty much	1 (5,6)
		A lot	1 (5,6)
	Pre-cycle 61 (n=11)	Not at all	9 (81,8)
		A little	0
		Some	1 (9,1)
		Pretty much	1 (9,1)
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	13 (65,0)
		A little	5 (25,0)
		Some	1 (5,0)
		Pretty much	1 (5,0)
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	6 (31,6)
		A little	12 (63,2)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	10 (55,6)
		A little	7 (38,9)
		Some	1 (5,6)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	6 (54,5)
		A little	4 (36,4)
		Some	1 (9,1)
		Pretty much	0
		A lot	0

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

root/cdar/dl53/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	19 (95,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (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 61 (n=11)	Not at all	8 (72,7)
		A little	2 (18,2)
		Some	1 (9,1)
		Pretty much	0
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	19 (95,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	17 (94,4)
		A little	1 (5,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	10 (90,9)
		A little	1 (9,1)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	18 (90,0)
		A little	2 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (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 49 (n=18)	Not at all	17 (94,4)
		A little	0
		Some	1 (5,6)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	9 (81,8)
		A little	2 (18,2)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	19 (95,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	17 (94,4)
		A little	1 (5,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	20 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	18 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	17 (85,0)
		A little	3 (15,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	13 (72,2)
		A little	3 (16,7)
		Some	2 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	9 (81,8)
		A little	1 (9,1)
		Some	1 (9,1)
		Pretty much	0
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	18 (90,0)
		A little	2 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (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 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	15 (75,0)
		A little	4 (20,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	13 (68,4)
		A little	4 (21,1)
		Some	1 (5,3)
		Pretty much	0
		A lot	1 (5,3)
	Pre-cycle 49 (n=18)	Not at all	14 (77,8)
		A little	3 (16,7)
		Some	0
		Pretty much	1 (5,6)
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	20 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	18 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	19 (95,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	17 (94,4)
		A little	1 (5,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	20 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	18 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

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Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	20 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	18 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

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Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	18 (90,0)
		A little	1 (5,0)
		Some	0
		Pretty much	1 (5,0)
		A lot	0
	Pre-cycle 37 (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 49 (n=18)	Not at all	14 (77,8)
		A little	2 (11,1)
		Some	2 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	9 (81,8)
		A little	1 (9,1)
		Some	1 (9,1)
		Pretty much	0
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	19 (95,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	17 (94,4)
		A little	1 (5,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

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Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	20 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	17 (94,4)
		A little	1 (5,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	12 (60,0)
		A little	6 (30,0)
		Some	2 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (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 49 (n=18)	Not at all	14 (77,8)
		A little	1 (5,6)
		Some	3 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	9 (81,8)
		A little	2 (18,2)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	19 (95,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	18 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	14 (70,0)
		A little	5 (25,0)
		Some	1 (5,0)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	16 (84,2)
		A little	3 (15,8)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	15 (83,3)
		A little	2 (11,1)
		Some	1 (5,6)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	10 (90,9)
		A little	1 (9,1)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	17 (85,0)
		A little	3 (15,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	15 (83,3)
		A little	3 (16,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	10 (90,9)
		A little	1 (9,1)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	14 (70,0)
		A little	6 (30,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	15 (78,9)
		A little	4 (21,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	15 (83,3)
		A little	3 (16,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	10 (90,9)
		A little	1 (9,1)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	14 (70,0)
		A little	5 (25,0)
		Some	0
		Pretty much	0
		A lot	1 (5,0)
	Pre-cycle 37 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	13 (72,2)
		A little	3 (16,7)
		Some	2 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	18 (90,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	1 (5,0)
	Pre-cycle 37 (n=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (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 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	19 (95,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	17 (94,4)
		A little	0
		Some	1 (5,6)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

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Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	20 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	18 (94,7)
		A little	1 (5,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	17 (94,4)
		A little	1 (5,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

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Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=19)	Not at all	17 (89,5)
		A little	1 (5,3)
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	17 (94,4)
		A little	0
		Some	1 (5,6)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=19)	Not at all	17 (89,5)
		A little	2 (10,5)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	17 (89,5)
		A little	0
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	16 (88,9)
		A little	2 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	19 (95,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (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 49 (n=18)	Not at all	13 (72,2)
		A little	2 (11,1)
		Some	1 (5,6)
		Pretty much	2 (11,1)
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	10 (90,9)
		A little	0
		Some	1 (9,1)
		Pretty much	0
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	17 (85,0)
		A little	3 (15,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	17 (89,5)
		A little	0
		Some	2 (10,5)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	14 (77,8)
		A little	3 (16,7)
		Some	0
		Pretty much	1 (5,6)
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	10 (90,9)
		A little	1 (9,1)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	17 (85,0)
		A little	3 (15,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	18 (94,7)
		A little	0
		Some	1 (5,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	17 (94,4)
		A little	1 (5,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	10 (90,9)
		A little	1 (9,1)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	20 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	18 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	10 (90,9)
		A little	1 (9,1)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.1 Distribution of General PN symptoms item responses over time - Gender = Male
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=20)	Not at all	19 (95,0)
		A little	1 (5,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=19)	Not at all	19 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=18)	Not at all	18 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n=11)	Not at all	10 (90,9)
		A little	1 (9,1)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsuba.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	2 (16,7)
		A little	7 (58,3)
		Some	2 (16,7)
		Pretty much	0
		A lot	1 (8,3)
	Pre-cycle 49 (n= 9)	Not at all	1 (11,1)
		A little	3 (33,3)
		Some	3 (33,3)
		Pretty much	0
		A lot	2 (22,2)
	Pre-cycle 61 (n= 6)	Not at all	2 (33,3)
		A little	1 (16,7)
		Some	2 (33,3)
		Pretty much	0
		A lot	1 (16,7)

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

root/cdar/dl53/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	7 (58,3)
		A little	2 (16,7)
		Some	3 (25,0)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	4 (44,4)
		A little	1 (11,1)
		Some	2 (22,2)
		Pretty much	0
		A lot	2 (22,2)
	Pre-cycle 61 (n= 6)	Not at all	3 (50,0)
		A little	2 (33,3)
		Some	0
		Pretty much	0
		A lot	1 (16,7)

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	6 (66,7)
		A little	1 (11,1)
		Some	1 (11,1)
		Pretty much	0
		A lot	1 (11,1)
	Pre-cycle 61 (n= 6)	Not at all	3 (50,0)
		A little	2 (33,3)
		Some	0
		Pretty much	1 (16,7)
		A lot	0

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

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Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	9 (75,0)
		A little	0
		Some	0
		Pretty much	1 (8,3)
		A lot	2 (16,7)
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (11,1)
	Pre-cycle 61 (n= 6)	Not at all	5 (83,3)
		A little	1 (16,7)
		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.

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Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	8 (66,7)
		A little	2 (16,7)
		Some	2 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	4 (44,4)
		A little	4 (44,4)
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

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Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	0
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

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Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	0
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

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Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	9 (75,0)
		A little	3 (25,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	5 (83,3)
		A little	1 (16,7)
		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.

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Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	7 (77,8)
		A little	1 (11,1)
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	5 (83,3)
		A little	1 (16,7)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

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Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	9 (75,0)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	1 (8,3)
	Pre-cycle 49 (n= 9)	Not at all	5 (55,6)
		A little	3 (33,3)
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	5 (83,3)
		A little	1 (16,7)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	6 (50,0)
		A little	4 (33,3)
		Some	2 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	7 (77,8)
		A little	0
		Some	0
		Pretty much	1 (11,1)
		A lot	1 (11,1)
	Pre-cycle 61 (n= 6)	Not at all	4 (66,7)
		A little	2 (33,3)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	8 (66,7)
		A little	3 (25,0)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	5 (55,6)
		A little	2 (22,2)
		Some	2 (22,2)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	0
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

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Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/dl53/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	5 (83,3)
		A little	1 (16,7)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	8 (66,7)
		A little	2 (16,7)
		Some	2 (16,7)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	7 (77,8)
		A little	2 (22,2)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	2 (33,3)
		A little	3 (50,0)
		Some	1 (16,7)
		Pretty much	0
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	0
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	0
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	5 (83,3)
		A little	0
		Some	1 (16,7)
		Pretty much	0
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	9 (75,0)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	1 (8,3)
	Pre-cycle 49 (n= 9)	Not at all	6 (66,7)
		A little	1 (11,1)
		Some	1 (11,1)
		Pretty much	0
		A lot	1 (11,1)
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	1 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	7 (77,8)
		A little	1 (11,1)
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	5 (83,3)
		A little	1 (16,7)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	0
		Pretty much	1 (8,3)
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	6 (66,7)
		A little	1 (11,1)
		Some	1 (11,1)
		Pretty much	1 (11,1)
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	9 (75,0)
		A little	2 (16,7)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	7 (77,8)
		A little	0
		Some	2 (22,2)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	5 (83,3)
		A little	0
		Some	1 (16,7)
		Pretty much	0
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	7 (77,8)
		A little	2 (22,2)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	4 (66,7)
		A little	2 (33,3)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	4 (66,7)
		A little	2 (33,3)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	10 (83,3)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	7 (77,8)
		A little	2 (22,2)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	5 (83,3)
		A little	1 (16,7)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	11 (91,7)
		A little	0
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	5 (83,3)
		A little	1 (16,7)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	8 (66,7)
		A little	4 (33,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	4 (66,7)
		A little	1 (16,7)
		Some	0
		Pretty much	1 (16,7)
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	9 (75,0)
		A little	3 (25,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	7 (77,8)
		A little	1 (11,1)
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	4 (66,7)
		A little	1 (16,7)
		Some	1 (16,7)
		Pretty much	0
		A lot	0

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

root/cdar/dl53/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.2 Distribution of General PN symptoms item responses over time - Gender = Female
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=12)	Not at all	10 (83,3)
		A little	1 (8,3)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 6)	Not at all	6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubb.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	7 (53,8)
		A little	4 (30,8)
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	5 (41,7)
		A little	4 (33,3)
		Some	3 (25,0)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	6 (60,0)
		A little	1 (10,0)
		Some	3 (30,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 4)	Not at all	2 (50,0)
		A little	1 (25,0)
		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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (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 49 (n=10)	Not at all	7 (70,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	1 (10,0)
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	10 (83,3)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	8 (61,5)
		A little	3 (23,1)
		Some	1 (7,7)
		Pretty much	1 (7,7)
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	8 (66,7)
		A little	1 (8,3)
		Some	2 (16,7)
		Pretty much	0
		A lot	1 (8,3)
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	0
		Some	0
		Pretty much	1 (10,0)
		A lot	1 (10,0)
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	6 (46,2)
		A little	6 (46,2)
		Some	0
		Pretty much	1 (7,7)
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	1 (8,3)
		A little	8 (66,7)
		Some	3 (25,0)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	5 (50,0)
		A little	4 (40,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (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 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (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 49 (n=10)	Not at all	9 (90,0)
		A little	0
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	10 (76,9)
		A little	3 (23,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	9 (75,0)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	1 (8,3)
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubc.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	9 (69,2)
		A little	2 (15,4)
		Some	1 (7,7)
		Pretty much	1 (7,7)
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	5 (41,7)
		A little	6 (50,0)
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	7 (70,0)
		A little	2 (20,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	11 (84,6)
		A little	1 (7,7)
		Some	0
		Pretty much	1 (7,7)
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	0
		Some	2 (20,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 4)	Not at all	2 (50,0)
		A little	1 (25,0)
		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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubc.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubc.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	9 (69,2)
		A little	3 (23,1)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	9 (75,0)
		A little	2 (16,7)
		Some	0
		Pretty much	0
		A lot	1 (8,3)
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubc.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubc.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	9 (69,2)
		A little	2 (15,4)
		Some	2 (15,4)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (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 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	10 (76,9)
		A little	2 (15,4)
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	7 (58,3)
		A little	5 (41,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	0
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	0
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	11 (84,6)
		A little	2 (15,4)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 3)	Not at all	3 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	11 (91,7)
		A little	0
		Some	1 (8,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubc.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	0
		Some	1 (7,7)
		Pretty much	0
		A lot	0
	Pre-cycle 37 (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 49 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	0
		Pretty much	1 (10,0)
		A lot	0
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubc.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	12 (92,3)
		A little	1 (7,7)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	11 (91,7)
		A little	1 (8,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubc.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.3 Distribution of General PN symptoms item responses over time - PN status at enrollment = Progressive (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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=13)	Not at all	13 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 37 (n=12)	Not at all	12 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	5 (50,0)
		A little	3 (30,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	1 (10,0)
	Pre-cycle 49 (n=10)	Not at all	5 (50,0)
		A little	3 (30,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	1 (10,0)
	Pre-cycle 61 (n= 8)	Not at all	5 (62,5)
		A little	1 (12,5)
		Some	1 (12,5)
		Pretty much	0
		A lot	1 (12,5)

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubd.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	6 (60,0)
		A little	3 (30,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	7 (70,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	1 (10,0)
	Pre-cycle 61 (n= 8)	Not at all	4 (50,0)
		A little	2 (25,0)
		Some	0
		Pretty much	0
		A lot	2 (25,0)

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

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	6 (60,0)
		A little	3 (30,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	4 (50,0)
		A little	3 (37,5)
		Some	0
		Pretty much	1 (12,5)
		A lot	0

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

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	6 (60,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	1 (10,0)
		A lot	1 (10,0)
	Pre-cycle 49 (n=10)	Not at all	6 (60,0)
		A little	1 (10,0)
		Some	2 (20,0)
		Pretty much	0
		A lot	1 (10,0)
	Pre-cycle 61 (n= 8)	Not at all	6 (75,0)
		A little	1 (12,5)
		Some	1 (12,5)
		Pretty much	0
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubd.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	6 (60,0)
		A little	4 (40,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	5 (50,0)
		A little	4 (40,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	4 (50,0)
		A little	3 (37,5)
		Some	1 (12,5)
		Pretty much	0
		A lot	0

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubd.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	6 (75,0)
		A little	2 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubd.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubd.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	8 (80,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubd.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubd.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	7 (70,0)
		A little	2 (20,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	6 (60,0)
		A little	4 (40,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	0
		Some	0
		Pretty much	1 (10,0)
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	9 (90,0)
		A little	0
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	9 (90,0)
		A little	0
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	8 (80,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	0
		Some	2 (20,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubd.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	8 (80,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	7 (70,0)
		A little	2 (20,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	9 (90,0)
		A little	0
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	7 (70,0)
		A little	3 (30,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	8 (80,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	0
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubd.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	8 (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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	9 (90,0)
		A little	1 (10,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsubd.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	8 (80,0)
		A little	1 (10,0)
		Some	1 (10,0)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	8 (80,0)
		A little	2 (20,0)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	0
		Some	1 (12,5)
		Pretty much	0
		A lot	0

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

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

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Table 2.1.4.4 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: 31 March 2021 (DC02)

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=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n=10)	Not at all	10 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 8)	Not at all	7 (87,5)
		A little	1 (12,5)
		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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	3 (33,3)
		A little	5 (55,6)
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	2 (28,6)
		A little	3 (42,9)
		Some	1 (14,3)
		Pretty much	0
		A lot	1 (14,3)
	Pre-cycle 61 (n= 5)	Not at all	3 (60,0)
		A little	1 (20,0)
		Some	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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)
	Pre-cycle 37 (n= 9)	Not at all	5 (55,6)
		A little	1 (11,1)
		Some	3 (33,3)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	3 (42,9)
		A little	1 (14,3)
		Some	2 (28,6)
		Pretty much	0
		A lot	1 (14,3)
	Pre-cycle 61 (n= 5)	Not at all	3 (60,0)
		A little	2 (40,0)
		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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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)
	Pre-cycle 37 (n= 9)	Not at all	7 (77,8)
		A little	1 (11,1)
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	0
		Some	0
		Pretty much	0
		A lot	1 (14,3)
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	1 (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.

root/cdar/dl53/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	0
		Some	0
		Pretty much	1 (11,1)
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	0
		Some	1 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	0
		Some	0
		Pretty much	1 (20,0)
		A lot	0

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

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	7 (77,8)
		A little	2 (22,2)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	4 (57,1)
		A little	3 (42,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	0
		Some	1 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	0
		Some	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	1 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	1 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	1 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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)
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	5 (71,4)
		A little	1 (14,3)
		Some	1 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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)
	Pre-cycle 37 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	1 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	6 (66,7)
		A little	3 (33,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	3 (42,9)
		A little	3 (42,9)
		Some	1 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	3 (60,0)
		A little	1 (20,0)
		Some	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	5 (55,6)
		A little	2 (22,2)
		Some	2 (22,2)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	5 (71,4)
		A little	0
		Some	0
		Pretty much	1 (14,3)
		A lot	1 (14,3)
	Pre-cycle 61 (n= 5)	Not at all	3 (60,0)
		A little	2 (40,0)
		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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	6 (66,7)
		A little	1 (11,1)
		Some	1 (11,1)
		Pretty much	0
		A lot	1 (11,1)
	Pre-cycle 49 (n= 7)	Not at all	3 (42,9)
		A little	3 (42,9)
		Some	1 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	7 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	0
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	7 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	7 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	1 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	5 (55,6)
		A little	2 (22,2)
		Some	2 (22,2)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	5 (71,4)
		A little	2 (28,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	2 (40,0)
		A little	2 (40,0)
		Some	1 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	1 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	0
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	0
		Some	1 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	0
		Some	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	5 (55,6)
		A little	3 (33,3)
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	4 (57,1)
		A little	0
		Some	2 (28,6)
		Pretty much	0
		A lot	1 (14,3)
	Pre-cycle 61 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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)
	Pre-cycle 37 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	5 (71,4)
		A little	1 (14,3)
		Some	1 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	5 (71,4)
		A little	0
		Some	1 (14,3)
		Pretty much	1 (14,3)
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	7 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	0
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	5 (71,4)
		A little	0
		Some	2 (28,6)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	0
		Some	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	4 (57,1)
		A little	3 (42,9)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	5 (71,4)
		A little	2 (28,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	1 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

root/cdar/dl53/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	7 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	7 (77,8)
		A little	1 (11,1)
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	0
		Some	1 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	1 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	0
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	5 (71,4)
		A little	2 (28,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptfsub.sas pnsmptfsube.rtf 22FEB2023:15:44 icesas68PD

Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	7 (77,8)
		A little	0
		Some	2 (22,2)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	4 (57,1)
		A little	1 (14,3)
		Some	0
		Pretty much	2 (28,6)
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	0
		Some	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	7 (77,8)
		A little	2 (22,2)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	5 (71,4)
		A little	2 (28,6)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	3 (60,0)
		A little	1 (20,0)
		Some	0
		Pretty much	1 (20,0)
		A lot	0

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

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown
(Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	8 (88,9)
		A little	1 (11,1)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	0
		Some	1 (14,3)
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	4 (80,0)
		A little	1 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	9 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	7 (100,0)
		A little	0
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

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Table 2.1.4.5 Distribution of General PN symptoms item responses over time - PN status at enrollment = Unknown (Full analysis set), Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n= 9)	Not at all	7 (77,8)
		A little	1 (11,1)
		Some	1 (11,1)
		Pretty much	0
		A lot	0
	Pre-cycle 49 (n= 7)	Not at all	6 (85,7)
		A little	1 (14,3)
		Some	0
		Pretty much	0
		A lot	0
	Pre-cycle 61 (n= 5)	Not at all	5 (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.

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1.14.1.2 Subgruppenanalyse zur Symptomcheckliste: Responderanalyse

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: 31 March 2021 (DC02)

		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=20)	14/20 (70,0)	6/20 (30,0)
	Pre-cycle 37 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 49 (N=18)	10/18 (55,6)	8/18 (44,4)
	Pre-cycle 61 (N=11)	5/11 (45,5)	6/11 (54,5)
	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=20)	11/20 (55,0)	9/20 (45,0)
	Pre-cycle 37 (N=19)	11/19 (57,9)	8/19 (42,1)
	Pre-cycle 49 (N=18)	10/18 (55,6)	8/18 (44,4)
	Pre-cycle 61 (N=11)	4/11 (36,4)	7/11 (63,6)
	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=20)	16/20 (80,0)	4/20 (20,0)
	Pre-cycle 37 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 49 (N=18)	13/18 (72,2)	5/18 (27,8)
	Pre-cycle 61 (N=11)	6/11 (54,5)	5/11 (45,5)
	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=20)	17/20 (85,0)	3/20 (15,0)
	Pre-cycle 37 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 49 (N=18)	15/18 (83,3)	3/18 (16,7)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	Overall (N=30)	22/30 (73,3)	8/30 (26,7)

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

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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: 31 March 2021 (DC02)

		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 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=20)	14/20 (70,0)	6/20 (30,0)
	Pre-cycle 37 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 49 (N=18)	12/18 (66,7)	6/18 (33,3)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsuba.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	11/11 (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=20)	18/20 (90,0)	2/20 (10,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	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=20)	17/20 (85,0)	3/20 (15,0)
	Pre-cycle 37 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 49 (N=18)	15/18 (83,3)	3/18 (16,7)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	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=20)	18/20 (90,0)	2/20 (10,0)
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)

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

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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: 31 March 2021 (DC02)

		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 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=20)	17/20 (85,0)	3/20 (15,0)
	Pre-cycle 37 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 49 (N=18)	15/18 (83,3)	3/18 (16,7)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsuba.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=20)	13/20 (65,0)	7/20 (35,0)
	Pre-cycle 37 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 49 (N=18)	13/18 (72,2)	5/18 (27,8)
	Pre-cycle 61 (N=11)	6/11 (54,5)	5/11 (45,5)
	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=20)	10/20 (50,0)	10/20 (50,0)
	Pre-cycle 37 (N=19)	9/19 (47,4)	10/19 (52,6)
	Pre-cycle 49 (N=18)	9/18 (50,0)	9/18 (50,0)
	Pre-cycle 61 (N=11)	4/11 (36,4)	7/11 (63,6)
	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=20)	13/20 (65,0)	7/20 (35,0)
	Pre-cycle 37 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 49 (N=18)	12/18 (66,7)	6/18 (33,3)
	Pre-cycle 61 (N=11)	4/11 (36,4)	7/11 (63,6)
	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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	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.

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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: 31 March 2021 (DC02)

		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 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=20)	18/20 (90,0)	2/20 (10,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	11/11 (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.

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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: 31 March 2021 (DC02)

		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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	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=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (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=20)	15/20 (75,0)	5/20 (25,0)
	Pre-cycle 37 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)

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

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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: 31 March 2021 (DC02)

		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 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=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (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.

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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: 31 March 2021 (DC02)

		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=20)	17/20 (85,0)	3/20 (15,0)
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	14/18 (77,8)	4/18 (22,2)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	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=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	Overall (N=30)	24/30 (80,0)	6/30 (20,0)
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=20)	18/20 (90,0)	2/20 (10,0)
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	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.

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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: 31 March 2021 (DC02)

		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 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=20)	16/20 (80,0)	4/20 (20,0)
	Pre-cycle 37 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 49 (N=18)	14/18 (77,8)	4/18 (22,2)
	Pre-cycle 61 (N=11)	8/11 (72,7)	3/11 (27,3)
	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.

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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: 31 March 2021 (DC02)

		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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	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=20)	16/20 (80,0)	4/20 (20,0)
	Pre-cycle 37 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 49 (N=18)	15/18 (83,3)	3/18 (16,7)
	Pre-cycle 61 (N=11)	8/11 (72,7)	3/11 (27,3)
	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=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (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=20)	18/20 (90,0)	2/20 (10,0)
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	Overall (N=30)	25/30 (83,3)	5/30 (16,7)

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

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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: 31 March 2021 (DC02)

		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 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=19)	19/19 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=10)	10/10 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsuba.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	11/11 (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=20)	16/20 (80,0)	4/20 (20,0)
	Pre-cycle 37 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 49 (N=18)	15/18 (83,3)	3/18 (16,7)
	Pre-cycle 61 (N=11)	8/11 (72,7)	3/11 (27,3)
	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=20)	17/20 (85,0)	3/20 (15,0)
	Pre-cycle 37 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 49 (N=18)	14/18 (77,8)	4/18 (22,2)
	Pre-cycle 61 (N=11)	6/11 (54,5)	5/11 (45,5)
	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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)

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

root/cdar/dl53/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsuba.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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 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=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsuba.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	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.

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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: 31 March 2021 (DC02)

		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=12)	6/12 (50,0)	6/12 (50,0)
	Pre-cycle 49 (N=9)	5/ 9 (55,6)	4/ 9 (44,4)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	Overall (N=19)	7/19 (36,8)	12/19 (63,2)
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=12)	5/12 (41,7)	7/12 (58,3)
	Pre-cycle 49 (N=9)	5/ 9 (55,6)	4/ 9 (44,4)
	Pre-cycle 61 (N=6)	3/ 6 (50,0)	3/ 6 (50,0)
	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=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	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.

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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: 31 March 2021 (DC02)

		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 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=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	2/ 6 (33,3)	4/ 6 (66,7)
	Overall (N=19)	10/19 (52,6)	9/19 (47,4)

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

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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: 31 March 2021 (DC02)

		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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	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=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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.

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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: 31 March 2021 (DC02)

		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 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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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.

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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: 31 March 2021 (DC02)

		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=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 49 (N=9)	5/ 9 (55,6)	4/ 9 (44,4)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	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=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 49 (N=9)	5/ 9 (55,6)	4/ 9 (44,4)
	Pre-cycle 61 (N=6)	3/ 6 (50,0)	3/ 6 (50,0)
	Overall (N=19)	9/19 (47,4)	10/19 (52,6)
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=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	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.

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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: 31 March 2021 (DC02)

		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 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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubb.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (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.

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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: 31 March 2021 (DC02)

		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 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=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubb.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)
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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	17/19 (89,5)	2/19 (10,5)

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

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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: 31 March 2021 (DC02)

		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 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=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 49 (N=9)	5/ 9 (55,6)	4/ 9 (44,4)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubb.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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.

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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: 31 March 2021 (DC02)

		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 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=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubb.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	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=12)	6/12 (50,0)	6/12 (50,0)
	Pre-cycle 49 (N=9)	4/ 9 (44,4)	5/ 9 (55,6)
	Pre-cycle 61 (N=6)	3/ 6 (50,0)	3/ 6 (50,0)
	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=12)	4/12 (33,3)	8/12 (66,7)
	Pre-cycle 49 (N=9)	4/ 9 (44,4)	5/ 9 (55,6)
	Pre-cycle 61 (N=6)	3/ 6 (50,0)	3/ 6 (50,0)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	17/19 (89,5)	2/19 (10,5)

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

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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: 31 March 2021 (DC02)

		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 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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	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.

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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: 31 March 2021 (DC02)

		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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	3/ 6 (50,0)	3/ 6 (50,0)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubb.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 37 (N=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 49 (N=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 61 (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=13)	4/13 (30,8)	9/13 (69,2)
	Pre-cycle 37 (N=12)	6/12 (50,0)	6/12 (50,0)
	Pre-cycle 49 (N=10)	5/10 (50,0)	5/10 (50,0)
	Pre-cycle 61 (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=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 37 (N=12)	6/12 (50,0)	6/12 (50,0)
	Pre-cycle 49 (N=10)	5/10 (50,0)	5/10 (50,0)
	Pre-cycle 61 (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=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 61 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	15/21 (71,4)	6/21 (28,6)

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubc.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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 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=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubc.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 37 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubc.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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 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=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 37 (N=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 49 (N=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 61 (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.

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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: 31 March 2021 (DC02)

		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=13)	6/13 (46,2)	7/13 (53,8)
	Pre-cycle 37 (N=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 49 (N=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 61 (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=13)	4/13 (30,8)	9/13 (69,2)
	Pre-cycle 37 (N=12)	4/12 (33,3)	8/12 (66,7)
	Pre-cycle 49 (N=10)	3/10 (30,0)	7/10 (70,0)
	Pre-cycle 61 (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=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	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=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (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.

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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: 31 March 2021 (DC02)

		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 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=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubc.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 37 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

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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: 31 March 2021 (DC02)

		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 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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (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.

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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: 31 March 2021 (DC02)

		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=13)	7/13 (53,8)	6/13 (46,2)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	Overall (N=21)	14/21 (66,7)	7/21 (33,3)
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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	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.

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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: 31 March 2021 (DC02)

		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 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=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 37 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 61 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubc.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 37 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

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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: 31 March 2021 (DC02)

		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 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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=3)	3/ 3 (100,0)	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubc.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 37 (N=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 49 (N=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 61 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	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=13)	8/13 (61,5)	5/13 (38,5)
	Pre-cycle 37 (N=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 49 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 61 (N=4)	2/ 4 (50,0)	2/ 4 (50,0)
	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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

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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: 31 March 2021 (DC02)

		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 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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubc.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubc.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 49 (N=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 61 (N=8)	4/ 8 (50,0)	4/ 8 (50,0)
	Overall (N=14)	7/14 (50,0)	7/14 (50,0)
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=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 49 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 61 (N=8)	5/ 8 (62,5)	3/ 8 (37,5)
	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=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	5/ 8 (62,5)	3/ 8 (37,5)
	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.

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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: 31 March 2021 (DC02)

		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 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=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 49 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 61 (N=8)	5/ 8 (62,5)	3/ 8 (37,5)
	Overall (N=14)	7/14 (50,0)	7/14 (50,0)

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubd.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	6/ 8 (75,0)	2/ 8 (25,0)
	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

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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: 31 March 2021 (DC02)

		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 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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubd.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	5/ 8 (62,5)	3/ 8 (37,5)
	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=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 49 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 61 (N=8)	5/ 8 (62,5)	3/ 8 (37,5)
	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=10)	4/10 (40,0)	6/10 (60,0)
	Pre-cycle 49 (N=10)	5/10 (50,0)	5/10 (50,0)
	Pre-cycle 61 (N=8)	3/ 8 (37,5)	5/ 8 (62,5)
	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubd.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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 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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubd.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	6/ 8 (75,0)	2/ 8 (25,0)
	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubd.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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 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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

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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: 31 March 2021 (DC02)

		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=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	6/ 8 (75,0)	2/ 8 (25,0)
	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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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=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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

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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: 31 March 2021 (DC02)

		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 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=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	5/ 8 (62,5)	3/ 8 (37,5)
	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.

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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: 31 March 2021 (DC02)

		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=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 61 (N=8)	6/ 8 (75,0)	2/ 8 (25,0)
	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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	6/ 8 (75,0)	2/ 8 (25,0)
	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.

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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: 31 March 2021 (DC02)

		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 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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

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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: 31 March 2021 (DC02)

		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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 49 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 61 (N=8)	4/ 8 (50,0)	4/ 8 (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=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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

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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: 31 March 2021 (DC02)

		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 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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubd.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsubd.rtf 22FEB2023:18:09 icesas370PD

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: 31 March 2021 (DC02)

		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)
	Pre-cycle 37 (N=9)	4/ 9 (44,4)	5/ 9 (55,6)
	Pre-cycle 49 (N=7)	3/ 7 (42,9)	4/ 7 (57,1)
	Pre-cycle 61 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
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)
	Pre-cycle 37 (N=9)	3/ 9 (33,3)	6/ 9 (66,7)
	Pre-cycle 49 (N=7)	3/ 7 (42,9)	4/ 7 (57,1)
	Pre-cycle 61 (N=5)	1/ 5 (20,0)	4/ 5 (80,0)
	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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (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)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	5/ 5 (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.

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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: 31 March 2021 (DC02)

		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 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)
	Pre-cycle 37 (N=9)	5/ 9 (55,6)	4/ 9 (44,4)
	Pre-cycle 49 (N=7)	4/ 7 (57,1)	3/ 7 (42,9)
	Pre-cycle 61 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsube.rtf 22FEB2023:18:10 icesas370PD

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: 31 March 2021 (DC02)

		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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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.

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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: 31 March 2021 (DC02)

		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 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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsube.rtf 22FEB2023:18:10 icesas370PD

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: 31 March 2021 (DC02)

		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)
	Pre-cycle 37 (N=9)	5/ 9 (55,6)	4/ 9 (44,4)
	Pre-cycle 49 (N=7)	4/ 7 (57,1)	3/ 7 (42,9)
	Pre-cycle 61 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	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)
	Pre-cycle 37 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 49 (N=7)	4/ 7 (57,1)	3/ 7 (42,9)
	Pre-cycle 61 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
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)
	Pre-cycle 37 (N=9)	5/ 9 (55,6)	4/ 9 (44,4)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	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)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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.

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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: 31 March 2021 (DC02)

		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 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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsube.rtf 22FEB2023:18:10 icesas370PD

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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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.

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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: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsube.rtf 22FEB2023:18:10 icesas370PD

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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	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
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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.

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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: 31 March 2021 (DC02)

		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 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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsube.rtf 22FEB2023:18:10 icesas370PD

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: 31 March 2021 (DC02)

		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)
	Pre-cycle 37 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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.

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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: 31 March 2021 (DC02)

		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 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)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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)
	Pre-cycle 37 (N=9)	5/ 9 (55,6)	4/ 9 (44,4)
	Pre-cycle 49 (N=7)	4/ 7 (57,1)	3/ 7 (42,9)
	Pre-cycle 61 (N=5)	2/ 5 (40,0)	3/ 5 (60,0)
	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)
	Pre-cycle 37 (N=9)	4/ 9 (44,4)	5/ 9 (55,6)
	Pre-cycle 49 (N=7)	4/ 7 (57,1)	3/ 7 (42,9)
	Pre-cycle 61 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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.

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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: 31 March 2021 (DC02)

		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 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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	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.

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub.sas pnsmptrsube.rtf 22FEB2023:18:10 icesas370PD

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: 31 March 2021 (DC02)

		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)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	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.

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 1.Fatigue/feeling tired	Pre-cycle 3 (N=30)	18/30 (60,0)	12/30 (40,0)
	Pre-cycle 5 (N=29)	21/29 (72,4)	8/29 (27,6)
	Pre-cycle 9 (N=28)	20/28 (71,4)	8/28 (28,6)
	Pre-cycle 13 (N=27)	19/27 (70,4)	8/27 (29,6)
	Pre-cycle 25 (N=20)	15/20 (75,0)	5/20 (25,0)
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	11/30 (36,7)	19/30 (63,3)
Item 2.Sleep problems	Pre-cycle 3 (N=30)	25/30 (83,3)	5/30 (16,7)
	Pre-cycle 5 (N=29)	26/29 (89,7)	3/29 (10,3)
	Pre-cycle 9 (N=28)	22/28 (78,6)	6/28 (21,4)
	Pre-cycle 13 (N=27)	23/27 (85,2)	4/27 (14,8)
	Pre-cycle 25 (N=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	Overall (N=30)	14/30 (46,7)	16/30 (53,3)
Item 3.Less appetite	Pre-cycle 3 (N=30)	25/30 (83,3)	5/30 (16,7)
	Pre-cycle 5 (N=29)	26/29 (89,7)	3/29 (10,3)
	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=20)	18/20 (90,0)	2/20 (10,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	Overall (N=30)	14/30 (46,7)	16/30 (53,3)
Item 4.More appetite	Pre-cycle 3 (N=30)	17/30 (56,7)	13/30 (43,3)
	Pre-cycle 5 (N=29)	13/29 (44,8)	16/29 (55,2)
	Pre-cycle 9 (N=28)	24/28 (85,7)	4/28 (14,3)
	Pre-cycle 13 (N=27)	18/27 (66,7)	9/27 (33,3)
	Pre-cycle 25 (N=20)	14/20 (70,0)	6/20 (30,0)
	Pre-cycle 37 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 49 (N=18)	12/18 (66,7)	6/18 (33,3)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	Overall (N=30)	8/30 (26,7)	22/30 (73,3)

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

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 5.Headaches	Pre-cycle 3 (N=30)	25/30 (83,3)	5/30 (16,7)
	Pre-cycle 5 (N=29)	25/29 (86,2)	4/29 (13,8)
	Pre-cycle 9 (N=28)	22/28 (78,6)	6/28 (21,4)
	Pre-cycle 13 (N=27)	24/27 (88,9)	3/27 (11,1)
	Pre-cycle 25 (N=20)	15/20 (75,0)	5/20 (25,0)
	Pre-cycle 37 (N=19)	10/19 (52,6)	9/19 (47,4)
	Pre-cycle 49 (N=18)	14/18 (77,8)	4/18 (22,2)
	Pre-cycle 61 (N=11)	9/11 (81,8)	2/11 (18,2)
	Overall (N=30)	14/30 (46,7)	16/30 (53,3)

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

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 6.Vision changes	Pre-cycle 3 (N=30)	29/30 (96,7)	1/30 (3,3)
	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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	8/11 (72,7)	3/11 (27,3)
	Overall (N=30)	23/30 (76,7)	7/30 (23,3)
Item 7.Decreased hearing	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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	Overall (N=30)	23/30 (76,7)	7/30 (23,3)
Item 8.Mouth sores	Pre-cycle 3 (N=30)	26/30 (86,7)	4/30 (13,3)
	Pre-cycle 5 (N=29)	28/29 (96,6)	1/29 (3,4)
	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=20)	18/20 (90,0)	2/20 (10,0)
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	Overall (N=30)	22/30 (73,3)	8/30 (26,7)
Item 9.Trouble swallowing	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)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)

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

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 10.Choking	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)	28/28 (100,0)	0
	Pre-cycle 13 (N=27)	27/27 (100,0)	0
	Pre-cycle 25 (N=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)

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

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 11.Snoring	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)	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=20)	18/20 (90,0)	2/20 (10,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	Overall (N=30)	18/30 (60,0)	12/30 (40,0)
Item 12.Frequent awakenings at night	Pre-cycle 3 (N=30)	23/30 (76,7)	7/30 (23,3)
	Pre-cycle 5 (N=29)	25/29 (86,2)	4/29 (13,8)
	Pre-cycle 9 (N=28)	24/28 (85,7)	4/28 (14,3)
	Pre-cycle 13 (N=27)	21/27 (77,8)	6/27 (22,2)
	Pre-cycle 25 (N=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	15/30 (50,0)	15/30 (50,0)
Item 13.Cough	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)	20/28 (71,4)	8/28 (28,6)
	Pre-cycle 13 (N=27)	21/27 (77,8)	6/27 (22,2)
	Pre-cycle 25 (N=20)	17/20 (85,0)	3/20 (15,0)
	Pre-cycle 37 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 49 (N=18)	15/18 (83,3)	3/18 (16,7)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	14/30 (46,7)	16/30 (53,3)
Item 14.Wheezing	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)	27/27 (100,0)	0
	Pre-cycle 25 (N=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	23/30 (76,7)	7/30 (23,3)

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

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 15.Difficulty breathing	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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	11/11 (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.

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	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)	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=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	26/30 (86,7)	4/30 (13,3)
Item 17.Palpitations/fluttering	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)	25/27 (92,6)	2/27 (7,4)
	Pre-cycle 25 (N=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	27/30 (90,0)	3/30 (10,0)
Item 18.Shortness of breath with activity	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	28/29 (96,6)	1/29 (3,4)
	Pre-cycle 9 (N=28)	26/28 (92,9)	2/28 (7,1)
	Pre-cycle 13 (N=27)	27/27 (100,0)	0
	Pre-cycle 25 (N=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	Overall (N=30)	23/30 (76,7)	7/30 (23,3)
Item 19.Shortness of breath at rest	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)	27/28 (96,4)	1/28 (3,6)
	Pre-cycle 13 (N=27)	27/27 (100,0)	0
	Pre-cycle 25 (N=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)

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

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 20.Swelling in hands/feet	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	28/29 (96,6)	1/29 (3,4)
	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=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	20/30 (66,7)	10/30 (33,3)

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

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 21.Abdominal pain	Pre-cycle 3 (N=30)	18/30 (60,0)	12/30 (40,0)
	Pre-cycle 5 (N=29)	24/29 (82,8)	5/29 (17,2)
	Pre-cycle 9 (N=28)	20/28 (71,4)	8/28 (28,6)
	Pre-cycle 13 (N=27)	21/27 (77,8)	6/27 (22,2)
	Pre-cycle 25 (N=20)	14/20 (70,0)	6/20 (30,0)
	Pre-cycle 37 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 49 (N=18)	15/18 (83,3)	3/18 (16,7)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	Overall (N=30)	10/30 (33,3)	20/30 (66,7)
Item 22.Heartburn	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	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)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	24/30 (80,0)	6/30 (20,0)
Item 23.Nausea	Pre-cycle 3 (N=30)	20/30 (66,7)	10/30 (33,3)
	Pre-cycle 5 (N=29)	20/29 (69,0)	9/29 (31,0)
	Pre-cycle 9 (N=28)	21/28 (75,0)	7/28 (25,0)
	Pre-cycle 13 (N=27)	20/27 (74,1)	7/27 (25,9)
	Pre-cycle 25 (N=20)	15/20 (75,0)	5/20 (25,0)
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	12/30 (40,0)	18/30 (60,0)
Item 24.Vomiting	Pre-cycle 3 (N=30)	25/30 (83,3)	5/30 (16,7)
	Pre-cycle 5 (N=29)	22/29 (75,9)	7/29 (24,1)
	Pre-cycle 9 (N=28)	23/28 (82,1)	5/28 (17,9)
	Pre-cycle 13 (N=27)	24/27 (88,9)	3/27 (11,1)
	Pre-cycle 25 (N=20)	17/20 (85,0)	3/20 (15,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	16/30 (53,3)	14/30 (46,7)

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

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 25.Diarrhea	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)	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=20)	16/20 (80,0)	4/20 (20,0)
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	10/30 (33,3)	20/30 (66,7)

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

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 26.Constipation	Pre-cycle 3 (N=30)	23/30 (76,7)	7/30 (23,3)
	Pre-cycle 5 (N=29)	24/29 (82,8)	5/29 (17,2)
	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=20)	17/20 (85,0)	3/20 (15,0)
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	15/18 (83,3)	3/18 (16,7)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	12/30 (40,0)	18/30 (60,0)
Item 27.Stool incontinence	Pre-cycle 3 (N=30)	26/30 (86,7)	4/30 (13,3)
	Pre-cycle 5 (N=29)	29/29 (100,0)	0
	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=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	21/30 (70,0)	9/30 (30,0)
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)	28/28 (100,0)	0
	Pre-cycle 13 (N=27)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	28/30 (93,3)	2/30 (6,7)
Item 29.Increased urinary frequency/urgency	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)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	25/30 (83,3)	5/30 (16,7)

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

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 30.Difficulty beginning 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)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=10)	9/10 (90,0)	1/10 (10,0)
	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.

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	Pre-cycle 3 (N=29)	28/29 (96,6)	1/29 (3,4)
	Pre-cycle 5 (N=28)	28/28 (100,0)	0
	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=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	27/30 (90,0)	3/30 (10,0)
Item 32.Weakness	Pre-cycle 3 (N=30)	28/30 (93,3)	2/30 (6,7)
	Pre-cycle 5 (N=29)	28/29 (96,6)	1/29 (3,4)
	Pre-cycle 9 (N=28)	25/28 (89,3)	3/28 (10,7)
	Pre-cycle 13 (N=27)	26/27 (96,3)	1/27 (3,7)
	Pre-cycle 25 (N=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	15/18 (83,3)	3/18 (16,7)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	20/30 (66,7)	10/30 (33,3)
Item 33.Muscle pain	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=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 49 (N=18)	16/18 (88,9)	2/18 (11,1)
	Pre-cycle 61 (N=11)	11/11 (100,0)	0
	Overall (N=30)	16/30 (53,3)	14/30 (46,7)
Item 34.Dizziness	Pre-cycle 3 (N=30)	26/30 (86,7)	4/30 (13,3)
	Pre-cycle 5 (N=29)	28/29 (96,6)	1/29 (3,4)
	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=20)	17/20 (85,0)	3/20 (15,0)
	Pre-cycle 37 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 49 (N=18)	17/18 (94,4)	1/18 (5,6)
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	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.

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 35.Numbness	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)	27/28 (96,4)	1/28 (3,6)
	Pre-cycle 13 (N=27)	27/27 (100,0)	0
	Pre-cycle 25 (N=20)	20/20 (100,0)	0
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	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.

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Table 2.1.3.1 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Male

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=30) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	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)	28/28 (100,0)	0
	Pre-cycle 13 (N=27)	27/27 (100,0)	0
	Pre-cycle 25 (N=20)	19/20 (95,0)	1/20 (5,0)
	Pre-cycle 37 (N=19)	19/19 (100,0)	0
	Pre-cycle 49 (N=18)	18/18 (100,0)	0
	Pre-cycle 61 (N=11)	10/11 (90,9)	1/11 (9,1)
	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.

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 1.Fatigue/feeling tired	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)	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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	5/ 9 (55,6)	4/ 9 (44,4)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	Overall (N=19)	5/19 (26,3)	14/19 (73,7)
Item 2.Sleep problems	Pre-cycle 3 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 5 (N=19)	18/19 (94,7)	1/19 (5,3)
	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=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	Overall (N=19)	10/19 (52,6)	9/19 (47,4)
Item 3.Less appetite	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)	16/17 (94,1)	1/17 (5,9)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	Overall (N=19)	11/19 (57,9)	8/19 (42,1)
Item 4.More appetite	Pre-cycle 3 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 5 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 9 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 13 (N=17)	16/17 (94,1)	1/17 (5,9)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	7/19 (36,8)	12/19 (63,2)

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

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 5.Headaches	Pre-cycle 3 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 5 (N=19)	14/19 (73,7)	5/19 (26,3)
	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)	11/15 (73,3)	4/15 (26,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	8/19 (42,1)	11/19 (57,9)

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

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened 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)	15/19 (78,9)	4/19 (21,1)
	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)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	13/19 (68,4)	6/19 (31,6)
Item 7.Decreased hearing	Pre-cycle 3 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 5 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 9 (N=19)	19/19 (100,0)	0
	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=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	14/19 (73,7)	5/19 (26,3)
Item 8.Mouth sores	Pre-cycle 3 (N=19)	18/19 (94,7)	1/19 (5,3)
	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)	15/15 (100,0)	0
	Pre-cycle 37 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	Overall (N=19)	10/19 (52,6)	9/19 (47,4)
Item 9.Trouble swallowing	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=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	17/19 (89,5)	2/19 (10,5)

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

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 10.Choking	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)	19/19 (100,0)	0
	Pre-cycle 13 (N=17)	17/17 (100,0)	0
	Pre-cycle 25 (N=15)	14/15 (93,3)	1/15 (6,7)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	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.

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 11.Snoring	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)	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=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	15/19 (78,9)	4/19 (21,1)
Item 12.Frequent awakenings at night	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)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 13 (N=17)	16/17 (94,1)	1/17 (5,9)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=12)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	9/19 (47,4)	10/19 (52,6)
Item 13.Cough	Pre-cycle 3 (N=19)	12/19 (63,2)	7/19 (36,8)
	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)	11/15 (73,3)	4/15 (26,7)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	8/19 (42,1)	11/19 (57,9)
Item 14.Wheezing	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)	19/19 (100,0)	0
	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=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	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.

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 15.Difficulty breathing	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)	16/17 (94,1)	1/17 (5,9)
	Pre-cycle 25 (N=15)	15/15 (100,0)	0
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (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.

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	Pre-cycle 3 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 5 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 9 (N=19)	17/19 (89,5)	2/19 (10,5)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	10/19 (52,6)	9/19 (47,4)
Item 17.Palpitations/fluttering	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=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	Overall (N=19)	14/19 (73,7)	5/19 (26,3)
Item 18.Shortness of breath with activity	Pre-cycle 3 (N=19)	18/19 (94,7)	1/19 (5,3)
	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)	14/15 (93,3)	1/15 (6,7)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	3/ 6 (50,0)	3/ 6 (50,0)
	Overall (N=19)	9/19 (47,4)	10/19 (52,6)
Item 19.Shortness of breath at rest	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)	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	13/19 (68,4)	6/19 (31,6)

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

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 20.Swelling in hands/feet	Pre-cycle 3 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 5 (N=19)	15/19 (78,9)	4/19 (21,1)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	Overall (N=19)	13/19 (68,4)	6/19 (31,6)

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

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 21.Abdominal pain	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)	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=19)	13/19 (68,4)	6/19 (31,6)
Item 22.Heartburn	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)	19/19 (100,0)	0
	Pre-cycle 13 (N=17)	16/17 (94,1)	1/17 (5,9)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	14/19 (73,7)	5/19 (26,3)
Item 23.Nausea	Pre-cycle 3 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 5 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 9 (N=19)	13/19 (68,4)	6/19 (31,6)
	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=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	7/19 (36,8)	12/19 (63,2)
Item 24.Vomiting	Pre-cycle 3 (N=19)	12/19 (63,2)	7/19 (36,8)
	Pre-cycle 5 (N=19)	15/19 (78,9)	4/19 (21,1)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	10/19 (52,6)	9/19 (47,4)

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

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 25.Diarrhea	Pre-cycle 3 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 5 (N=19)	17/19 (89,5)	2/19 (10,5)
	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)	14/15 (93,3)	1/15 (6,7)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	10/19 (52,6)	9/19 (47,4)

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

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 26.Constipation	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)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 13 (N=17)	14/17 (82,4)	3/17 (17,6)
	Pre-cycle 25 (N=15)	15/15 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	13/19 (68,4)	6/19 (31,6)
Item 27.Stool incontinence	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)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 13 (N=17)	16/17 (94,1)	1/17 (5,9)
	Pre-cycle 25 (N=15)	15/15 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	4/ 6 (66,7)	2/ 6 (33,3)
	Overall (N=19)	13/19 (68,4)	6/19 (31,6)
Item 28.Pain with urination	Pre-cycle 3 (N=19)	19/19 (100,0)	0
	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)	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)
Item 29.Increased urinary frequency/urgency	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)	16/19 (84,2)	3/19 (15,8)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (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.

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 30.Difficulty beginning urination	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)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 13 (N=17)	16/17 (94,1)	1/17 (5,9)
	Pre-cycle 25 (N=15)	13/15 (86,7)	2/15 (13,3)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	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.

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	Pre-cycle 3 (N=19)	19/19 (100,0)	0
	Pre-cycle 5 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 9 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 13 (N=17)	17/17 (100,0)	0
	Pre-cycle 25 (N=15)	15/15 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	16/19 (84,2)	3/19 (15,8)
Item 32.Weakness	Pre-cycle 3 (N=19)	19/19 (100,0)	0
	Pre-cycle 5 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 9 (N=19)	17/19 (89,5)	2/19 (10,5)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	Overall (N=19)	12/19 (63,2)	7/19 (36,8)
Item 33.Muscle pain	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	Overall (N=19)	13/19 (68,4)	6/19 (31,6)
Item 34.Dizziness	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)	12/15 (80,0)	3/15 (20,0)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 61 (N=6)	5/ 6 (83,3)	1/ 6 (16,7)
	Overall (N=19)	9/19 (47,4)	10/19 (52,6)

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

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 35.Numbness	Pre-cycle 3 (N=19)	19/19 (100,0)	0
	Pre-cycle 5 (N=19)	18/19 (94,7)	1/19 (5,3)
	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=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	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.

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Table 2.1.3.2 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - Gender = Female

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=20) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	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)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 13 (N=17)	17/17 (100,0)	0
	Pre-cycle 25 (N=15)	15/15 (100,0)	0
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 61 (N=6)	6/ 6 (100,0)	0
	Overall (N=19)	13/19 (68,4)	6/19 (31,6)

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

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 1.Fatigue/feeling tired	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)	15/21 (71,4)	6/21 (28,6)
	Pre-cycle 13 (N=19)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	8/21 (38,1)	13/21 (61,9)
Item 2.Sleep problems	Pre-cycle 3 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 5 (N=21)	21/21 (100,0)	0
	Pre-cycle 9 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 13 (N=19)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 25 (N=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	13/21 (61,9)	8/21 (38,1)
Item 3.Less appetite	Pre-cycle 3 (N=21)	20/21 (95,2)	1/21 (4,8)
	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)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 25 (N=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	11/21 (52,4)	10/21 (47,6)
Item 4.More appetite	Pre-cycle 3 (N=21)	13/21 (61,9)	8/21 (38,1)
	Pre-cycle 5 (N=21)	14/21 (66,7)	7/21 (33,3)
	Pre-cycle 9 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 13 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 25 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 37 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	5/21 (23,8)	16/21 (76,2)

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

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 5.Headaches	Pre-cycle 3 (N=21)	18/21 (85,7)	3/21 (14,3)
	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)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 25 (N=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 37 (N=12)	5/12 (41,7)	7/12 (58,3)
	Pre-cycle 49 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	9/21 (42,9)	12/21 (57,1)

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

root/cdar/d153/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub_det.sas pnsmptrsubc_det.rtf 22FEB2023:18:09 icesas78PD

Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened 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)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 9 (N=21)	21/21 (100,0)	0
	Pre-cycle 13 (N=19)	19/19 (100,0)	0
	Pre-cycle 25 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	16/21 (76,2)	5/21 (23,8)
Item 7.Decreased hearing	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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	16/21 (76,2)	5/21 (23,8)
Item 8.Mouth sores	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)	15/19 (78,9)	4/19 (21,1)
	Pre-cycle 25 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	12/21 (57,1)	9/21 (42,9)
Item 9.Trouble swallowing	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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 10.Choking	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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	20/21 (95,2)	1/21 (4,8)

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

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 11.Snoring	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)	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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	13/21 (61,9)	8/21 (38,1)
Item 12.Frequent awakenings at night	Pre-cycle 3 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 5 (N=21)	21/21 (100,0)	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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	13/21 (61,9)	8/21 (38,1)
Item 13.Cough	Pre-cycle 3 (N=21)	17/21 (81,0)	4/21 (19,0)
	Pre-cycle 5 (N=21)	15/21 (71,4)	6/21 (28,6)
	Pre-cycle 9 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 13 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 25 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	8/21 (38,1)	13/21 (61,9)
Item 14.Wheezing	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)	19/19 (100,0)	0
	Pre-cycle 25 (N=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 15.Difficulty breathing	Pre-cycle 3 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 5 (N=21)	21/21 (100,0)	0
	Pre-cycle 9 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 13 (N=19)	19/19 (100,0)	0
	Pre-cycle 25 (N=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

root/cdar/dl53/_iemt/ar/payer2023/tlf_gp/dev/program/pnsmptrsub_det.sas pnsmptrsubc_det.rtf 22FEB2023:18:09 icesas78PD

Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	Pre-cycle 3 (N=21)	20/21 (95,2)	1/21 (4,8)
	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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	18/21 (85,7)	3/21 (14,3)
Item 17.Palpitations/fluttering	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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	20/21 (95,2)	1/21 (4,8)
Item 18.Shortness of breath with activity	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)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	19/19 (100,0)	0
	Pre-cycle 25 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=21)	16/21 (76,2)	5/21 (23,8)
Item 19.Shortness of breath at rest	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)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 13 (N=19)	19/19 (100,0)	0
	Pre-cycle 25 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 20.Swelling in hands/feet	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)	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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	15/21 (71,4)	6/21 (28,6)

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

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 21.Abdominal pain	Pre-cycle 3 (N=21)	11/21 (52,4)	10/21 (47,6)
	Pre-cycle 5 (N=21)	18/21 (85,7)	3/21 (14,3)
	Pre-cycle 9 (N=21)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 13 (N=19)	17/19 (89,5)	2/19 (10,5)
	Pre-cycle 25 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	8/21 (38,1)	13/21 (61,9)
Item 22.Heartburn	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)	19/19 (100,0)	0
	Pre-cycle 25 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	17/21 (81,0)	4/21 (19,0)
Item 23.Nausea	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)	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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	10/21 (47,6)	11/21 (52,4)
Item 24.Vomiting	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)	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=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	11/21 (52,4)	10/21 (47,6)

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

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 25.Diarrhea	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)	16/21 (76,2)	5/21 (23,8)
	Pre-cycle 13 (N=19)	14/19 (73,7)	5/19 (26,3)
	Pre-cycle 25 (N=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	7/21 (33,3)	14/21 (66,7)

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

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 26.Constipation	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)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	16/19 (84,2)	3/19 (15,8)
	Pre-cycle 25 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	12/21 (57,1)	9/21 (42,9)
Item 27.Stool incontinence	Pre-cycle 3 (N=21)	20/21 (95,2)	1/21 (4,8)
	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)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 25 (N=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	18/21 (85,7)	3/21 (14,3)
Item 28.Pain with urination	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)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 13 (N=19)	19/19 (100,0)	0
	Pre-cycle 25 (N=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	19/21 (90,5)	2/21 (9,5)
Item 29.Increased urinary frequency/urgency	Pre-cycle 3 (N=21)	20/21 (95,2)	1/21 (4,8)
	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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	20/21 (95,2)	1/21 (4,8)

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

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 30.Difficulty beginning urination	Pre-cycle 3 (N=21)	20/21 (95,2)	1/21 (4,8)
	Pre-cycle 5 (N=21)	21/21 (100,0)	0
	Pre-cycle 9 (N=21)	19/21 (90,5)	2/21 (9,5)
	Pre-cycle 13 (N=19)	19/19 (100,0)	0
	Pre-cycle 25 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=3)	3/ 3 (100,0)	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.

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	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)	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=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	19/21 (90,5)	2/21 (9,5)
Item 32.Weakness	Pre-cycle 3 (N=21)	21/21 (100,0)	0
	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)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 25 (N=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	14/21 (66,7)	7/21 (33,3)
Item 33.Muscle pain	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)	18/19 (94,7)	1/19 (5,3)
	Pre-cycle 25 (N=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	0
	Overall (N=21)	14/21 (66,7)	7/21 (33,3)
Item 34.Dizziness	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=13)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 37 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	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.

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 35.Numbness	Pre-cycle 3 (N=21)	21/21 (100,0)	0
	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)	19/19 (100,0)	0
	Pre-cycle 25 (N=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

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Table 2.1.3.3 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=21) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	Pre-cycle 3 (N=21)	21/21 (100,0)	0
	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)	19/19 (100,0)	0
	Pre-cycle 25 (N=13)	13/13 (100,0)	0
	Pre-cycle 37 (N=12)	12/12 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=4)	4/ 4 (100,0)	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.

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 1.Fatigue/feeling tired	Pre-cycle 3 (N=14)	8/14 (57,1)	6/14 (42,9)
	Pre-cycle 5 (N=14)	9/14 (64,3)	5/14 (35,7)
	Pre-cycle 9 (N=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 13 (N=12)	6/12 (50,0)	6/12 (50,0)
	Pre-cycle 25 (N=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 37 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 61 (N=8)	6/ 8 (75,0)	2/ 8 (25,0)
	Overall (N=14)	4/14 (28,6)	10/14 (71,4)
Item 2.Sleep problems	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)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	6/ 8 (75,0)	2/ 8 (25,0)
	Overall (N=14)	5/14 (35,7)	9/14 (64,3)
Item 3.Less appetite	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)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 61 (N=8)	5/ 8 (62,5)	3/ 8 (37,5)
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)
Item 4.More appetite	Pre-cycle 3 (N=14)	9/14 (64,3)	5/14 (35,7)
	Pre-cycle 5 (N=14)	6/14 (42,9)	8/14 (57,1)
	Pre-cycle 9 (N=13)	11/13 (84,6)	2/13 (15,4)
	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=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 49 (N=10)	6/10 (60,0)	4/10 (40,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	Overall (N=14)	4/14 (28,6)	10/14 (71,4)

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

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 5.Headaches	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 9 (N=13)	8/13 (61,5)	5/13 (38,5)
	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=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	6/ 8 (75,0)	2/ 8 (25,0)
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)

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

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 6.Vision changes	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	6/ 8 (75,0)	2/ 8 (25,0)
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)
Item 7.Decreased hearing	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)	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 8.Mouth sores	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)	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)	12/12 (100,0)	0
	Pre-cycle 37 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
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)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 10.Choking	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)	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 11.Snoring	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)	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	8/ 8 (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)	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)	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=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)
Item 13.Cough	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 5 (N=14)	13/14 (92,9)	1/14 (7,1)
	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)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
Item 14.Wheezing	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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 15.Difficulty breathing	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	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)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	8/ 8 (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.

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	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)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 25 (N=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 37 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
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)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)
Item 18.Shortness of breath with activity	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=14)	11/14 (78,6)	3/14 (21,4)
	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)	12/12 (100,0)	0
	Pre-cycle 37 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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=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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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.

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
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)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=12)	12/12 (100,0)	0
	Pre-cycle 37 (N=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	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.

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 21.Abdominal pain	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	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)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 37 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
Item 22.Heartburn	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)	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	11/14 (78,6)	3/14 (21,4)
Item 23.Nausea	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	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)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 25 (N=12)	7/12 (58,3)	5/12 (41,7)
	Pre-cycle 37 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	4/14 (28,6)	10/14 (71,4)
Item 24.Vomiting	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)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=12)	12/12 (100,0)	0
	Pre-cycle 25 (N=12)	10/12 (83,3)	2/12 (16,7)
	Pre-cycle 37 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	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.

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 25.Diarrhea	Pre-cycle 3 (N=14)	9/14 (64,3)	5/14 (35,7)
	Pre-cycle 5 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 9 (N=13)	8/13 (61,5)	5/13 (38,5)
	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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)

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

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 26.Constipation	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)	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)
Item 27.Stool incontinence	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	Pre-cycle 5 (N=14)	14/14 (100,0)	0
	Pre-cycle 9 (N=13)	10/13 (76,9)	3/13 (23,1)
	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
Item 28.Pain with urination	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)	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 29.Increased urinary frequency/urgency	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=14)	10/14 (71,4)	4/14 (28,6)
	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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	7/14 (50,0)	7/14 (50,0)

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

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 30.Difficulty beginning urination	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)	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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.

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	Pre-cycle 3 (N=13)	12/13 (92,3)	1/13 (7,7)
	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=12)	11/12 (91,7)	1/12 (8,3)
	Pre-cycle 25 (N=11)	11/11 (100,0)	0
	Pre-cycle 37 (N=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (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)	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
Item 33.Muscle pain	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=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	8/ 8 (100,0)	0
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)
Item 34.Dizziness	Pre-cycle 3 (N=14)	8/14 (57,1)	6/14 (42,9)
	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)	8/12 (66,7)	4/12 (33,3)
	Pre-cycle 25 (N=12)	9/12 (75,0)	3/12 (25,0)
	Pre-cycle 37 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 49 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	Overall (N=14)	5/14 (35,7)	9/14 (64,3)

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

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 35.Numbness	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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.

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Table 2.1.3.4 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Non-progressive

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=15) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	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)	11/13 (84,6)	2/13 (15,4)
	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=10)	10/10 (100,0)	0
	Pre-cycle 49 (N=10)	10/10 (100,0)	0
	Pre-cycle 61 (N=8)	7/ 8 (87,5)	1/ 8 (12,5)
	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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 1.Fatigue/feeling tired	Pre-cycle 3 (N=14)	9/14 (64,3)	5/14 (35,7)
	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)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	4/14 (28,6)	10/14 (71,4)
Item 2.Sleep problems	Pre-cycle 3 (N=14)	8/14 (57,1)	6/14 (42,9)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 9 (N=13)	10/13 (76,9)	3/13 (23,1)
	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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)
Item 3.Less appetite	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)	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)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
Item 4.More appetite	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)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)

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

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 5.Headaches	Pre-cycle 3 (N=14)	10/14 (71,4)	4/14 (28,6)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	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)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	7/14 (50,0)	7/14 (50,0)

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

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 6.Vision changes	Pre-cycle 3 (N=14)	14/14 (100,0)	0
	Pre-cycle 5 (N=13)	10/13 (76,9)	3/13 (23,1)
	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)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)
Item 7.Decreased hearing	Pre-cycle 3 (N=14)	13/14 (92,9)	1/14 (7,1)
	Pre-cycle 5 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 9 (N=13)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
Item 8.Mouth sores	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)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=14)	11/14 (78,6)	3/14 (21,4)
Item 9.Trouble swallowing	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
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	5/ 5 (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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 10.Choking	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)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened 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=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)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
Item 12.Frequent awakenings at night	Pre-cycle 3 (N=14)	9/14 (64,3)	5/14 (35,7)
	Pre-cycle 5 (N=13)	10/13 (76,9)	3/13 (23,1)
	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)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 37 (N=9)	6/ 9 (66,7)	3/ 9 (33,3)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	5/14 (35,7)	9/14 (64,3)
Item 13.Cough	Pre-cycle 3 (N=14)	8/14 (57,1)	6/14 (42,9)
	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)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	6/14 (42,9)	8/14 (57,1)
Item 14.Wheezing	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)
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 15.Difficulty breathing	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
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 16.Chest pain	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	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)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
Item 17.Palpitations/fluttering	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)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	11/14 (78,6)	3/14 (21,4)
Item 18.Shortness of breath with activity	Pre-cycle 3 (N=14)	12/14 (85,7)	2/14 (14,3)
	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)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	3/ 5 (60,0)	2/ 5 (40,0)
	Overall (N=14)	7/14 (50,0)	7/14 (50,0)
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)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 20.Swelling in hands/feet	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)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened 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=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)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 25 (N=10)	7/10 (70,0)	3/10 (30,0)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	4/ 7 (57,1)	3/ 7 (42,9)
	Pre-cycle 61 (N=4)	3/ 4 (75,0)	1/ 4 (25,0)
	Overall (N=14)	7/14 (50,0)	7/14 (50,0)
Item 22.Heartburn	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)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)
Item 23.Nausea	Pre-cycle 3 (N=14)	8/14 (57,1)	6/14 (42,9)
	Pre-cycle 5 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 9 (N=13)	10/13 (76,9)	3/13 (23,1)
	Pre-cycle 13 (N=13)	9/13 (69,2)	4/13 (30,8)
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	5/14 (35,7)	9/14 (64,3)
Item 24.Vomiting	Pre-cycle 3 (N=14)	9/14 (64,3)	5/14 (35,7)
	Pre-cycle 5 (N=13)	10/13 (76,9)	3/13 (23,1)
	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)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	7/14 (50,0)	7/14 (50,0)

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

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 25.Diarrhea	Pre-cycle 3 (N=14)	11/14 (78,6)	3/14 (21,4)
	Pre-cycle 5 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 9 (N=13)	10/13 (76,9)	3/13 (23,1)
	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)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	7/14 (50,0)	7/14 (50,0)

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

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened 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)	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)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	7/14 (50,0)	7/14 (50,0)
Item 27.Stool incontinence	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)	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
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=14)	8/14 (57,1)	6/14 (42,9)
Item 28.Pain with urination	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)	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
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	13/14 (92,9)	1/14 (7,1)
Item 29.Increased urinary frequency/urgency	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)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
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)
	Pre-cycle 37 (N=9)	7/ 9 (77,8)	2/ 9 (22,2)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 31.Urinary incontinence	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)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	9/10 (90,0)	1/10 (10,0)
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	5/ 7 (71,4)	2/ 7 (28,6)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	12/14 (85,7)	2/14 (14,3)
Item 32.Weakness	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)	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)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	0
	Overall (N=14)	10/14 (71,4)	4/14 (28,6)
Item 33.Muscle pain	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)	13/13 (100,0)	0
	Pre-cycle 13 (N=13)	11/13 (84,6)	2/13 (15,4)
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	4/ 5 (80,0)	1/ 5 (20,0)
	Overall (N=14)	9/14 (64,3)	5/14 (35,7)
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)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	8/10 (80,0)	2/10 (20,0)
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	6/ 7 (85,7)	1/ 7 (14,3)
	Pre-cycle 61 (N=5)	5/ 5 (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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 35.Numbness	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)	12/13 (92,3)	1/13 (7,7)
	Pre-cycle 13 (N=13)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	9/ 9 (100,0)	0
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (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.

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Table 2.1.3.5 General PN symptoms responder analyses (Deterioration by >= 0.6 pts) - PN status at enrollment = Unknown

(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]	
		Not worsened	Worsened by >= 0.6 points
Parameter	Time point	n/N (%) [b]	n/N (%) [b]
Item 36.Tingling	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)	13/13 (100,0)	0
	Pre-cycle 25 (N=10)	10/10 (100,0)	0
	Pre-cycle 37 (N=9)	8/ 9 (88,9)	1/ 9 (11,1)
	Pre-cycle 49 (N=7)	7/ 7 (100,0)	0
	Pre-cycle 61 (N=5)	5/ 5 (100,0)	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.

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1.15 Endpunkt Allgemeiner Gesundheitszustand: Gehfähigkeit anhand 6 Minute Walking Test (6MWT)

1.15.1 Subgruppenanalysen zum 6MWT

1.15.1.1 Subgruppenanalyse zum 6MWT: Veränderung gegenüber Baseline

Table 4.4.1.1 Motor function secondary outcomes test score mean change from baseline - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=14)	501.80	219.661	448.00	135.0	836.0	26.3							
	Pre-cycle 5 (n=13)	506.05	182.017	483.00	186.6	860.0	31.6	13	24.24	86.308	6.00	-117.0	236.2	31.6
	Pre-cycle 9 (n=13)	520.60	158.172	495.00	263.0	845.0	31.6	13	38.79	109.306	9.00	-117.0	297.2	31.6
	Pre-cycle 13 (n=13)	459.58	200.699	464.82	101.0	861.0	31.6	12	12.25	131.465	23.00	-174.0	281.9	36.8
	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
	Pre-cycle 37 (n=7)	420.45	169.858	460.50	82.9	584.0	63.2	6	28.89	108.114	70.25	-121.0	144.8	68.4
	Pre-cycle 49 (n=5)	461.03	80.363	500.00	356.0	532.0	73.7	5	-29.75	232.254	-86.00	-258.0	339.9	73.7

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.1 Motor function secondary outcomes test score mean change from baseline - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % normal distance achieved - all	Baseline (n=13)	70.75	26.053	71.50	20.5	114.4	31.6							
	Pre-cycle 5 (n=12)	71.60	18.166	76.32	28.2	95.6	36.8	12	4.49	13.109	1.35	-16.1	35.4	36.8
	Pre-cycle 9 (n=12)	72.39	16.058	73.30	36.6	92.1	36.8	12	5.28	16.609	-0.55	-13.3	44.0	36.8
	Pre-cycle 13 (n=12)	67.37	18.155	68.98	30.8	93.6	36.8	12	0.26	20.011	0.70	-32.6	40.7	36.8
	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
	Pre-cycle 37 (n=6)	72.92	13.442	76.70	46.5	83.7	68.4	5	2.77	12.654	5.55	-16.1	18.5	73.7
	Pre-cycle 49 (n=3)	71.60	7.758	73.40	63.1	78.3	84.2	3	-11.05	9.319	-8.05	-21.5	-3.6	84.2

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.1 Motor function secondary outcomes test score mean change from baseline - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 velocity achieved (m/min) - all	Baseline (n=14)	83.63	36.610	74.67	22.5	139.3	26.3							
	Pre-cycle 5 (n=13)	84.34	30.336	80.50	31.1	143.3	31.6	13	4.04	14.385	1.00	-19.5	39.4	31.6
	Pre-cycle 9 (n=13)	86.77	26.362	82.50	43.8	140.8	31.6	13	6.47	18.217	1.50	-19.5	49.5	31.6
	Pre-cycle 13 (n=13)	76.60	33.450	77.47	16.8	143.5	31.6	12	2.04	21.911	3.84	-29.0	47.0	36.8
	Pre-cycle 25 (n=9)	75.95	40.350	82.83	7.6	128.3	52.6	8	-4.68	30.741	-13.08	-52.8	44.2	57.9
	Pre-cycle 37 (n=7)	70.07	28.308	76.75	13.8	97.3	63.2	6	4.81	18.020	11.71	-20.2	24.1	68.4
	Pre-cycle 49 (n=5)	76.84	13.396	83.33	59.3	88.7	73.7	5	-4.96	38.709	-14.34	-43.0	56.6	73.7

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.1 Motor function secondary outcomes test score mean change from baseline - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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	4	53.81	126.482	16.50	-54.0	236.2	78.9
	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
	Pre-cycle 37 (n=3)	442.57	111.326	450.00	327.7	550.0	84.2	3	51.28	122.218	96.00	-87.0	144.8	84.2
	Pre-cycle 49 (n=2)	NC	NC	NC	500.0	522.7	89.5	2	NC	NC	NC	-258.0	339.9	89.5

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.1 Motor function secondary outcomes test score mean change from baseline - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - Unilateral Lower	Baseline (n=4)	447.03	163.189	392.55	319.0	684.0	78.9							
	Pre-cycle 5 (n=4)	449.66	127.571	460.32	311.0	567.0	78.9	4	2.64	100.899	-1.00	-117.0	129.5	78.9
	Pre-cycle 9 (n=4)	485.60	124.688	514.20	311.0	603.0	78.9	4	38.58	100.629	53.15	-81.0	129.0	78.9
	Pre-cycle 13 (n=4)	500.88	131.043	502.75	354.0	644.0	78.9	4	53.85	79.740	51.50	-40.0	152.4	78.9
	Pre-cycle 25 (n=1)	NC	NC	NC	497.0	497.0	94.7	1	NC	NC	NC	131.0	131.0	94.7
	Pre-cycle 37 (n=1)	NC	NC	NC	460.5	460.5	94.7	1	NC	NC	NC	94.5	94.5	94.7
	Pre-cycle 49 (n=1)	NC	NC	NC	394.4	394.4	94.7	1	NC	NC	NC	28.4	28.4	94.7

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.1 Motor function secondary outcomes test score mean change from baseline - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=3)	384.97	265.965	488.00	82.9	584.0	84.2	2	NC	NC	NC	-121.0	46.0	89.5
	Pre-cycle 49 (n=2)	NC	NC	NC	356.0	532.0	89.5	2	NC	NC	NC	-173.0	-86.0	89.5

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.1 Motor function secondary outcomes test score mean change from baseline - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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 patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.2 Motor function secondary outcomes test score mean change from baseline - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=13)	497.65	76.520	467.00	386.0	603.0	7.1							
	Pre-cycle 5 (n=13)	502.19	105.987	551.00	354.0	660.0	7.1	13	4.54	63.885	-4.00	-92.0	123.0	7.1
	Pre-cycle 9 (n=13)	493.54	89.673	510.00	350.0	607.0	7.1	13	-4.12	63.111	-19.50	-89.0	114.0	7.1
	Pre-cycle 13 (n=11)	486.36	95.884	485.00	333.0	596.0	21.4	11	-17.23	86.698	-39.00	-134.0	146.0	21.4
	Pre-cycle 25 (n=9)	534.68	67.967	556.00	433.1	604.0	35.7	9	27.68	49.754	10.00	-33.9	106.0	35.7
	Pre-cycle 37 (n=7)	502.93	80.836	500.00	397.5	604.0	50.0	7	-29.50	47.240	-34.00	-95.0	46.0	50.0
	Pre-cycle 49 (n=4)	596.25	41.844	588.50	554.0	654.0	71.4	4	6.25	37.854	7.50	-41.0	51.0	71.4

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.2 Motor function secondary outcomes test score mean change from baseline - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % normal distance achieved - all	Baseline (n=13)	78.54	9.062	78.86	67.1	91.1	7.1							
	Pre-cycle 5 (n=13)	78.77	14.445	83.00	54.1	97.5	7.1	13	0.23	10.832	-1.80	-21.9	17.5	7.1
	Pre-cycle 9 (n=13)	77.39	12.863	83.12	56.5	92.0	7.1	13	-1.14	10.144	-3.25	-18.0	17.8	7.1
	Pre-cycle 13 (n=11)	75.76	16.662	73.15	45.7	107.2	21.4	11	-3.53	13.585	-7.21	-22.0	21.3	21.4
	Pre-cycle 25 (n=9)	83.92	10.137	86.00	65.2	95.2	35.7	9	3.22	6.692	2.20	-5.5	16.8	35.7
	Pre-cycle 37 (n=7)	77.23	12.981	80.40	57.8	93.9	50.0	7	-4.16	9.570	-4.02	-17.3	10.5	50.0
	Pre-cycle 49 (n=4)	92.58	7.883	88.65	88.6	104.4	71.4	4	3.90	7.955	1.29	-2.5	15.5	71.4

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.2 Motor function secondary outcomes test score mean change from baseline - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 velocity achieved (m/min) - all	Baseline (n=13)	82.94	12.753	77.83	64.3	100.5	7.1							
	Pre-cycle 5 (n=13)	83.70	17.664	91.83	59.0	110.0	7.1	13	0.76	10.648	-0.67	-15.3	20.5	7.1
	Pre-cycle 9 (n=13)	82.26	14.945	85.00	58.3	101.2	7.1	13	-0.69	10.518	-3.25	-14.8	19.0	7.1
	Pre-cycle 13 (n=11)	81.06	15.981	80.83	55.5	99.3	21.4	11	-2.87	14.449	-6.50	-22.3	24.3	21.4
	Pre-cycle 25 (n=9)	89.11	11.328	92.67	72.2	100.7	35.7	9	4.61	8.292	1.67	-5.6	17.7	35.7
	Pre-cycle 37 (n=7)	83.82	13.475	83.33	66.3	100.7	50.0	7	-4.92	7.874	-5.66	-15.8	7.7	50.0
	Pre-cycle 49 (n=4)	99.38	6.975	98.09	92.3	109.0	71.4	4	1.04	6.310	1.25	-6.8	8.5	71.4

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.2 Motor function secondary outcomes test score mean change from baseline - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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
	Pre-cycle 37 (n=3)	558.33	53.144	571.00	500.0	604.0	78.6	3	13.33	28.572	1.00	-7.0	46.0	78.6
	Pre-cycle 49 (n=2)	NC	NC	NC	591.0	654.0	85.7	2	NC	NC	NC	13.0	51.0	85.7

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.2 Motor function secondary outcomes test score mean change from baseline - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - Unilateral Lower	Baseline (n=8)	480.19	81.610	450.25	386.0	595.0	42.9							
	Pre-cycle 5 (n=8)	476.81	121.745	435.00	354.0	660.0	42.9	8	-3.38	68.937	-7.00	-92.0	123.0	42.9
	Pre-cycle 9 (n=8)	473.25	89.882	487.00	350.0	600.0	42.9	8	-6.94	56.073	-19.75	-89.0	97.0	42.9
	Pre-cycle 13 (n=6)	474.33	98.291	441.50	383.0	596.0	57.1	6	-10.92	89.194	-21.00	-119.0	146.0	57.1
	Pre-cycle 25 (n=5)	525.60	65.767	556.00	453.0	584.0	64.3	5	33.40	50.974	10.00	-11.0	106.0	64.3
	Pre-cycle 37 (n=3)	482.67	77.468	500.00	398.0	550.0	78.6	3	-59.00	31.953	-48.00	-95.0	-34.0	78.6
	Pre-cycle 49 (n=2)	NC	NC	NC	554.0	586.0	85.7	2	NC	NC	NC	-41.0	2.0	85.7

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.2 Motor function secondary outcomes test score mean change from baseline - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=1)	NC	NC	NC	397.5	397.5	92.9	1	NC	NC	NC	-69.5	-69.5	92.9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.3 Motor function secondary outcomes test score mean change from baseline - PN status = Progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=10)	500.91	129.770	448.25	366.0	758.0	9.1							
	Pre-cycle 5 (n=10)	501.24	134.876	480.15	354.0	762.0	9.1	10	0.33	87.275	5.00	-117.0	129.5	9.1
	Pre-cycle 9 (n=10)	520.67	103.382	502.50	357.0	728.0	9.1	10	19.76	79.817	10.67	-89.0	129.0	9.1
	Pre-cycle 13 (n=8)	485.73	107.520	434.65	383.0	644.0	27.3	8	-6.16	87.436	-21.00	-139.0	152.4	27.3
	Pre-cycle 25 (n=5)	537.80	96.264	497.00	453.0	644.0	54.5	5	39.20	99.595	67.00	-119.0	131.0	54.5
	Pre-cycle 37 (n=3)	436.17	33.468	450.00	398.0	460.5	72.7	3	-13.50	95.542	-48.00	-87.0	94.5	72.7
	Pre-cycle 49 (n=2)	NC	NC	NC	394.4	500.0	81.8	2	NC	NC	NC	-258.0	28.4	81.8

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.3 Motor function secondary outcomes test score mean change from baseline - PN status = Progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % normal distance achieved - all	Baseline (n=9)	75.95	8.647	71.50	67.1	96.0	18.2							
	Pre-cycle 5 (n=9)	76.12	14.244	78.00	54.1	97.5	18.2	9	0.17	14.739	1.00	-21.9	20.6	18.2
	Pre-cycle 9 (n=9)	78.01	10.744	77.10	60.8	92.1	18.2	9	2.06	13.251	-2.60	-18.0	21.0	18.2
	Pre-cycle 13 (n=8)	72.99	14.009	68.93	56.0	93.6	27.3	8	-2.45	12.977	-3.90	-21.0	22.1	27.3
	Pre-cycle 25 (n=5)	80.80	19.157	76.50	57.9	109.7	54.5	4	-0.84	14.884	0.15	-19.1	15.5	63.6
	Pre-cycle 37 (n=3)	70.47	7.960	73.20	61.5	76.7	72.7	2	NC	NC	NC	-17.3	5.6	81.8
	Pre-cycle 49 (n=2)	NC	NC	NC	63.1	73.4	81.8	2	NC	NC	NC	-8.1	-3.6	81.8

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.3 Motor function secondary outcomes test score mean change from baseline - PN status = Progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 velocity achieved (m/min) - all	Baseline (n=10)	83.48	21.628	74.71	61.0	126.3	9.1						
	Pre-cycle 5 (n=10)	83.54	22.479	80.03	59.0	127.0	9.1	10	0.06	14.546	0.83	-19.5	21.6	9.1
	Pre-cycle 9 (n=10)	86.78	17.230	83.75	59.5	121.3	9.1	10	3.29	13.303	1.78	-14.8	21.5	9.1
	Pre-cycle 13 (n=8)	80.95	17.920	72.44	63.8	107.3	27.3	8	-1.03	14.573	-3.50	-23.2	25.4	27.3
	Pre-cycle 25 (n=5)	89.63	16.044	82.83	75.5	107.3	54.5	5	6.53	16.599	11.17	-19.8	21.8	54.5
	Pre-cycle 37 (n=3)	72.69	5.580	75.00	66.3	76.8	72.7	3	-2.25	15.924	-8.00	-14.5	15.8	72.7
	Pre-cycle 49 (n=2)	NC	NC	NC	65.7	83.3	81.8	2	NC	NC	NC	-43.0	4.7	81.8

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.3 Motor function secondary outcomes test score mean change from baseline - PN status = Progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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	2	NC	NC	NC	-54.0	4.0	81.8
	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
	Pre-cycle 37 (n=1)	NC	NC	NC	450.0	450.0	90.9	1	NC	NC	NC	-87.0	-87.0	90.9
	Pre-cycle 49 (n=1)	NC	NC	NC	500.0	500.0	90.9	1	NC	NC	NC	-258.0	-258.0	90.9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.3 Motor function secondary outcomes test score mean change from baseline - PN status = Progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - Unilateral Lower	Baseline (n=7)	469.80	109.319	446.00	366.0	684.0	36.4						
	Pre-cycle 5 (n=7)	470.02	121.106	424.00	354.0	660.0	36.4	7	0.22	102.419	6.00	-117.0	129.5	36.4
	Pre-cycle 9 (n=7)	487.49	77.731	495.00	357.0	603.0	36.4	7	17.69	93.556	-19.50	-89.0	129.0	36.4
	Pre-cycle 13 (n=6)	471.92	109.063	420.50	383.0	644.0	45.5	6	13.32	81.655	-21.00	-58.5	152.4	45.5
	Pre-cycle 25 (n=3)	468.67	24.583	456.00	453.0	497.0	72.7	3	69.33	60.534	67.00	10.0	131.0	72.7
	Pre-cycle 37 (n=2)	NC	NC	NC	398.0	460.5	81.8	2	NC	NC	NC	-48.0	94.5	81.8
	Pre-cycle 49 (n=1)	NC	NC	NC	394.4	394.4	90.9	1	NC	NC	NC	28.4	28.4	90.9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.3 Motor function secondary outcomes test score mean change from baseline - PN status = Progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.4 Motor function secondary outcomes test score mean change from baseline - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	456.95	188.657	550.00	82.9	604.0	36.4	6	-1.36	104.887	-16.50	-121.0	144.8	45.5
	Pre-cycle 49 (n=5)	569.75	53.024	554.00	522.7	654.0	54.5	5	35.77	189.285	2.00	-173.0	339.9	54.5

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.4 Motor function secondary outcomes test score mean change from baseline - PN status = Non-progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % 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
	Pre-cycle 37 (n=6)	77.98	16.203	81.70	46.5	93.9	45.5	6	-0.10	12.673	0.49	-16.1	18.5	45.5
	Pre-cycle 49 (n=4)	89.98	10.773	88.60	78.3	104.4	63.6	4	-1.66	15.290	-0.31	-21.5	15.5	63.6

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.4 Motor function secondary outcomes test score mean change from baseline - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=7)	76.16	31.442	91.67	13.8	100.7	36.4	6	-0.23	17.483	-2.75	-20.2	24.1	45.5
	Pre-cycle 49 (n=5)	94.96	8.838	92.33	87.1	109.0	54.5	5	5.96	31.546	0.34	-28.8	56.6	54.5

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.4 Motor function secondary outcomes test score mean change from baseline - PN status = Non-progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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
	Pre-cycle 37 (n=3)	493.91	146.433	550.00	327.7	604.0	72.7	3	80.61	73.144	96.00	1.0	144.8	72.7
	Pre-cycle 49 (n=2)	NC	NC	NC	522.7	654.0	81.8	2	NC	NC	NC	51.0	339.9	81.8

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.4 Motor function secondary outcomes test score mean change from baseline - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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
	Pre-cycle 37 (n=2)	NC	NC	NC	500.0	550.0	81.8	2	NC	NC	NC	-95.0	-34.0	81.8
	Pre-cycle 49 (n=2)	NC	NC	NC	554.0	586.0	81.8	2	NC	NC	NC	-41.0	2.0	81.8

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.4 Motor function secondary outcomes test score mean change from baseline - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=2)	NC	NC	NC	82.9	584.0	81.8	1	NC	NC	NC	-121.0	-121.0	90.9
	Pre-cycle 49 (n=1)	NC	NC	NC	532.0	532.0	90.9	1	NC	NC	NC	-173.0	-173.0	90.9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.5 Motor function secondary outcomes test score mean change from baseline - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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)	502.08	212.335	467.00	135.0	836.0	18.2							
	Pre-cycle 5 (n=8)	492.58	203.551	492.50	186.6	860.0	27.3	8	22.95	44.071	24.50	-37.0	108.0	27.3
	Pre-cycle 9 (n=8)	480.50	185.469	460.00	263.0	845.0	27.3	8	10.88	78.184	0.50	-89.0	128.0	27.3
	Pre-cycle 13 (n=8)	450.86	209.928	419.50	203.9	861.0	27.3	8	-18.76	101.159	-8.00	-174.0	123.0	27.3
	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
	Pre-cycle 37 (n=4)	489.13	71.223	494.00	397.5	571.0	63.6	4	3.88	54.928	19.50	-69.5	46.0	63.6
	Pre-cycle 49 (n=2)	NC	NC	NC	356.0	591.0	81.8	2	NC	NC	NC	-86.0	13.0	81.8

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.5 Motor function secondary outcomes test score mean change from baseline - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % normal distance achieved - all	Baseline (n=9)	70.46	25.396	68.50	20.5	114.4	18.2							
	Pre-cycle 5 (n=8)	67.86	20.575	70.32	28.2	92.5	27.3	8	2.90	6.412	2.46	-3.7	15.3	27.3
	Pre-cycle 9 (n=8)	65.95	17.445	66.43	36.6	86.3	27.3	8	0.99	11.565	-1.15	-11.3	17.8	27.3
	Pre-cycle 13 (n=8)	60.28	19.199	61.15	30.8	88.1	27.3	8	-4.69	16.953	-3.61	-32.6	19.6	27.3
	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
	Pre-cycle 37 (n=4)	74.70	11.839	77.85	57.8	85.3	63.6	4	-0.73	8.451	-1.76	-9.9	10.5	63.6
	Pre-cycle 49 (n=1)	NC	NC	NC	88.7	88.7	90.9	1	NC	NC	NC	0.7	0.7	90.9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.5 Motor function secondary outcomes test score mean change from baseline - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 velocity achieved (m/min) - all	Baseline (n=9)	83.68	35.388	77.83	22.5	139.3	18.2						
	Pre-cycle 5 (n=8)	82.10	33.925	82.08	31.1	143.3	27.3	8	3.83	7.344	4.08	-6.2	18.0	27.3
	Pre-cycle 9 (n=8)	80.08	30.911	76.67	43.8	140.8	27.3	8	1.81	13.029	0.08	-14.8	21.3	27.3
	Pre-cycle 13 (n=8)	75.14	34.989	69.92	34.0	143.5	27.3	8	-3.13	16.859	-1.33	-29.0	20.5	27.3
	Pre-cycle 25 (n=5)	82.50	39.947	91.67	20.8	128.3	54.5	5	-10.06	26.002	-5.65	-52.8	16.0	54.5
	Pre-cycle 37 (n=4)	81.52	11.872	82.33	66.3	95.2	63.6	4	0.65	9.151	3.25	-11.6	7.7	63.6
	Pre-cycle 49 (n=2)	NC	NC	NC	59.3	98.5	81.8	2	NC	NC	NC	-14.3	2.2	81.8

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.5 Motor function secondary outcomes test score mean change from baseline - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - 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
	Pre-cycle 37 (n=2)	NC	NC	NC	500.0	571.0	81.8	2	NC	NC	NC	-7.0	46.0	81.8
	Pre-cycle 49 (n=1)	NC	NC	NC	591.0	591.0	90.9	1	NC	NC	NC	13.0	13.0	90.9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.5 Motor function secondary outcomes test score mean change from baseline - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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) - Unilateral Lower	Baseline (n=1)	NC	NC	NC	319.0	319.0	90.9							
	Pre-cycle 5 (n=1)	NC	NC	NC	311.0	311.0	90.9	1	NC	NC	NC	-8.0	-8.0	90.9
	Pre-cycle 9 (n=1)	NC	NC	NC	311.0	311.0	90.9	1	NC	NC	NC	-8.0	-8.0	90.9
	Pre-cycle 13 (n=1)	NC	NC	NC	354.0	354.0	90.9	1	NC	NC	NC	35.0	35.0	90.9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.4.1.5 Motor function secondary outcomes test score mean change from baseline - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=2)	NC	NC	NC	397.5	488.0	81.8	2	NC	NC	NC	-69.5	46.0	81.8
	Pre-cycle 49 (n=1)	NC	NC	NC	356.0	356.0	90.9	1	NC	NC	NC	-86.0	-86.0	90.9

[a] Patients with motor PN-related morbidity at enrolment.
[b] Calculated from the number of patients who completed each item at each time point (n) and the number of expected completed forms from the FAS with motor PN-related morbidity (N) [N-n]/N * 100.
NC = Not calculated. Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.1 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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=16)	505.14	216.773	448.00	135.0	850.0	11.1						
	Pre-cycle 5 (n=15)	481.71	157.223	477.30	186.6	860.0	16.7	15	-6.32	133.085	-2.00	-389.0	236.2	16.7
	Pre-cycle 9 (n=15)	518.12	151.826	495.00	263.0	845.0	16.7	15	30.09	110.961	9.00	-145.0	297.2	16.7
	Pre-cycle 13 (n=15)	462.30	185.195	464.82	101.0	861.0	16.7	14	3.57	142.827	23.00	-296.0	281.9	22.2
	Pre-cycle 25 (n=11)	477.14	235.552	497.00	45.5	805.0	38.9	10	-13.48	166.095	-55.50	-317.0	265.2	44.4
	Pre-cycle 37 (n=10)	480.81	186.428	474.25	82.9	761.0	44.4	9	24.82	97.256	60.00	-121.0	144.8	50.0
	Pre-cycle 49 (n=6)	506.86	110.803	527.37	356.0	632.0	66.7	6	-15.13	200.052	-34.00	-218.0	339.9	66.7

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.1 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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 % normal distance achieved	Baseline (n=15)	72.42	25.047	71.50	20.5	114.4	16.7							
	Pre-cycle 5 (n=13)	72.11	18.335	74.64	28.2	95.6	27.8	13	3.36	12.999	-0.65	-16.1	35.4	27.8
	Pre-cycle 9 (n=14)	73.49	17.107	72.10	36.6	102.4	22.2	14	4.07	16.079	-0.05	-14.0	44.0	22.2
	Pre-cycle 13 (n=14)	69.85	18.102	72.33	30.8	93.6	22.2	14	0.43	18.788	0.70	-32.6	40.7	22.2
	Pre-cycle 25 (n=9)	76.09	16.837	78.60	54.4	109.7	50.0	8	-0.70	20.187	-6.55	-19.6	36.6	55.6
	Pre-cycle 37 (n=9)	75.32	14.373	76.70	46.5	100.8	50.0	8	1.35	10.572	3.32	-16.1	18.5	55.6
	Pre-cycle 49 (n=4)	80.78	13.208	84.10	63.1	91.8	77.8	4	-5.59	14.562	-7.33	-21.5	13.8	77.8

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.1 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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 velocity achieved (m/min)	Baseline (n=16)	84.19	36.129	74.67	22.5	141.7	11.1							
	Pre-cycle 5 (n=15)	80.28	26.203	79.55	31.1	143.3	16.7	15	-1.05	22.181	-0.33	-64.8	39.4	16.7
	Pre-cycle 9 (n=15)	86.35	25.304	82.50	43.8	140.8	16.7	15	5.01	18.493	1.50	-24.2	49.5	16.7
	Pre-cycle 13 (n=15)	77.05	30.866	77.47	16.8	143.5	16.7	14	0.60	23.804	3.84	-49.3	47.0	22.2
	Pre-cycle 25 (n=11)	79.52	39.259	82.83	7.6	134.2	38.9	10	-2.25	27.684	-9.25	-52.8	44.2	44.4
	Pre-cycle 37 (n=10)	80.14	31.070	79.04	13.8	126.8	44.4	9	4.14	16.210	10.00	-20.2	24.1	50.0
	Pre-cycle 49 (n=6)	84.48	18.469	87.90	59.3	105.3	66.7	6	-2.52	33.342	-5.67	-36.3	56.6	66.7

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.2 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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=16)	480.27	83.706	455.00	308.8	603.0	0.0							
	Pre-cycle 5 (n=16)	490.30	98.634	453.50	354.0	660.0	0.0	16	10.03	62.040	0.50	-92.0	123.0	0.0
	Pre-cycle 9 (n=16)	486.82	82.564	487.00	350.0	607.0	0.0	16	6.55	63.316	4.50	-89.0	114.0	0.0
	Pre-cycle 13 (n=14)	486.29	88.847	480.50	333.0	596.0	12.5	14	3.84	91.001	-11.00	-134.0	146.0	12.5
	Pre-cycle 25 (n=12)	537.13	65.023	553.00	433.1	611.0	25.0	12	55.65	67.837	43.00	-33.9	165.7	25.0
	Pre-cycle 37 (n=10)	522.45	81.318	525.00	397.5	642.0	37.5	10	28.27	102.156	-3.00	-95.0	186.0	37.5
	Pre-cycle 49 (n=6)	571.13	62.942	583.00	461.8	654.0	62.5	6	50.33	74.886	32.00	-41.0	153.0	62.5

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.2 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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 % normal distance achieved	Baseline (n=15)	76.94	10.318	78.80	55.2	91.1	6.3							
	Pre-cycle 5 (n=15)	78.46	13.399	82.07	54.1	97.5	6.3	15	1.51	11.448	-1.65	-21.9	21.4	6.3
	Pre-cycle 9 (n=15)	77.44	11.915	78.74	56.5	92.0	6.3	15	0.50	11.060	0.80	-18.0	21.5	6.3
	Pre-cycle 13 (n=13)	75.90	15.246	74.20	45.7	107.2	18.8	13	-1.44	14.545	-3.74	-22.0	23.9	18.8
	Pre-cycle 25 (n=12)	83.02	9.396	85.65	65.2	95.2	25.0	11	5.88	9.239	2.40	-5.5	26.4	31.3
	Pre-cycle 37 (n=10)	79.25	12.059	80.65	57.8	95.2	37.5	9	1.53	14.168	-2.70	-17.3	25.7	43.8
	Pre-cycle 49 (n=6)	84.62	14.037	88.60	64.3	104.4	62.5	5	6.69	9.299	1.88	-2.5	17.9	68.8

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.2 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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 velocity achieved (m/min)	Baseline (n=16)	80.04	13.950	75.83	51.5	100.5	0.0							
	Pre-cycle 5 (n=16)	81.72	16.439	75.58	59.0	110.0	0.0	16	1.67	10.340	0.08	-15.3	20.5	0.0
	Pre-cycle 9 (n=16)	81.14	13.761	81.17	58.3	101.2	0.0	16	1.09	10.552	0.75	-14.8	19.0	0.0
	Pre-cycle 13 (n=14)	81.05	14.808	80.08	55.5	99.3	12.5	14	0.64	15.166	-1.83	-22.3	24.3	12.5
	Pre-cycle 25 (n=12)	89.52	10.837	92.17	72.2	101.8	25.0	12	9.28	11.305	7.17	-5.6	27.6	25.0
	Pre-cycle 37 (n=10)	87.08	13.555	87.50	66.3	107.0	37.5	10	4.71	17.025	-0.50	-15.8	31.0	37.5
	Pre-cycle 49 (n=6)	95.19	10.490	97.17	77.0	109.0	62.5	6	8.39	12.482	5.34	-6.8	25.5	62.5

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.3 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=13)	501.70	138.877	450.50	366.0	850.0	0.0							
	Pre-cycle 5 (n=13)	470.50	94.569	461.00	354.0	660.0	0.0	13	-31.20	131.476	-2.00	-389.0	129.5	0.0
	Pre-cycle 9 (n=13)	514.83	99.932	495.00	357.0	705.0	0.0	13	13.13	83.013	26.00	-145.0	129.0	0.0
	Pre-cycle 13 (n=11)	492.35	91.482	450.00	383.0	644.0	15.4	11	-2.94	118.396	-3.00	-296.0	152.4	15.4
	Pre-cycle 25 (n=8)	555.88	122.836	498.50	453.0	805.0	38.5	8	55.13	86.799	84.50	-86.0	155.0	38.5
	Pre-cycle 37 (n=7)	545.07	141.112	460.50	398.0	761.0	46.2	7	27.93	104.643	60.00	-89.0	186.0	46.2
	Pre-cycle 49 (n=4)	552.60	107.586	592.00	394.4	632.0	69.2	4	-11.90	145.447	23.20	-218.0	124.0	69.2

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.3 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % normal distance achieved	Baseline (n=11)	77.27	10.262	71.50	67.1	96.5	15.4							
	Pre-cycle 5 (n=10)	76.33	14.874	78.03	54.1	97.5	23.1	10	-0.87	14.034	-2.50	-21.9	20.6	23.1
	Pre-cycle 9 (n=11)	78.39	13.405	77.10	60.8	102.4	15.4	11	1.11	12.861	-0.80	-18.0	21.0	15.4
	Pre-cycle 13 (n=10)	75.33	13.795	73.88	55.4	93.6	23.1	10	-1.67	12.404	-3.90	-22.6	22.1	23.1
	Pre-cycle 25 (n=8)	81.16	12.549	77.55	72.0	109.7	38.5	6	0.58	12.588	0.15	-17.9	15.5	53.8
	Pre-cycle 37 (n=7)	75.37	12.331	73.20	61.5	100.8	46.2	5	-2.96	10.052	2.33	-17.3	5.6	61.5
	Pre-cycle 49 (n=4)	77.28	15.702	77.10	63.1	91.8	69.2	3	-0.28	12.218	-6.60	-8.1	13.8	76.9

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.3 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 velocity achieved (m/min)	Baseline (n=13)	83.62	23.146	75.08	61.0	141.7	0.0							
	Pre-cycle 5 (n=13)	78.42	15.761	76.83	59.0	110.0	0.0	13	-5.20	21.913	-0.33	-64.8	21.6	0.0
	Pre-cycle 9 (n=13)	85.80	16.655	82.50	59.5	117.5	0.0	13	2.19	13.835	4.33	-24.2	21.5	0.0
	Pre-cycle 13 (n=11)	82.06	15.247	75.00	63.8	107.3	15.4	11	-0.49	19.733	-0.50	-49.3	25.4	15.4
	Pre-cycle 25 (n=8)	92.65	20.472	83.08	75.5	134.2	38.5	8	9.19	14.467	14.09	-14.3	25.8	38.5
	Pre-cycle 37 (n=7)	90.85	23.519	76.75	66.3	126.8	46.2	7	4.65	17.441	10.00	-14.8	31.0	46.2
	Pre-cycle 49 (n=4)	92.10	17.933	98.67	65.7	105.3	69.2	4	-1.98	24.244	3.87	-36.3	20.7	69.2

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.4 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = 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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	456.95	188.657	550.00	82.9	604.0	22.2	6	-1.36	104.887	-16.50	-121.0	144.8	33.3
	Pre-cycle 49 (n=5)	569.75	53.024	554.00	522.7	654.0	44.4	5	35.77	189.285	2.00	-173.0	339.9	44.4

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.4 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = 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: 31 March 2021 (DC02)

		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 % 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
	Pre-cycle 37 (n=6)	77.98	16.203	81.70	46.5	93.9	33.3	6	-0.10	12.673	0.49	-16.1	18.5	33.3
	Pre-cycle 49 (n=4)	89.98	10.773	88.60	78.3	104.4	55.6	4	-1.66	15.290	-0.31	-21.5	15.5	55.6

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.4 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = 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: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=7)	76.16	31.442	91.67	13.8	100.7	22.2	6	-0.23	17.483	-2.75	-20.2	24.1	33.3
	Pre-cycle 49 (n=5)	94.96	8.838	92.33	87.1	109.0	44.4	5	5.96	31.546	0.34	-28.8	56.6	44.4

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.1.5 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=11)	479.78	198.819	454.00	135.0	836.0	8.3							
	Pre-cycle 5 (n=10)	479.99	181.718	442.00	186.6	860.0	16.7	10	28.41	46.949	24.50	-37.0	108.0	16.7
	Pre-cycle 9 (n=10)	473.51	164.818	445.53	263.0	845.0	16.7	10	21.93	75.318	17.00	-89.0	128.0	16.7
	Pre-cycle 13 (n=10)	449.49	185.191	444.00	203.9	861.0	16.7	10	-2.09	100.466	13.00	-174.0	128.2	16.7
	Pre-cycle 25 (n=7)	499.66	197.004	548.00	125.0	770.0	41.7	7	-5.46	159.386	19.00	-317.0	165.7	41.7
	Pre-cycle 37 (n=6)	503.08	64.430	495.50	397.5	571.0	50.0	6	53.12	89.466	46.00	-69.5	182.2	50.0
	Pre-cycle 49 (n=3)	469.60	117.694	461.80	356.0	591.0	75.0	3	26.67	120.085	13.00	-86.0	153.0	75.0

[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.

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Table 4.5.1.1.5 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % normal distance achieved	Baseline (n=11)	69.75	23.327	68.50	20.5	114.4	8.3							
	Pre-cycle 5 (n=10)	69.58	18.505	75.47	28.2	92.5	16.7	10	4.29	8.376	2.46	-3.7	21.4	16.7
	Pre-cycle 9 (n=10)	68.32	16.177	72.32	36.6	86.3	16.7	10	3.02	12.098	0.75	-11.3	21.5	16.7
	Pre-cycle 13 (n=10)	63.55	18.321	67.98	30.8	88.1	16.7	10	-1.74	17.450	-1.87	-32.6	23.9	16.7
	Pre-cycle 25 (n=6)	77.63	13.220	83.45	57.2	89.2	50.0	6	7.35	12.638	5.28	-7.1	26.4	50.0
	Pre-cycle 37 (n=6)	79.15	12.332	79.95	57.8	95.2	50.0	6	6.67	13.463	4.84	-9.9	25.7	50.0
	Pre-cycle 49 (n=2)	NC	NC	NC	73.1	88.7	83.3	2	NC	NC	NC	0.7	17.9	83.3

[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.

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Table 4.5.1.1.5 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 velocity achieved (m/min)	Baseline (n=11)	79.96	33.135	75.67	22.5	139.3	8.3							
	Pre-cycle 5 (n=10)	80.00	30.286	73.67	31.1	143.3	16.7	10	4.74	7.824	4.08	-6.2	18.0	16.7
	Pre-cycle 9 (n=10)	78.92	27.469	74.25	43.8	140.8	16.7	10	3.65	12.551	2.83	-14.8	21.3	16.7
	Pre-cycle 13 (n=10)	74.91	30.866	74.00	34.0	143.5	16.7	10	-0.35	16.743	2.17	-29.0	21.4	16.7
	Pre-cycle 25 (n=7)	83.27	32.834	91.33	20.8	128.3	41.7	7	-0.91	26.564	3.17	-52.8	27.6	41.7
	Pre-cycle 37 (n=6)	83.85	10.740	82.58	66.3	95.2	50.0	6	8.85	14.908	7.66	-11.6	30.4	50.0
	Pre-cycle 49 (n=3)	78.27	19.617	76.97	59.3	98.5	75.0	3	4.44	20.015	2.17	-14.3	25.5	75.0

[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.

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Table 4.5.1.2.1 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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)	477.25	217.044	425.50	135.0	836.0	7.1							
	Pre-cycle 5 (n=12)	479.97	174.604	480.15	186.6	860.0	14.3	12	26.43	89.732	15.00	-117.0	236.2	14.3
	Pre-cycle 9 (n=12)	502.15	152.744	487.53	263.0	845.0	14.3	12	48.61	109.613	24.92	-117.0	297.2	14.3
	Pre-cycle 13 (n=11)	494.23	167.197	464.82	203.9	861.0	21.4	11	48.28	110.328	35.00	-162.0	281.9	21.4
	Pre-cycle 25 (n=7)	539.01	135.229	497.00	363.0	770.0	50.0	7	44.74	145.020	102.00	-135.0	265.2	50.0
	Pre-cycle 37 (n=6)	468.54	90.640	455.25	327.7	584.0	57.1	6	31.22	108.706	77.25	-121.0	144.8	57.1
	Pre-cycle 49 (n=3)	483.04	76.907	522.73	394.4	532.0	78.6	3	65.08	258.385	28.40	-173.0	339.9	78.6

[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.

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Table 4.5.1.2.1 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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 % normal distance achieved	Baseline (n=12)	69.52	27.044	71.23	20.5	114.4	14.3						
	Pre-cycle 5 (n=11)	70.11	18.984	70.50	28.2	95.6	21.4	11	4.67	13.789	1.70	-16.1	35.4	21.4
	Pre-cycle 9 (n=11)	72.24	16.821	72.20	36.6	92.1	21.4	11	6.80	16.614	0.70	-13.3	44.0	21.4
	Pre-cycle 13 (n=11)	71.46	17.126	75.40	30.8	93.6	21.4	11	6.02	16.109	3.70	-23.1	40.7	21.4
	Pre-cycle 25 (n=7)	76.31	19.341	80.60	54.4	109.7	50.0	6	3.05	22.109	2.27	-19.6	36.6	57.1
	Pre-cycle 37 (n=6)	72.02	13.318	74.95	46.5	83.7	57.1	5	3.40	12.508	5.55	-16.1	18.5	64.3
	Pre-cycle 49 (n=2)	NC	NC	NC	63.1	78.3	85.7	2	NC	NC	NC	-21.5	-8.1	85.7

[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.

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Table 4.5.1.2.1 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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 velocity achieved (m/min)	Baseline (n=13)	79.54	36.173	70.92	22.5	139.3	7.1							
	Pre-cycle 5 (n=12)	79.99	29.100	80.03	31.1	143.3	14.3	12	4.40	14.955	2.50	-19.5	39.4	14.3
	Pre-cycle 9 (n=12)	83.69	25.457	81.26	43.8	140.8	14.3	12	8.10	18.269	4.15	-19.5	49.5	14.3
	Pre-cycle 13 (n=11)	82.37	27.867	77.47	34.0	143.5	21.4	11	8.05	18.388	5.83	-27.0	47.0	21.4
	Pre-cycle 25 (n=7)	89.84	22.537	82.83	60.5	128.3	50.0	7	7.46	24.171	17.00	-22.5	44.2	50.0
	Pre-cycle 37 (n=6)	78.09	15.106	75.88	54.6	97.3	57.1	6	5.20	18.119	12.88	-20.2	24.1	57.1
	Pre-cycle 49 (n=3)	80.51	12.820	87.12	65.7	88.7	78.6	3	10.85	43.062	4.73	-28.8	56.6	78.6

[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.

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Table 4.5.1.2.2 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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=14)	484.16	89.177	460.50	308.8	603.0	0.0						
	Pre-cycle 5 (n=14)	495.56	104.811	498.50	354.0	660.0	0.0	14	11.39	66.521	9.00	-92.0	123.0	0.0
	Pre-cycle 9 (n=14)	488.00	88.609	500.50	350.0	607.0	0.0	14	3.84	67.546	-7.75	-89.0	114.0	0.0
	Pre-cycle 13 (n=12)	482.25	92.525	480.50	333.0	596.0	14.3	12	-5.11	92.712	-29.00	-134.0	146.0	14.3
	Pre-cycle 25 (n=10)	528.66	66.846	553.00	433.1	604.0	28.6	10	41.48	64.074	14.50	-33.9	165.7	28.6
	Pre-cycle 37 (n=8)	501.44	74.959	500.00	397.5	604.0	42.9	8	-3.04	86.689	-20.50	-95.0	182.2	42.9
	Pre-cycle 49 (n=5)	569.36	70.204	586.00	461.8	654.0	64.3	5	35.60	73.361	13.00	-41.0	153.0	64.3

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.2.2 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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 % normal distance achieved	Baseline (n=14)	76.87	10.704	78.83	55.2	91.1	0.0							
	Pre-cycle 5 (n=14)	78.61	13.890	82.54	54.1	97.5	0.0	14	1.74	11.845	0.71	-21.9	21.4	0.0
	Pre-cycle 9 (n=14)	77.35	12.359	80.76	56.5	92.0	0.0	14	0.48	11.477	-1.18	-18.0	21.5	0.0
	Pre-cycle 13 (n=12)	76.04	15.915	75.93	45.7	107.2	14.3	12	-1.25	15.174	-5.06	-22.0	23.9	14.3
	Pre-cycle 25 (n=10)	83.69	9.585	85.65	65.2	95.2	28.6	10	5.53	9.662	2.30	-5.5	26.4	28.6
	Pre-cycle 37 (n=8)	77.69	12.088	80.65	57.8	93.9	42.9	8	-0.43	13.772	-3.36	-17.3	25.7	42.9
	Pre-cycle 49 (n=5)	88.68	11.066	88.60	73.1	104.4	64.3	5	6.69	9.299	1.88	-2.5	17.9	64.3

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.2.2 Endurance evaluation secondary outcome test scores and 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: 31 March 2021 (DC02)

		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 velocity achieved (m/min)	Baseline (n=14)	80.69	14.862	76.75	51.5	100.5	0.0							
	Pre-cycle 5 (n=14)	82.59	17.468	83.08	59.0	110.0	0.0	14	1.90	11.087	1.50	-15.3	20.5	0.0
	Pre-cycle 9 (n=14)	81.33	14.768	83.42	58.3	101.2	0.0	14	0.64	11.257	-1.29	-14.8	19.0	0.0
	Pre-cycle 13 (n=12)	80.37	15.421	80.08	55.5	99.3	14.3	12	-0.85	15.451	-4.83	-22.3	24.3	14.3
	Pre-cycle 25 (n=10)	88.11	11.141	92.17	72.2	100.7	28.6	10	6.91	10.677	2.42	-5.6	27.6	28.6
	Pre-cycle 37 (n=8)	83.57	12.495	83.33	66.3	100.7	42.9	8	-0.51	14.446	-3.41	-15.8	30.4	42.9
	Pre-cycle 49 (n=5)	94.89	11.700	97.67	77.0	109.0	64.3	5	5.93	12.227	2.17	-6.8	25.5	64.3

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.2.3 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=10)	463.01	97.733	435.75	366.0	684.0	0.0							
	Pre-cycle 5 (n=10)	462.74	103.465	450.65	354.0	660.0	0.0	10	-0.27	87.268	2.00	-117.0	129.5	0.0
	Pre-cycle 9 (n=10)	486.67	81.138	489.00	357.0	603.0	0.0	10	23.66	78.048	24.92	-89.0	129.0	0.0
	Pre-cycle 13 (n=8)	464.60	93.249	434.65	383.0	644.0	20.0	8	20.09	72.023	3.40	-58.5	152.4	20.0
	Pre-cycle 25 (n=5)	506.20	79.150	481.00	453.0	644.0	50.0	5	83.40	46.971	102.00	10.0	131.0	50.0
	Pre-cycle 37 (n=4)	436.88	27.363	444.50	398.0	460.5	60.0	4	4.88	86.233	6.00	-87.0	94.5	60.0
	Pre-cycle 49 (n=1)	NC	NC	NC	394.4	394.4	90.0	1	NC	NC	NC	28.4	28.4	90.0

[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.

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Table 4.5.1.2.3 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % normal distance achieved	Baseline (n=9)	75.06	8.934	71.30	67.1	96.0	10.0							
	Pre-cycle 5 (n=9)	74.63	14.714	77.80	54.1	97.5	10.0	9	-0.42	14.809	-0.65	-21.9	20.6	10.0
	Pre-cycle 9 (n=9)	77.32	11.196	77.10	60.8	92.1	10.0	9	2.26	13.186	-0.80	-18.0	21.0	10.0
	Pre-cycle 13 (n=8)	75.80	12.260	73.88	57.9	93.6	20.0	8	1.36	11.096	-2.47	-10.2	22.1	20.0
	Pre-cycle 25 (n=5)	85.34	14.496	80.60	73.3	109.7	50.0	4	6.85	9.137	8.72	-5.5	15.5	60.0
	Pre-cycle 37 (n=4)	70.68	6.513	72.25	61.5	76.7	60.0	3	-3.14	12.368	2.33	-17.3	5.6	70.0
	Pre-cycle 49 (n=1)	NC	NC	NC	63.1	63.1	90.0	1	NC	NC	NC	-8.1	-8.1	90.0

[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.

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Table 4.5.1.2.3 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 velocity achieved (m/min)	Baseline (n=10)	77.17	16.289	72.63	61.0	114.0	0.0							
	Pre-cycle 5 (n=10)	77.12	17.244	75.11	59.0	110.0	0.0	10	-0.04	14.545	0.33	-19.5	21.6	0.0
	Pre-cycle 9 (n=10)	81.11	13.523	81.50	59.5	100.5	0.0	10	3.94	13.008	4.15	-14.8	21.5	0.0
	Pre-cycle 13 (n=8)	77.43	15.541	72.44	63.8	107.3	20.0	8	3.35	12.004	0.57	-9.8	25.4	20.0
	Pre-cycle 25 (n=5)	84.37	13.191	80.17	75.5	107.3	50.0	5	13.90	7.829	17.00	1.7	21.8	50.0
	Pre-cycle 37 (n=4)	72.81	4.562	74.09	66.3	76.8	60.0	4	0.81	14.373	1.00	-14.5	15.8	60.0
	Pre-cycle 49 (n=1)	NC	NC	NC	65.7	65.7	90.0	1	NC	NC	NC	4.7	4.7	90.0

[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.

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Table 4.5.1.2.4 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = Non-progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=6)	519.29	100.320	550.00	327.7	604.0	25.0	6	-1.36	104.887	-16.50	-121.0	144.8	25.0
	Pre-cycle 49 (n=5)	569.75	53.024	554.00	522.7	654.0	37.5	5	35.77	189.285	2.00	-173.0	339.9	37.5

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.2.4 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = Non-progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % 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
	Pre-cycle 37 (n=6)	77.98	16.203	81.70	46.5	93.9	25.0	6	-0.10	12.673	0.49	-16.1	18.5	25.0
	Pre-cycle 49 (n=4)	89.98	10.773	88.60	78.3	104.4	50.0	4	-1.66	15.290	-0.31	-21.5	15.5	50.0

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.2.4 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = Non-progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=6)	86.55	16.721	91.67	54.6	100.7	25.0	6	-0.23	17.483	-2.75	-20.2	24.1	25.0
	Pre-cycle 49 (n=5)	94.96	8.838	92.33	87.1	109.0	37.5	5	5.96	31.546	0.34	-28.8	56.6	37.5

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.2.5 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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)	487.28	221.491	467.00	135.0	836.0	10.0							
	Pre-cycle 5 (n=8)	489.49	204.750	490.50	186.6	860.0	20.0	8	36.51	49.540	26.50	-37.0	108.0	20.0
	Pre-cycle 9 (n=8)	482.26	184.684	467.03	263.0	845.0	20.0	8	29.28	81.747	21.00	-89.0	128.0	20.0
	Pre-cycle 13 (n=8)	471.99	197.003	461.00	203.9	861.0	20.0	8	19.01	90.802	30.00	-134.0	128.2	20.0
	Pre-cycle 25 (n=5)	564.92	131.208	550.00	433.1	770.0	50.0	5	36.16	94.870	19.00	-66.0	165.7	50.0
	Pre-cycle 37 (n=4)	489.88	71.223	495.50	397.5	571.0	60.0	4	37.93	107.143	19.50	-69.5	182.2	60.0
	Pre-cycle 49 (n=2)	NC	NC	NC	461.8	591.0	80.0	2	NC	NC	NC	13.0	153.0	80.0

[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.

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Table 4.5.1.2.5 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % normal distance achieved	Baseline (n=9)	67.98	25.705	67.71	20.5	114.4	10.0						
	Pre-cycle 5 (n=8)	68.11	20.681	71.32	28.2	92.5	20.0	8	5.93	8.645	3.86	-3.7	21.4	20.0
	Pre-cycle 9 (n=8)	67.07	17.864	70.89	36.6	86.3	20.0	8	4.89	12.668	3.78	-11.3	21.5	20.0
	Pre-cycle 13 (n=8)	64.55	19.097	67.98	30.8	88.1	20.0	8	2.36	15.353	1.85	-22.0	23.9	20.0
	Pre-cycle 25 (n=5)	75.70	13.800	81.60	57.2	89.2	50.0	5	6.95	14.087	1.20	-7.1	26.4	50.0
	Pre-cycle 37 (n=4)	75.75	12.254	79.95	57.8	85.3	60.0	4	5.89	15.658	3.90	-9.9	25.7	60.0
	Pre-cycle 49 (n=2)	NC	NC	NC	73.1	88.7	80.0	2	NC	NC	NC	0.7	17.9	80.0

[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.

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Table 4.5.1.2.5 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 velocity achieved (m/min)	Baseline (n=9)	81.21	36.914	77.83	22.5	139.3	10.0							
	Pre-cycle 5 (n=8)	81.58	34.124	81.75	31.1	143.3	20.0	8	6.09	8.256	4.42	-6.2	18.0	20.0
	Pre-cycle 9 (n=8)	80.37	30.780	77.84	43.8	140.8	20.0	8	4.88	13.623	3.50	-14.8	21.3	20.0
	Pre-cycle 13 (n=8)	78.66	32.835	76.83	34.0	143.5	20.0	8	3.17	15.131	5.00	-22.3	21.4	20.0
	Pre-cycle 25 (n=5)	94.15	21.867	91.67	72.2	128.3	50.0	5	6.03	15.809	3.17	-11.0	27.6	50.0
	Pre-cycle 37 (n=4)	81.65	11.872	82.58	66.3	95.2	60.0	4	6.32	17.852	3.25	-11.6	30.4	60.0
	Pre-cycle 49 (n=2)	NC	NC	NC	77.0	98.5	80.0	2	NC	NC	NC	2.2	25.5	80.0

[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.

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Table 4.5.1.3.1 Endurance evaluation secondary outcome test scores and change from baseline over time - Gender = Male (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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	8	-22.40	173.501	-11.50	-389.0	236.2	20.0
	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=8)	488.58	210.494	519.00	82.9	761.0	20.0	7	9.83	106.463	46.00	-121.0	144.8	30.0
	Pre-cycle 49 (n=5)	529.35	107.483	532.00	356.0	632.0	50.0	5	-23.83	222.391	-86.00	-218.0	339.9	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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.3.1 Endurance evaluation secondary outcome test scores and change from baseline over time - Gender = Male (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % 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=7)	75.70	16.501	76.70	46.5	100.8	30.0	6	0.49	12.323	1.74	-16.1	18.5	40.0
	Pre-cycle 49 (n=3)	86.67	7.308	89.90	78.3	91.8	70.0	3	-4.77	17.721	-6.60	-21.5	13.8	70.0

[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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.3.1 Endurance evaluation secondary outcome test scores and change from baseline over time - Gender = Male (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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	8	-3.73	28.917	-1.92	-64.8	39.4	20.0
	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	42.546	79.01	7.6	134.2	20.0	7	-7.19	30.822	-14.33	-52.8	44.2	30.0
	Pre-cycle 37 (n=8)	81.43	35.081	86.50	13.8	126.8	20.0	7	1.64	17.745	7.66	-20.2	24.1	30.0
	Pre-cycle 49 (n=5)	88.22	17.915	88.67	59.3	105.3	50.0	5	-3.97	37.065	-14.34	-36.3	56.6	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.
Min = Minimum. Max = Maximum. SD = Standard deviation.

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Table 4.5.1.3.2 Endurance evaluation secondary outcome test scores and change from baseline over time - Gender = Female (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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=6)	547.58	87.159	571.00	397.5	642.0	0.0	6	46.25	93.165	23.50	-69.5	186.0	0.0
	Pre-cycle 49 (n=3)	608.33	39.929	591.00	580.0	654.0	50.0	3	62.67	56.412	51.00	13.0	124.0	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.

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Table 4.5.1.3.2 Endurance evaluation secondary outcome test scores and change from baseline over time - Gender = Female (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % 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=6)	81.17	13.825	82.15	57.8	95.2	0.0	5	4.03	10.694	5.00	-9.9	17.3	16.7
	Pre-cycle 49 (n=3)	85.80	20.207	88.70	64.3	104.4	50.0	2	NC	NC	NC	0.7	15.5	66.7

[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.

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Table 4.5.1.3.2 Endurance evaluation secondary outcome test scores and change from baseline over time - Gender = Female (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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=6)	91.27	14.528	95.17	66.3	107.0	0.0	6	7.71	15.526	3.92	-11.6	31.0	0.0
	Pre-cycle 49 (n=3)	101.39	6.654	98.50	96.7	109.0	50.0	3	10.45	9.402	8.50	2.2	20.7	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.

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Table 4.5.1.3.3 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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	4	-114.25	184.617	-34.50	-389.0	1.0	0.0
	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=4)	629.50	130.293	653.50	450.0	761.0	0.0	4	22.25	134.594	-4.00	-89.0	186.0	0.0
	Pre-cycle 49 (n=3)	605.33	26.026	604.00	580.0	632.0	25.0	3	-25.33	175.070	18.00	-218.0	124.0	25.0

[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.

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Table 4.5.1.3.3 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % 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=4)	79.53	14.520	74.50	68.3	100.8	0.0	2	NC	NC	NC	-9.7	4.3	50.0
	Pre-cycle 49 (n=3)	82.00	15.358	89.90	64.3	91.8	25.0	2	NC	NC	NC	-6.6	13.8	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.

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Table 4.5.1.3.3 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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	4	-19.04	30.770	-5.75	-64.8	0.2	0.0
	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=4)	104.92	21.716	108.92	75.0	126.8	0.0	4	3.71	22.432	-0.67	-14.8	31.0	0.0
	Pre-cycle 49 (n=3)	100.89	4.334	100.67	96.7	105.3	25.0	3	-4.22	29.182	3.00	-36.3	20.7	25.0

[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.

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Table 4.5.1.3.4 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Non-progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=5)	429.72	223.233	550.00	82.9	604.0	0.0	4	30.21	117.169	48.50	-121.0	144.8	20.0
	Pre-cycle 49 (n=3)	569.58	73.260	532.00	522.7	654.0	40.0	3	72.62	257.107	51.00	-173.0	339.9	40.0

[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.

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Table 4.5.1.3.4 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = Non-progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % 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
	Pre-cycle 37 (n=4)	76.20	20.590	82.20	46.5	93.9	20.0	4	3.53	14.405	5.85	-16.1	18.5	20.0
	Pre-cycle 49 (n=2)	NC	NC	NC	78.3	104.4	60.0	2	NC	NC	NC	-21.5	15.5	60.0

[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.

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Table 4.5.1.3.4 Endurance evaluation secondary outcome test scores and change from baseline over time – PN status = Non-progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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
	Pre-cycle 37 (n=5)	71.62	37.205	91.67	13.8	100.7	0.0	4	5.04	19.530	8.09	-20.2	24.1	20.0
	Pre-cycle 49 (n=3)	94.93	12.210	88.67	87.1	109.0	40.0	3	12.10	42.849	8.50	-28.8	56.6	40.0

[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.

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Table 4.5.1.3.5 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Unknown (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=5)	505.50	71.730	500.00	397.5	571.0	28.6	5	27.30	70.756	46.00	-69.5	121.0	28.6
	Pre-cycle 49 (n=2)	NC	NC	NC	356.0	591.0	71.4	2	NC	NC	NC	-86.0	13.0	71.4

[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.

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Table 4.5.1.3.5 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Unknown (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 % 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
	Pre-cycle 37 (n=5)	78.80	13.754	79.00	57.8	95.2	28.6	5	2.87	10.877	-0.82	-9.9	17.3	28.6
	Pre-cycle 49 (n=1)	NC	NC	NC	88.7	88.7	85.7	1	NC	NC	NC	0.7	0.7	85.7

[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.

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Table 4.5.1.3.5 Endurance evaluation secondary outcome test scores and change from baseline over time - PN status = Unknown (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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 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	31.965	91.33	20.8	99.5	28.6	5	-4.60	28.508	3.17	-52.8	16.3	28.6
	Pre-cycle 37 (n=5)	84.25	11.957	83.33	66.3	95.2	28.6	5	4.55	11.791	7.66	-11.6	20.2	28.6
	Pre-cycle 49 (n=2)	NC	NC	NC	59.3	98.5	71.4	2	NC	NC	NC	-14.3	2.2	71.4

[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.

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1.15.1.2 Subgruppenanalyse zum 6MWT: Responderanalyse

Table 4.4.2.1 Motor function secondary outcomes test score categories of change over time - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - all	Pre-cycle 5 (n=13)	Categories of change [d]			
		Improvement	4	30.8	9.1, 61.4
		No improvement or deterioration	6	46.2	19.2, 74.9
		Deterioration	3	23.1	5.0, 53.8
	Pre-cycle 9 (n=13)	Categories of change [d]			
		Improvement	6	46.2	19.2, 74.9
		No improvement or deterioration	3	23.1	5.0, 53.8
		Deterioration	4	30.8	9.1, 61.4
	Pre-cycle 13 (n=12)	Categories of change [d]			
		Improvement	5	41.7	15.2, 72.3
		No improvement or deterioration	3	25.0	5.5, 57.2
		Deterioration	4	33.3	9.9, 65.1
	Pre-cycle 25 (n=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		No improvement or deterioration	0	0	0, 36.9
		Deterioration	5	62.5	24.5, 91.5

[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.
NC = Not calculated.

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Table 4.4.2.1 Motor function secondary outcomes test score categories of change over time - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - all	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		No improvement or deterioration	0	0	0, 45.9
		Deterioration	2	33.3	4.3, 77.7
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	3	60.0	14.7, 94.7
	Overall (n=13)	Categories of change [d]			
		Improvement	9	69.2	38.6, 90.9
		No improvement or deterioration	0	0	0, 24.7
		Deterioration	7	53.8	25.1, 80.8
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6

[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.
NC = Not calculated.

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Table 4.4.2.1 Motor function secondary outcomes test score categories of change over time - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	1	33.3	0.8, 90.6

[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.
NC = Not calculated.

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Table 4.4.2.1 Motor function secondary outcomes test score categories of change over time - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	3	75.0	19.4, 99.4
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6

[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.
NC = Not calculated.

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Table 4.4.2.1 Motor function secondary outcomes test score categories of change over time - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.1 Motor function secondary outcomes test score categories of change over time - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Lower	Overall (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	1	25.0	0.6, 80.6
6-minute walk test distance achieved (m) - Bilateral Upper	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2

[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.
NC = Not calculated.

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Table 4.4.2.1 Motor function secondary outcomes test score categories of change over time - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Bilateral Upper	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	3	100	29.2, 100
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.1 Motor function secondary outcomes test score categories of change over time - Gender = Male
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=19) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Bilateral Lower	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.2 Motor function secondary outcomes test score categories of change over time - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - all	Pre-cycle 5 (n=13)	Categories of change [d]			
		Improvement	3	23.1	5.0, 53.8
		No improvement or deterioration	6	46.2	19.2, 74.9
		Deterioration	4	30.8	9.1, 61.4
	Pre-cycle 9 (n=13)	Categories of change [d]			
		Improvement	4	30.8	9.1, 61.4
		No improvement or deterioration	5	38.5	13.9, 68.4
		Deterioration	4	30.8	9.1, 61.4
	Pre-cycle 13 (n=11)	Categories of change [d]			
		Improvement	2	18.2	2.3, 51.8
		No improvement or deterioration	3	27.3	6.0, 61.0
		Deterioration	6	54.5	23.4, 83.3
	Pre-cycle 25 (n=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		No improvement or deterioration	5	55.6	21.2, 86.3
		Deterioration	1	11.1	0.3, 48.2

[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.
NC = Not calculated.

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Table 4.4.2.2 Motor function secondary outcomes test score categories of change over time - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - all	Pre-cycle 37 (n=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0
		Deterioration	4	57.1	18.4, 90.1
	Pre-cycle 49 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
	Overall (n=13)	Categories of change [d]			
		Improvement	6	46.2	19.2, 74.9
		No improvement or deterioration	0	0	0, 24.7
		Deterioration	9	69.2	38.6, 90.9
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6

[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.
NC = Not calculated.

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Table 4.4.2.2 Motor function secondary outcomes test score categories of change over time - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8

[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.
NC = Not calculated.

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Table 4.4.2.2 Motor function secondary outcomes test score categories of change over time - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	3	75.0	19.4, 99.4
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		No improvement or deterioration	4	50.0	15.7, 84.3
		Deterioration	2	25.0	3.2, 65.1
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		No improvement or deterioration	4	50.0	15.7, 84.3
		Deterioration	2	25.0	3.2, 65.1

[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.
NC = Not calculated.

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Table 4.4.2.2 Motor function secondary outcomes test score categories of change over time - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 13 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		No improvement or deterioration	2	33.3	4.3, 77.7
		Deterioration	3	50.0	11.8, 88.2
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		No improvement or deterioration	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	3	100	29.2, 100
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.2 Motor function secondary outcomes test score categories of change over time - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Lower	Overall (n=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		No improvement or deterioration	0	0	0, 36.9
		Deterioration	5	62.5	24.5, 91.5
6-minute walk test distance achieved (m) - Bilateral Upper	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.2 Motor function secondary outcomes test score categories of change over time - Gender = Female
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Bilateral Upper	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.3 Motor function secondary outcomes test score categories of change over time - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - all	Pre-cycle 5 (n=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		No improvement or deterioration	2	20.0	2.5, 55.6
		Deterioration	4	40.0	12.2, 73.8
	Pre-cycle 9 (n=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		No improvement or deterioration	2	20.0	2.5, 55.6
		Deterioration	3	30.0	6.7, 65.2
	Pre-cycle 13 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		No improvement or deterioration	2	25.0	3.2, 65.1
		Deterioration	4	50.0	15.7, 84.3
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6

[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.
NC = Not calculated.

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Table 4.4.2.3 Motor function secondary outcomes test score categories of change over time - PN status = Progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - all	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Overall (n=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		No improvement or deterioration	0	0	0, 30.8
		Deterioration	5	50.0	18.7, 81.3
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 5 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.3 Motor function secondary outcomes test score categories of change over time - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 9 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.3 Motor function secondary outcomes test score categories of change over time - PN status = Progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 5 (n=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		No improvement or deterioration	1	14.3	0.4, 57.9
		Deterioration	3	42.9	9.9, 81.6
	Pre-cycle 9 (n=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		No improvement or deterioration	2	28.6	3.7, 71.0
		Deterioration	2	28.6	3.7, 71.0

[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.
NC = Not calculated.

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Table 4.4.2.3 Motor function secondary outcomes test score categories of change over time - PN status = Progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 13 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		No improvement or deterioration	1	16.7	0.4, 64.1
		Deterioration	3	50.0	11.8, 88.2
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.3 Motor function secondary outcomes test score categories of change over time - PN status = Progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Lower	Overall (n=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		No improvement or deterioration	0	0	0, 41.0
		Deterioration	3	42.9	9.9, 81.6
6-minute walk test distance achieved (m) - Bilateral Lower	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.3 Motor function secondary outcomes test score categories of change over time - PN status = Progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Bilateral Lower	Overall (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.4 Motor function secondary outcomes test score categories of change over time - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - all	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	1	12.5	0.3, 52.7
		No improvement or deterioration	5	62.5	24.5, 91.5
		Deterioration	2	25.0	3.2, 65.1
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		No improvement or deterioration	4	50.0	15.7, 84.3
		Deterioration	2	25.0	3.2, 65.1
	Pre-cycle 13 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		No improvement or deterioration	3	42.9	9.9, 81.6
		Deterioration	2	28.6	3.7, 71.0
	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		No improvement or deterioration	3	42.9	9.9, 81.6
		Deterioration	2	28.6	3.7, 71.0

[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.
NC = Not calculated.

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Table 4.4.2.4 Motor function secondary outcomes test score categories of change over time - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - all	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		No improvement or deterioration	1	16.7	0.4, 64.1
		Deterioration	3	50.0	11.8, 88.2
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	2	40.0	5.3, 85.3
	Overall (n=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		No improvement or deterioration	0	0	0, 36.9
		Deterioration	6	75.0	34.9, 96.8
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6

[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.
NC = Not calculated.

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Table 4.4.2.4 Motor function secondary outcomes test score categories of change over time - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8

[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.
NC = Not calculated.

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Table 4.4.2.4 Motor function secondary outcomes test score categories of change over time - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	2	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100
		Deterioration	0	0	0, 60.2
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6

[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.
NC = Not calculated.

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Table 4.4.2.4 Motor function secondary outcomes test score categories of change over time - PN status = Non-progressive
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	2	NC	NC
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.4 Motor function secondary outcomes test score categories of change over time - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
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 or deterioration	0	0	0, 60.2
		Deterioration	3	75.0	19.4, 99.4
6-minute walk test distance achieved (m) - Bilateral Upper	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.4 Motor function secondary outcomes test score categories of change over time - PN status = Non-progressive (Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Bilateral Upper	Pre-cycle 25 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 37 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.5 Motor function secondary outcomes test score categories of change over time - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - all	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		No improvement or deterioration	5	62.5	24.5, 91.5
		Deterioration	1	12.5	0.3, 52.7
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		No improvement or deterioration	2	25.0	3.2, 65.1
		Deterioration	3	37.5	8.5, 75.5
	Pre-cycle 13 (n=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		No improvement or deterioration	1	12.5	0.3, 52.7
		Deterioration	4	50.0	15.7, 84.3
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	3	60.0	14.7, 94.7

[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.
NC = Not calculated.

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Table 4.4.2.5 Motor function secondary outcomes test score categories of change over time - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - all	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Overall (n=8)	Categories of change [d]			
		Improvement	5	62.5	24.5, 91.5
		No improvement or deterioration	0	0	0, 36.9
		Deterioration	5	62.5	24.5, 91.5
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 5 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8

[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.
NC = Not calculated.

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Table 4.4.2.5 Motor function secondary outcomes test score categories of change over time - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 9 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
	Pre-cycle 25 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.5 Motor function secondary outcomes test score categories of change over time - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Upper	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	2	66.7	9.4, 99.2
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 5 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Pre-cycle 9 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.5 Motor function secondary outcomes test score categories of change over time - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Unilateral Lower	Pre-cycle 13 (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
	Overall (n=1)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	0	NC	NC
6-minute walk test distance achieved (m) - Bilateral Upper	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2

[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.
NC = Not calculated.

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Table 4.4.2.5 Motor function secondary outcomes test score categories of change over time - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Bilateral Upper	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 25 (n=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	3	100	29.2, 100
	Pre-cycle 37 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	1	NC	NC
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	0	NC	NC
		Deterioration	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.
NC = Not calculated.

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Table 4.4.2.5 Motor function secondary outcomes test score categories of change over time - PN status = Unknown
(Full analysis set with motor PN-related morbidity)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [a]			
Parameter	Time point	Response Category	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m) - Bilateral Upper	Overall (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	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.
NC = Not calculated.

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Table 4.5.2.1.1 Endurance evaluation secondary outcome test score categories of change over time - Gender = Male (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=18) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=15)	Categories of change [d]			
		Improvement	4	26.7	7.8, 55.1
		No improvement or deterioration	7	46.7	21.3, 73.4
		Deterioration	4	26.7	7.8, 55.1
	Pre-cycle 9 (n=15)	Categories of change [d]			
		Improvement	7	46.7	21.3, 73.4
		No improvement or deterioration	4	26.7	7.8, 55.1
		Deterioration	4	26.7	7.8, 55.1
	Pre-cycle 13 (n=14)	Categories of change [d]			
		Improvement	6	42.9	17.7, 71.1
		No improvement or deterioration	4	28.6	8.4, 58.1
		Deterioration	4	28.6	8.4, 58.1
	Pre-cycle 25 (n=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		No improvement or deterioration	0	0	0, 30.8
		Deterioration	6	60.0	26.2, 87.8

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.1.1 Endurance evaluation secondary outcome test score categories of change over time - Gender = Male (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=18) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=9)	Categories of change [d]			
		Improvement	6	66.7	29.9, 92.5
		No improvement or deterioration	0	0	0, 33.6
		Deterioration	3	33.3	7.5, 70.1
	Pre-cycle 49 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		No improvement or deterioration	2	33.3	4.3, 77.7
		Deterioration	3	50.0	11.8, 88.2
	Overall (n=15)	Categories of change [d]			
		Improvement	11	73.3	44.9, 92.2
		No improvement or deterioration	0	0	0, 21.8
		Deterioration	8	53.3	26.6, 78.7

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.1.2 Endurance evaluation secondary outcome test score categories of change over time - Gender = Female (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=16) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=16)	Categories of change [d]			
		Improvement	4	25.0	7.3, 52.4
		No improvement or deterioration	8	50.0	24.7, 75.3
		Deterioration	4	25.0	7.3, 52.4
	Pre-cycle 9 (n=16)	Categories of change [d]			
		Improvement	5	31.3	11.0, 58.7
		No improvement or deterioration	7	43.8	19.8, 70.1
		Deterioration	4	25.0	7.3, 52.4
	Pre-cycle 13 (n=14)	Categories of change [d]			
		Improvement	4	28.6	8.4, 58.1
		No improvement or deterioration	4	28.6	8.4, 58.1
		Deterioration	6	42.9	17.7, 71.1
	Pre-cycle 25 (n=12)	Categories of change [d]			
		Improvement	6	50.0	21.1, 78.9
		No improvement or deterioration	5	41.7	15.2, 72.3
		Deterioration	1	8.3	0.2, 38.5

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.1.2 Endurance evaluation secondary outcome test score categories of change over time – Gender = Female (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=16) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		No improvement or deterioration	2	20.0	2.5, 55.6
		Deterioration	4	40.0	12.2, 73.8
	Pre-cycle 49 (n=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		No improvement or deterioration	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
	Overall (n=16)	Categories of change [d]			
		Improvement	9	56.3	29.9, 80.2
		No improvement or deterioration	0	0	0, 20.6
		Deterioration	9	56.3	29.9, 80.2

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.1.3 Endurance evaluation secondary outcome test score categories of change over time - PN status = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=13) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=13)	Categories of change [d]			
		Improvement	4	30.8	9.1, 61.4
		No improvement or deterioration	4	30.8	9.1, 61.4
		Deterioration	5	38.5	13.9, 68.4
	Pre-cycle 9 (n=13)	Categories of change [d]			
		Improvement	6	46.2	19.2, 74.9
		No improvement or deterioration	4	30.8	9.1, 61.4
		Deterioration	3	23.1	5.0, 53.8
	Pre-cycle 13 (n=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		No improvement or deterioration	3	27.3	6.0, 61.0
		Deterioration	4	36.4	10.9, 69.2
	Pre-cycle 25 (n=8)	Categories of change [d]			
		Improvement	5	62.5	24.5, 91.5
		No improvement or deterioration	1	12.5	0.3, 52.7
		Deterioration	2	25.0	3.2, 65.1

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.1.3 Endurance evaluation secondary outcome test score categories of change over time - PN status = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=13) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		No improvement or deterioration	0	0	0, 41.0
		Deterioration	3	42.9	9.9, 81.6
	Pre-cycle 49 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
	Overall (n=13)	Categories of change [d]			
		Improvement	9	69.2	38.6, 90.9
		No improvement or deterioration	0	0	0, 24.7
		Deterioration	6	46.2	19.2, 74.9

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.1.4 Endurance evaluation secondary outcome test score categories of change over time - PN status = 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=9) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	1	12.5	0.3, 52.7
		No improvement or deterioration	5	62.5	24.5, 91.5
		Deterioration	2	25.0	3.2, 65.1
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		No improvement or deterioration	4	50.0	15.7, 84.3
		Deterioration	2	25.0	3.2, 65.1
	Pre-cycle 13 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		No improvement or deterioration	3	42.9	9.9, 81.6
		Deterioration	2	28.6	3.7, 71.0
	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		No improvement or deterioration	3	42.9	9.9, 81.6
		Deterioration	2	28.6	3.7, 71.0

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.1.4 Endurance evaluation secondary outcome test score categories of change over time - PN status = 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=9) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		No improvement or deterioration	1	16.7	0.4, 64.1
		Deterioration	3	50.0	11.8, 88.2
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	2	40.0	5.3, 85.3
	Overall (n=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		No improvement or deterioration	0	0	0, 36.9
		Deterioration	6	75.0	34.9, 96.8

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.1.5 Endurance evaluation secondary outcome test score categories of change over time -
PN status = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=12) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		No improvement or deterioration	6	60.0	26.2, 87.8
		Deterioration	1	10.0	0.3, 44.5
	Pre-cycle 9 (n=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		No improvement or deterioration	3	30.0	6.7, 65.2
		Deterioration	3	30.0	6.7, 65.2
	Pre-cycle 13 (n=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		No improvement or deterioration	2	20.0	2.5, 55.6
		Deterioration	4	40.0	12.2, 73.8
	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		No improvement or deterioration	1	14.3	0.4, 57.9
		Deterioration	3	42.9	9.9, 81.6

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years at enrolment.
[b] 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.1.5 Endurance evaluation secondary outcome test score categories of change over time -
PN status = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=12) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		No improvement or deterioration	1	16.7	0.4, 64.1
		Deterioration	1	16.7	0.4, 64.1
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Overall (n=10)	Categories of change [d]			
		Improvement	7	70.0	34.8, 93.3
		No improvement or deterioration	0	0	0, 30.8
		Deterioration	5	50.0	18.7, 81.3

[a] Patients with lower extremity PN (leg length discrepancy), cord compression or airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.2.1 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=12)	Categories of change [d]			
		Improvement	4	33.3	9.9, 65.1
		No improvement or deterioration	5	41.7	15.2, 72.3
		Deterioration	3	25.0	5.5, 57.2
	Pre-cycle 9 (n=12)	Categories of change [d]			
		Improvement	6	50.0	21.1, 78.9
		No improvement or deterioration	4	33.3	9.9, 65.1
		Deterioration	2	16.7	2.1, 48.4
	Pre-cycle 13 (n=11)	Categories of change [d]			
		Improvement	6	54.5	23.4, 83.3
		No improvement or deterioration	3	27.3	6.0, 61.0
		Deterioration	2	18.2	2.3, 51.8
	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		No improvement or deterioration	0	0	0, 41.0
		Deterioration	3	42.9	9.9, 81.6

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.2.1 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		No improvement or deterioration	0	0	0, 45.9
		Deterioration	2	33.3	4.3, 77.7
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Overall (n=12)	Categories of change [d]			
		Improvement	9	75.0	42.8, 94.5
		No improvement or deterioration	0	0	0, 26.5
		Deterioration	5	41.7	15.2, 72.3

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.2.2 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=14)	Categories of change [d]			
		Improvement	4	28.6	8.4, 58.1
		No improvement or deterioration	6	42.9	17.7, 71.1
		Deterioration	4	28.6	8.4, 58.1
	Pre-cycle 9 (n=14)	Categories of change [d]			
		Improvement	5	35.7	12.8, 64.9
		No improvement or deterioration	5	35.7	12.8, 64.9
		Deterioration	4	28.6	8.4, 58.1
	Pre-cycle 13 (n=12)	Categories of change [d]			
		Improvement	3	25.0	5.5, 57.2
		No improvement or deterioration	3	25.0	5.5, 57.2
		Deterioration	6	50.0	21.1, 78.9
	Pre-cycle 25 (n=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		No improvement or deterioration	5	50.0	18.7, 81.3
		Deterioration	1	10.0	0.3, 44.5

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.2.2 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		No improvement or deterioration	2	25.0	3.2, 65.1
		Deterioration	4	50.0	15.7, 84.3
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		No improvement or deterioration	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
	Overall (n=14)	Categories of change [d]			
		Improvement	7	50.0	23.0, 77.0
		No improvement or deterioration	0	0	0, 23.2
		Deterioration	9	64.3	35.1, 87.2

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.2.3 Endurance evaluation secondary outcome test score categories of change over time -
PN status = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		No improvement or deterioration	2	20.0	2.5, 55.6
		Deterioration	4	40.0	12.2, 73.8
	Pre-cycle 9 (n=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		No improvement or deterioration	3	30.0	6.7, 65.2
		Deterioration	2	20.0	2.5, 55.6
	Pre-cycle 13 (n=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		No improvement or deterioration	2	25.0	3.2, 65.1
		Deterioration	3	37.5	8.5, 75.5
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	4	80.0	28.4, 99.5
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

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Table 4.5.2.2.3 Endurance evaluation secondary outcome test score categories of change over time -
PN status = Progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 49 (n=1)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (n=10)	Categories of change [d]			
		Improvement	7	70.0	34.8, 93.3
		No improvement or deterioration	0	0	0, 30.8
		Deterioration	4	40.0	12.2, 73.8

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20e3.sas Executed: 2023-06-21T09:39

Table 4.5.2.2.4 Endurance evaluation secondary outcome test score categories of change over time - PN status = Non-progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=8) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	1	12.5	0.3, 52.7
		No improvement or deterioration	5	62.5	24.5, 91.5
		Deterioration	2	25.0	3.2, 65.1
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		No improvement or deterioration	4	50.0	15.7, 84.3
		Deterioration	2	25.0	3.2, 65.1
	Pre-cycle 13 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		No improvement or deterioration	3	42.9	9.9, 81.6
		Deterioration	2	28.6	3.7, 71.0
	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		No improvement or deterioration	3	42.9	9.9, 81.6
		Deterioration	2	28.6	3.7, 71.0

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.2.4 Endurance evaluation secondary outcome test score categories of change over time –
PN status = Non-progressive (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=8) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		No improvement or deterioration	1	16.7	0.4, 64.1
		Deterioration	3	50.0	11.8, 88.2
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	2	40.0	5.3, 85.3
	Overall (n=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		No improvement or deterioration	0	0	0, 36.9
		Deterioration	6	75.0	34.9, 96.8

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.2.5 Endurance evaluation secondary outcome test score categories of change over time -
PN status = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		No improvement or deterioration	4	50.0	15.7, 84.3
		Deterioration	1	12.5	0.3, 52.7
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		No improvement or deterioration	2	25.0	3.2, 65.1
		Deterioration	2	25.0	3.2, 65.1
	Pre-cycle 13 (n=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		No improvement or deterioration	1	12.5	0.3, 52.7
		Deterioration	3	37.5	8.5, 75.5
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	2	40.0	5.3, 85.3

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

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Table 4.5.2.2.5 Endurance evaluation secondary outcome test score categories of change over time -
PN status = Unknown (Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	1	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	0	NC	NC
	Overall (n=8)	Categories of change [d]			
		Improvement	5	62.5	24.5, 91.5
		No improvement or deterioration	0	0	0, 36.9
		Deterioration	4	50.0	15.7, 84.3

[a] Patients with lower extremity PN (leg length discrepancy) or cord compression who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

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Table 4.5.2.3.1 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		No improvement or deterioration	3	37.5	8.5, 75.5
		Deterioration	3	37.5	8.5, 75.5
	Pre-cycle 9 (n=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		No improvement or deterioration	1	12.5	0.3, 52.7
		Deterioration	3	37.5	8.5, 75.5
	Pre-cycle 13 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		No improvement or deterioration	2	28.6	3.7, 71.0
		Deterioration	3	42.9	9.9, 81.6
	Pre-cycle 25 (n=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		No improvement or deterioration	0	0	0, 41.0
		Deterioration	5	71.4	29.0, 96.3

[a] Patients with airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20f1.sas Executed: 2023-06-16T11:51

Table 4.5.2.3.1 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		No improvement or deterioration	0	0	0, 41.0
		Deterioration	3	42.9	9.9, 81.6
	Pre-cycle 49 (n=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	3	60.0	14.7, 94.7
	Overall (n=8)	Categories of change [d]			
		Improvement	6	75.0	34.9, 96.8
		No improvement or deterioration	0	0	0, 36.9
		Deterioration	6	75.0	34.9, 96.8

[a] Patients with airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.3.2 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
		Deterioration	2	33.3	4.3, 77.7
	Pre-cycle 9 (n=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
		Deterioration	2	33.3	4.3, 77.7
	Pre-cycle 13 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		No improvement or deterioration	2	33.3	4.3, 77.7
		Deterioration	2	33.3	4.3, 77.7
	Pre-cycle 25 (n=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		No improvement or deterioration	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1

[a] Patients with airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20f2.sas Executed: 2023-06-16T11:52

Table 4.5.2.3.2 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		No improvement or deterioration	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
	Overall (n=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		No improvement or deterioration	0	0	0, 45.9
		Deterioration	3	50.0	11.8, 88.2

[a] Patients with airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20f2.sas Executed: 2023-06-16T11:52

Table 4.5.2.3.3 Endurance evaluation secondary outcome test score categories of change over time - PN status = Progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 13 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	2	50.0	6.8, 93.2

[a] Patients with airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

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Table 4.5.2.3.3 Endurance evaluation secondary outcome test score categories of change over time - PN status = Progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
	Overall (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	3	75.0	19.4, 99.4

[a] Patients with airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20f3.sas Executed: 2023-06-16T11:52

Table 4.5.2.3.4 Endurance evaluation secondary outcome test score categories of change over time - PN status = Non-progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2
	Pre-cycle 9 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 13 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 25 (n=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	2	50.0	6.8, 93.2

[a] Patients with airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.3.4 Endurance evaluation secondary outcome test score categories of change over time - PN status = Non-progressive (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		No improvement or deterioration	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
	Pre-cycle 49 (n=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		No improvement or deterioration	0	0	0, 70.8
		Deterioration	1	33.3	0.8, 90.6
	Overall (n=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		No improvement or deterioration	0	0	0, 60.2
		Deterioration	3	75.0	19.4, 99.4

[a] Patients with airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.

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Table 4.5.2.3.5 Endurance evaluation secondary outcome test score categories of change over time - PN status = Unknown (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 5 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		No improvement or deterioration	3	50.0	11.8, 88.2
		Deterioration	1	16.7	0.4, 64.1
	Pre-cycle 9 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		No improvement or deterioration	1	16.7	0.4, 64.1
		Deterioration	3	50.0	11.8, 88.2
	Pre-cycle 13 (n=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		No improvement or deterioration	1	16.7	0.4, 64.1
		Deterioration	3	50.0	11.8, 88.2
	Pre-cycle 25 (n=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	2	40.0	5.3, 85.3

[a] Patients with airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20f5.sas Executed: 2023-06-16T11:53

Table 4.5.2.3.5 Endurance evaluation secondary outcome test score categories of change over time - PN status = Unknown (Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [a]			
Parameter	Time point	Parameter	n	% [b]	95% CI [c]
6-minute walk test distance achieved (m)	Pre-cycle 37 (n=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		No improvement or deterioration	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6
	Pre-cycle 49 (n=2)	Categories of change [d]			
		Improvement	0	NC	NC
		No improvement or deterioration	1	NC	NC
		Deterioration	1	NC	NC
	Overall (n=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		No improvement or deterioration	0	0	0, 45.9
		Deterioration	3	50.0	11.8, 88.2

[a] Patients with airway PN-related morbidity who are aged >= 5 years 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 change/deterioration are defined using a threshold of 30 m for the 6-minute walk test.
NC = Not Calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20f5.sas Executed: 2023-06-16T11:53

1.15.1.3 Subgruppenanalyse zum 6MWT: MMRM Analyse

Table 4.5.4.1.1 Change from baseline for 6-minute walk test, MMRM - 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=18)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	15	15	14
	Adjusted mean	-8.22	28.50	4.17
	Standard Error	26.806	20.162	28.156
	95% CI	-66.61, 50.17	-15.80, 72.81	-57.02, 65.36
	p-value	0.764	0.185	0.885

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20j1.sas Executed: 2023-06-19T13:08

Table 4.5.4.1.1 Change from baseline for 6-minute walk test, MMRM - 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=18)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	10	9	6
	Adjusted mean	-0.91	NC	NC
	Standard Error	38.379	NC	NC
	95% CI	-83.58, 81.77	NC	NC
	p-value	0.982	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20j1.sas Executed: 2023-06-19T13:08

Table 4.5.4.1.2 Change from baseline for 6-minute walk test, MMRM - 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=16)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	16	16	14
	Adjusted mean	9.10	5.02	0.22
	Standard Error	14.846	14.907	21.319
	95% CI	-23.43, 41.63	-27.28, 37.32	-46.13, 46.56
	p-value	0.552	0.742	0.992

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20j2.sas Executed: 2023-06-19T12:31

Table 4.5.4.1.2 Change from baseline for 6-minute walk test, MMRM - 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=16)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	12	10	6
	Adjusted mean	50.17	28.23	NC
	Standard Error	12.269	21.033	NC
	95% CI	22.60, 77.75	-18.93, 75.39	NC
	p-value	0.002	0.211	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20j2.sas Executed: 2023-06-19T12:31

Table 4.5.4.1.3 Change from baseline for 6-minute walk test, MMRM - PN status = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=13)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	13	13	11
	Adjusted mean	-29.49	14.27	7.95
	Standard Error	26.222	17.729	25.540
	95% CI	-89.89, 30.90	-25.87, 54.41	-52.84, 68.73
	p-value	0.293	0.442	0.765

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20j3.sas Executed: 2023-06-19T13:09

Table 4.5.4.1.3 Change from baseline for 6-minute walk test, MMRM - PN status = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=13)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	8	7	4
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20j3.sas Executed: 2023-06-19T13:09

Table 4.5.4.1.4 Change from baseline for 6-minute walk test, MMRM - PN status = 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=9)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	8	8	7
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20j4.sas Executed: 2023-06-19T13:09

Table 4.5.4.1.4 Change from baseline for 6-minute walk test, MMRM - PN status = 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: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=9)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	7	6	5
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20j4.sas Executed: 2023-06-19T13:09

Table 4.5.4.1.5 Change from baseline for 6-minute walk test, MMRM - PN status = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=12)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	10	10	10
	Adjusted mean	28.41	21.93	-2.09
	Standard Error	16.367	20.312	31.493
	95% CI	-11.05, 67.87	-29.63, 73.48	-75.41, 71.23
	p-value	0.130	0.328	0.949

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20j5.sas Executed: 2023-06-19T13:10

Table 4.5.4.1.5 Change from baseline for 6-minute walk test, MMRM - PN status = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN, cord compression, or airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=12)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	7	6	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20j5.sas Executed: 2023-06-19T13:10

Table 4.5.4.2.1 Change from baseline for 6-minute walk test, MMRM - Gender = Male
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	12	12	11
	Adjusted mean	27.99	50.47	49.38
	Standard Error	23.680	23.753	25.379
	95% CI	-26.35, 82.33	-3.93, 104.87	-8.80, 107.56
	p-value	0.270	0.065	0.086

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20k1.sas Executed: 2023-06-19T13:11

Table 4.5.4.2.1 Change from baseline for 6-minute walk test, MMRM - Gender = Male
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	7	6	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20k1.sas Executed: 2023-06-19T13:11

Table 4.5.4.2.2 Change from baseline for 6-minute walk test, MMRM - Gender = Female
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	14	14	12
	Adjusted mean	10.22	2.38	-7.72
	Standard Error	16.991	17.227	23.651
	95% CI	-27.43, 47.86	-35.49, 40.25	-59.75, 44.32
	p-value	0.561	0.893	0.750

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20k2.sas Executed: 2023-06-19T13:12

Table 4.5.4.2.2 Change from baseline for 6-minute walk test, MMRM - Gender = Female
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=14)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	10	8	5
	Adjusted mean	37.99	NC	NC
	Standard Error	11.934	NC	NC
	95% CI	11.51, 64.46	NC	NC
	p-value	0.009	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20k2.sas Executed: 2023-06-19T13:12

Table 4.5.4.2.3 Change from baseline for 6-minute walk test, MMRM - PN status = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	10	10	8
	Adjusted mean	-0.27	23.66	NC
	Standard Error	28.355	22.353	NC
	95% CI	-70.18, 69.65	-31.39, 78.72	NC
	p-value	0.993	0.332	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20k3.sas Executed: 2023-06-19T13:13

Table 4.5.4.2.3 Change from baseline for 6-minute walk test, MMRM - PN status = Progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	5	4	1
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20k3.sas Executed: 2023-06-19T13:13

Table 4.5.4.2.4 Change from baseline for 6-minute walk test, MMRM - PN status = Non-progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=8)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	8	8	7
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20k4.sas Executed: 2023-06-19T13:14

Table 4.5.4.2.4 Change from baseline for 6-minute walk test, MMRM - PN status = Non-progressive
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=8)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	7	6	5
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20k4.sas Executed: 2023-06-19T13:14

Table 4.5.4.2.5 Change from baseline for 6-minute walk test, MMRM - PN status = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	8	8	8
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20k5.sas Executed: 2023-06-19T13:14

Table 4.5.4.2.5 Change from baseline for 6-minute walk test, MMRM - PN status = Unknown
(Full analysis set >= 5 years at enrolment, with lower extremity PN or cord compression)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	5	4	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req20k5.sas Executed: 2023-06-19T13:14

Table 4.5.4.3.1 Change from baseline for 6-minute walk test, MMRM - Gender = Male
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	8	8	7
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req2011.sas Executed: 2023-06-19T13:15

Table 4.5.4.3.1 Change from baseline for 6-minute walk test, MMRM - Gender = Male
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	7	7	5
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req2011.sas Executed: 2023-06-19T13:15

Table 4.5.4.3.2 Change from baseline for 6-minute walk test, MMRM - Gender = Female
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	6	6	6
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req2012.sas Executed: 2023-06-19T13:16

Table 4.5.4.3.2 Change from baseline for 6-minute walk test, MMRM - Gender = Female
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=6)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	6	6	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req2012.sas Executed: 2023-06-19T13:16

Table 4.5.4.3.3 Change from baseline for 6-minute walk test, MMRM - PN status = Progressive
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	4	4	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req2013.sas Executed: 2023-06-19T13:16

Table 4.5.4.3.3 Change from baseline for 6-minute walk test, MMRM - PN status = Progressive
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	4	4	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req2013.sas Executed: 2023-06-19T13:16

Table 4.5.4.3.4 Change from baseline for 6-minute walk test, MMRM - PN status = Non-progressive
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	4	4	4
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req2014.sas Executed: 2023-06-19T13:17

Table 4.5.4.3.4 Change from baseline for 6-minute walk test, MMRM - PN status = Non-progressive
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=5)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	4	4	3
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

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Table 4.5.4.3.5 Change from baseline for 6-minute walk test, MMRM - PN status = Unknown
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7)		
Parameter	Statistic	Pre-cycle 5	Pre-cycle 9	Pre-cycle 13
6-minute walk test distance achieved (m)	n	6	6	6
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

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Table 4.5.4.3.5 Change from baseline for 6-minute walk test, MMRM - PN status = Unknown
(Full analysis set >= 5 years at enrolment, with airway PN)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7)		
Parameter	Statistic	Pre-cycle 25	Pre-cycle 37	Pre-cycle 49
6-minute walk test distance achieved (m)	n	5	5	2
	Adjusted mean	NC	NC	NC
	Standard Error	NC	NC	NC
	95% CI	NC	NC	NC
	p-value	NC	NC	NC

CI = Confidence interval. MMRM = Mixed Model Repeated Measures.
NC = Not calculated (less than 10 patients at all visits).
The model includes terms for pre-cycle, baseline score, age, the number of morbidities at baseline and baseline X pre-cycle interaction.

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1.16 Endpunkt Allgemeiner Gesundheitszustand: Global Impression of Change (GIC)

1.16.1 Rücklaufquoten für den GIC – Elternberichtet (8–18 Jahre)

Tabelle 8: Rücklaufquoten für Global Impression of Change (GIC) – Elternberichtet (8–18 Jahre)

Studie	**Selumetinib 25 mg/m² BID**		
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Patienten im Alter von 8–18 Jahren (FAS) N = 34**		
	Erwartete Antworten, N*	**Alle Fragen beantwortet, n/N* (%)**	**≥ eine Frage beantwortet, n (%)**
GIC – elternberichtet			
Zyklus 3	32	23 (71,9)	30 (93,8)
Zyklus 5	32	30 (93,8)	31 (96,9)
Zyklus 9	30	29 (96,7)	29 (96,7)
Zyklus 13	30	30 (100,0)	30 (100,0)
Zyklus 25	23	23 (100,0)	23 (100,0)
Zyklus 37	20	19 (95,0)	19 (95,0)
Zyklus 49	19	5 (26,3)	6 (31,6)

BID: Zweimal täglich; FAS: Full Analysis Set; GIC: Global Impression of Change; n: Patienten mit Antwort; N*: Patienten mit erwarteter Antwort

Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 5. Stand: 19.04.2023. 2023.

1.16.2 Zeitlicher Verlauf der Verteilung der Antwortkategorien des GIC – Elternberichtet (8–18 Jahre)

Tabelle 9: Ergebnisse für den Endpunkt „Allgemeiner Gesundheitszustand: GIC“ – elternberichtet (8–18 Jahre) – Zeitlicher Verlauf der Verteilung der Antwortkategorien

Studie	**Selumetinib 25 mg/m² BID**						
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Elternberichtet Patienten im Alter von 8–18 Jahren (FAS) N = 34**						
Antwortkategorien	**Sehr viel besser** n /N* (%)	**Viel besser** n/N* (%)	**Besser** n/N* (%)	**Keine Veränderung** n/N* (%)	**Schlechter** n/N*(%)	**Viel schlechter** n/N* (%)	**Sehr viel schlechter** n/N* (%)
Item 1: Tumorschmerz							
Zyklus 3	2/26 (7,7)	6/26 (23,1)	5/26 (19,2)	13/26 (50,0)	0/26 (0,0)	0/26 (0,0)	0/26 (0,0)
Zyklus 5	5/31 (16,1)	7/31 (22,6)	5/31 (16,1)	14/31 (45,2)	0/31 (0,0)	0/31 (0,0)	0/31 (0,0)
Zyklus 9	11/31 (35,5)	7/31 (22,6)	5/31 (16,1)	8/31 (25,8)	0/31 (0,0)	0/31 (0,0)	0/31 (0,0)
Zyklus 13	11/30 (36,7)	8/30 (26,7)	2/30 (6,7)	9/30 (30,0)	0/30 (0,0)	0/30 (0,0)	0/30 (0,0)
Zyklus 25	8/23 (34,8)	5/23 (21,7)	2/23 (8,7)	8/23 (34,8)	0/23 (0,0)	0/23 (0,0)	0/23 (0,0)
Zyklus 37	7/20 (35,0)	5/20 (25,0)	3/20 (15,0)	5/20 (25,0)	0/20 (0,0)	0/20 (0,0)	0/20 (0,0)
Zyklus 49	2/6 (33,3)	3/6 (50,0)	0/6 (0,0)	1/6 (16,7)	0/6 (0,0)	0/6 (0,0)	0/6 (0,0)
Item 2: Gesamtschmerz							
Zyklus 3	2/30 (6,7)	6/30 (20,0)	8/30 (26,7)	14/30 (46,7)	0/30 (0,0)	0/30 (0,0)	0/30 (0,0)
Zyklus 5	4/31 (12,9)	9/31 (29,0)	6/31 (19,4)	11/31 (35,5)	1/31 (3,2)	0/31 (0,0)	0/31 (0,0)
Zyklus 9	4/31 (12,9)	13/31 (41,9)	2/31 (6,5)	11/31 (35,5)	1/31 (3,2)	0/31 (0,0)	0/31 (0,0)
Zyklus 13	7/30 (23,3)	10/30 (33,3)	4/30 (13,3)	8/30 (26,7)	1/30 (3,3)	0/30 (0,0)	0/30 (0,0)
Zyklus 25	7/23 (30,4)	5/23 (21,7)	4/23 (17,4)	7/23 (30,4)	0/23 (0,0)	0/23 (0,0)	0/23 (0,0)
Zyklus 37	5/20 (25,0)	6/20 (30,0)	3/20 (15,0)	6/20 (20,0)	0/20 (0,0)	0/20 (0,0)	0/20 (0,0)
Zyklus 49	2/6 (33,3)	2/6 (33,3)	0/6 (0,0)	1/6 (16,7)	0/6 (0,0)	1/6 (16,7)	0/6 (0,0)

Studie	**Selumetinib 25 mg/m² BID**						
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Elternberichtet Patienten im Alter von 8–18 Jahren (FAS) N = 34**						
Antwortkategorien	**Sehr viel besser** n /N* (%)	**Viel besser** n/N* (%)	**Besser** n/N* (%)	**Keine Veränderung** n/N* (%)	**Schlechter** n/N*(%)	**Viel schlechter** n/N* (%)	**Sehr viel schlechter** n/N* (%)
Item 3: Tumor-assoziierte Morbidität							
Zyklus 3	0/23 (0,0)	4/23 (17,4)	8/23 (34,8)	10/23 (43,5)	1/23 (4,3)	0/23 (0,0)	0/23 (0,0)
Zyklus 5	4/30 (13,3)	8/30 (26,7)	9/30 (30,0)	8/30 (26,7)	1/30 (3,3)	0/30 (0,0)	0/30 (0,0)
Zyklus 9	6/31 (19,4)	13/31 (41,9)	5/31 (16,1)	7/31 (22,6)	0/31 (0,0)	0/31 (0,0)	0/31 (0,0)
Zyklus 13	9/30 (30,0)	13/30 (43,3)	5/30 (16,7)	3/30 (10,0)	0/30 (0,0)	0/30 (0,0)	0/30 (0,0)
Zyklus 25	9/23 (39,1)	7/23 (30,4)	4/23 (17,4)	3/23 (13,0)	0/23 (0,0)	0/23 (0,0)	0/23 (0,0)
Zyklus 37	4/20 (20,0)	13/20 (65,0)	2/20 (10,0)	0/20 (0,0)	1/20 (5,0)	0/20 (0,0)	0/20 (0,0)
Zyklus 49	0/5 (0,0)	2/5 (40,0)	2/5 (40,0)	1/5 (20,0)	0/5 (0,0)	0/5 (0,0)	0/5 (0,0)

BID: Zweimal täglich; FAS: Full Analysis Set

N*: Anzahl der in die Analyse mit eingeschlossenen Patienten. Patienten mit vorhandenen Werten bei der jeweiligen Visite gingen in die Analyse mit ein.

Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 5. Stand: 19.04.2023. 2023.

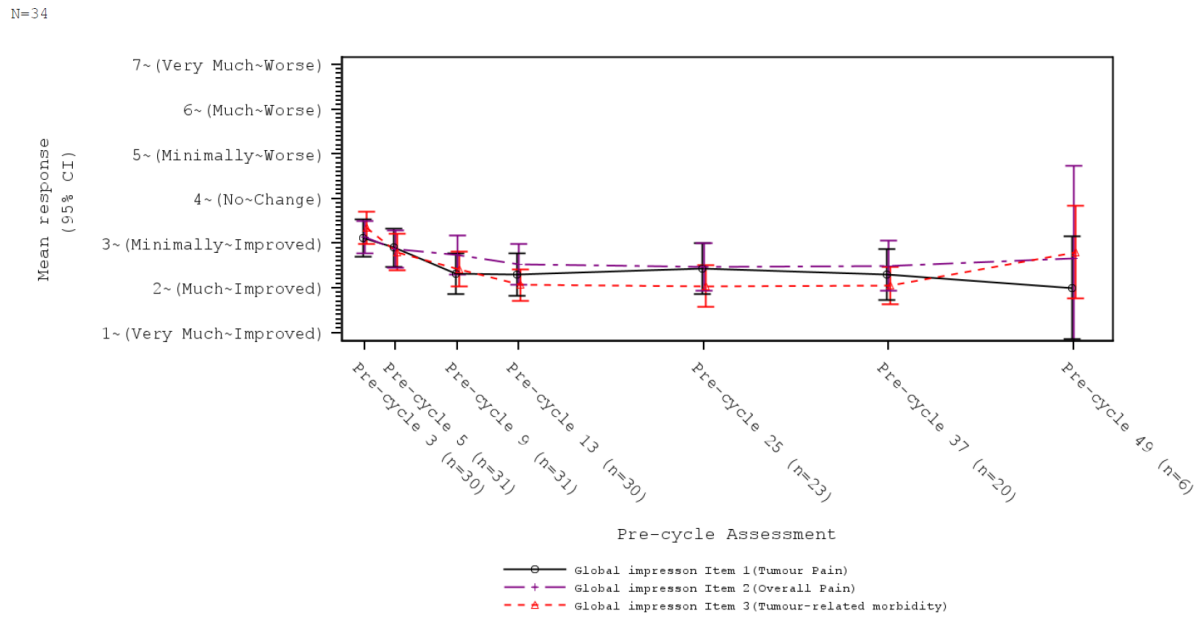

Abbildung 9: Global Impression of Change (GIC) – elternberichtet (8–18 Jahre) – Mittlere Veränderung gegenüber Baseline im Studienverlauf

Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 2 – 4. Stand: 17.03.2023. 2023.

1.16.3 GIC Responderanalysen – Elternberichtet (8–18 Jahre)

Tabelle 10: Ergebnisse für den Endpunkt „Allgemeiner Gesundheitszustand: GIC“ – elternberichtet (8–18 Jahre) – Responderanalysen

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Verbesserung[a] n/N* (%)**	**Verschlechterung[b] n/N (%)**
Elternberichtet (8–18 Jahre)		
Zyklus 3		
Item 1: Tumorschmerz	8/26 (30,8)	0/26 (0,0)
Item 2: Gesamtschmerz	8/30 (26,7)	0/30 (0,0)
Item 3: Tumor-assoziierte Morbidität	4/23 (17,4)	0/23 (0,0)
Zyklus 5		
Item 1: Tumorschmerz	12/31 (38,7)	0/31 (0,0)
Item 2: Gesamtschmerz	13/31 (41,9)	0/31 (0,0)
Item 3: Tumor-assoziierte Morbidität	12/30 (40,0)	0/30 (0,0)
Zyklus 9		
Item 1: Tumorschmerz	18/31 (58,1)	0/31 (0,0)
Item 2: Gesamtschmerz	17/31 (54,8)	0/31 (0,0)
Item 3: Tumor-assoziierte Morbidität	19/31 (61,3)	0/31 (0,0)
Zyklus 13		
Item 1: Tumorschmerz	19/30 (63,3)	0/30 (0,0)
Item 2: Gesamtschmerz	17/30 (56,7)	0/30 (0,0)
Item 3: Tumor-assoziierte Morbidität	22/30 (73,3)	0/30 (0,0)
Zyklus 25		
Item 1: Tumorschmerz	13/23 (56,5)	0/23 (0,0)
Item 2: Gesamtschmerz	12/23 (52,2)	0/23 (0,0)
Item 3: Tumor-assoziierte Morbidität	16/23 (69,6)	0/23 (0,0)
Zyklus 37		
Item 1: Tumorschmerz	12/20 (60,0)	0/20 (0,0)
Item 2: Gesamtschmerz	11/20 (55,0)	0/20 (0,0)
Item 3: Tumor-assoziierte Morbidität	17/20 (85,0)	0/20 (0,0)
Zyklus 49		
Item 1: Tumorschmerz	5/6 (83,3)	0/6 (0,0)
Item 2: Gesamtschmerz	4/6 (66,7)	1/6 (16,7)
Item 3: Tumor-assoziierte Morbidität	2/5 (40,0)	0/5 (0,0)
Gesamt		
Item 1: Tumorschmerz	24/32 (75,0)	0/32 (0,0)
Item 2: Gesamtschmerz	23/32 (71,9)	1/32 (3,1)
Item 3: Tumor-assoziierte Morbidität	26/32 (81,3)	0/32 (0,0)

BID: Zweimal täglich; GIC: Global Impression of Change

a: Erreichen der Kategorien „viel besser“ oder „sehr viel besser“

b: Erreichen der Kategorien „viel schlechter“ oder „sehr viel schlechter“

Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 5. Stand: 19.04.2023. 2023.

1.16.4 Subgruppenanalysen zum GIC

1.16.4.1 Subgruppenanalyse GIC – Selbstberichtet (8-18 Jahre)

Table 2.10.1.1.1.1 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male(Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=14)	1 = Much or Very Much Improved	9 (64.3)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (35.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=18)	1 = Much or Very Much Improved	11 (61.1)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (38.9)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=18)	1 = Much or Very Much Improved	12 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (27.8)
		3 = Much or Very Much Worsened	1 (5.6)
	Pre-cycle 13 (n=18)	1 = Much or Very Much Improved	10 (55.6)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (44.4)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.1 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n=14)	1 = Much or Very Much Improved	9 (64.3)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (35.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n=11)	1 = Much or Very Much Improved	5 (45.5)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (54.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Overall (n=19)	1 = Much or Very Much Improved	16 (84.2)
		2 = Minimally Improved, No Change, or Minimally Worse	12 (63.2)
		3 = Much or Very Much Worsened	1 (5.3)

[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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.1 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=18)	1 = Much or Very Much Improved	7 (38.9)
		2 = Minimally Improved, No Change, or Minimally Worse	11 (61.1)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=18)	1 = Much or Very Much Improved	8 (44.4)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (50.0)
		3 = Much or Very Much Worsened	1 (5.6)
	Pre-cycle 9 (n=18)	1 = Much or Very Much Improved	6 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	12 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=18)	1 = Much or Very Much Improved	8 (44.4)
		2 = Minimally Improved, No Change, or Minimally Worse	10 (55.6)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.1 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male(Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n=14)	1 = Much or Very Much Improved	5 (35.7)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (64.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n=12)	1 = Much or Very Much Improved	6 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	2 (100)
		3 = Much or Very Much Worsened	0
	Overall (n=19)	1 = Much or Very Much Improved	13 (68.4)
		2 = Minimally Improved, No Change, or Minimally Worse	15 (78.9)
		3 = Much or Very Much Worsened	1 (5.3)

[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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.1 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=12)	1 = Much or Very Much Improved	7 (58.3)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (41.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=17)	1 = Much or Very Much Improved	10 (58.8)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (41.2)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=18)	1 = Much or Very Much Improved	9 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=18)	1 = Much or Very Much Improved	13 (72.2)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (27.8)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.1 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male(Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n=14)	1 = Much or Very Much Improved	10 (71.4)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (28.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n=12)	1 = Much or Very Much Improved	9 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (25.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Overall (n=19)	1 = Much or Very Much Improved	17 (89.5)
		2 = Minimally Improved, No Change, or Minimally Worse	15 (78.9)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.2 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 = Much or Very Much Improved	3 (25.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (75.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=12)	1 = Much or Very Much Improved	3 (25.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (75.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=12)	1 = Much or Very Much Improved	4 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=11)	1 = Much or Very Much Improved	5 (45.5)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (54.5)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.2 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	7 (77.8)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (22.2)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	2 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (33.3)
		3 = Much or Very Much Worsened	0
	Overall (n=12)	1 = Much or Very Much Improved	9 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	11 (91.7)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.2 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=12)	1 = Much or Very Much Improved	2 (16.7)
		2 = Minimally Improved, No Change, or Minimally Worse	10 (83.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=12)	1 = Much or Very Much Improved	4 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=12)	1 = Much or Very Much Improved	4 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=11)	1 = Much or Very Much Improved	4 (36.4)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (63.6)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.2 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	4 (44.4)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (55.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 9)	1 = Much or Very Much Improved	3 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	2 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (33.3)
		3 = Much or Very Much Worsened	0
	Overall (n=12)	1 = Much or Very Much Improved	10 (83.3)
		2 = Minimally Improved, No Change, or Minimally Worse	11 (91.7)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.2 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 = Much or Very Much Improved	2 (18.2)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (81.8)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=12)	1 = Much or Very Much Improved	4 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=12)	1 = Much or Very Much Improved	4 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=11)	1 = Much or Very Much Improved	4 (36.4)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (63.6)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.2 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=13) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 9)	1 = Much or Very Much Improved	5 (55.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (44.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	2 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (33.3)
		3 = Much or Very Much Worsened	0
	Overall (n=12)	1 = Much or Very Much Improved	10 (83.3)
		2 = Minimally Improved, No Change, or Minimally Worse	12 (100)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.3 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 8)	1 = Much or Very Much Improved	3 (37.5)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (62.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	4 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=11)	1 = Much or Very Much Improved	6 (54.5)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (36.4)
		3 = Much or Very Much Worsened	1 (9.1)
	Pre-cycle 13 (n=10)	1 = Much or Very Much Improved	5 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (50.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.3 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 6)	1 = Much or Very Much Improved	5 (83.3)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (16.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 5)	1 = Much or Very Much Improved	2 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (60.0)
		3 = Much or Very Much Worsened	0
	Overall (n=11)	1 = Much or Very Much Improved	9 (81.8)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (72.7)
		3 = Much or Very Much Worsened	1 (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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.3 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Much or Very Much Improved	4 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	3 (30.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	1 (10.0)
	Pre-cycle 9 (n=11)	1 = Much or Very Much Improved	4 (36.4)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (63.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=10)	1 = Much or Very Much Improved	4 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.3 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 6)	1 = Much or Very Much Improved	3 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	3 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (50.0)
		3 = Much or Very Much Worsened	0
	Overall (n=11)	1 = Much or Very Much Improved	8 (72.7)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (72.7)
		3 = Much or Very Much Worsened	1 (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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.3 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 = Much or Very Much Improved	3 (60.0)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (40.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	6 (60.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (40.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=11)	1 = Much or Very Much Improved	6 (54.5)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (45.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=10)	1 = Much or Very Much Improved	7 (70.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (30.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.3 Distribution of Global Impression of Change self-report item responses over time – Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 6)	1 = Much or Very Much Improved	6 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	6 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n=11)	1 = Much or Very Much Improved	10 (90.9)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (72.7)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.4 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	6 (60.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (40.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 9)	1 = Much or Very Much Improved	5 (55.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (44.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 9)	1 = Much or Very Much Improved	4 (44.4)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (55.6)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.4 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	5 (55.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (44.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 8)	1 = Much or Very Much Improved	5 (62.5)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (37.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	2 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (33.3)
		3 = Much or Very Much Worsened	0
	Overall (n=10)	1 = Much or Very Much Improved	7 (70.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.4 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Much or Very Much Improved	2 (20.0)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (80.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	5 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 9)	1 = Much or Very Much Improved	1 (11.1)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (88.9)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 9)	1 = Much or Very Much Improved	3 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (66.7)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.4 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	2 (22.2)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (77.8)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 8)	1 = Much or Very Much Improved	2 (25.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (75.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	1 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (66.7)
		3 = Much or Very Much Worsened	0
	Overall (n=10)	1 = Much or Very Much Improved	6 (60.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (90.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.4 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 9)	1 = Much or Very Much Improved	3 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	4 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 9)	1 = Much or Very Much Improved	4 (44.4)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (55.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.4 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	4 (44.4)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (55.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 8)	1 = Much or Very Much Improved	4 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	2 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (33.3)
		3 = Much or Very Much Worsened	0
	Overall (n=10)	1 = Much or Very Much Improved	9 (90.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (90.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.5 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=12) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 9)	1 = Much or Very Much Improved	3 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	4 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=10)	1 = Much or Very Much Improved	5 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=10)	1 = Much or Very Much Improved	6 (60.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (40.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.5 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=12) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 8)	1 = Much or Very Much Improved	6 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (25.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 7)	1 = Much or Very Much Improved	4 (57.1)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (42.9)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Overall (n=10)	1 = Much or Very Much Improved	9 (90.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (90.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.5 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=12) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Much or Very Much Improved	3 (30.0)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (70.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	4 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=10)	1 = Much or Very Much Improved	5 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=10)	1 = Much or Very Much Improved	5 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (50.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.5 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=12) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 8)	1 = Much or Very Much Improved	4 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 7)	1 = Much or Very Much Improved	4 (57.1)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (42.9)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Overall (n=10)	1 = Much or Very Much Improved	9 (90.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (90.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.5 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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 = Much or Very Much Improved	3 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 9)	1 = Much or Very Much Improved	4 (44.4)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (55.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=10)	1 = Much or Very Much Improved	3 (30.0)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (70.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=10)	1 = Much or Very Much Improved	4 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.1.5 Distribution of Global Impression of Change self-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC self-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=12) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 8)	1 = Much or Very Much Improved	6 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (25.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 7)	1 = Much or Very Much Improved	4 (57.1)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (42.9)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Overall (n=10)	1 = Much or Very Much Improved	8 (80.0)
		2 = Minimally Improved, No Change, or Minimally Worse	10 (100)
		3 = Much or Very Much Worsened	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 and Worsened category includes patients with much or very much Worsened.

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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: 31 March 2021 (DC02)

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=11)	1 = Very Much Improved	4/11 (36,4)
		2 = Much Improved	1/11 (9,1)
		3 = Minimally Improved	1/11 (9,1)
		4 = No Change	5/11 (45,5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n=2)	2 = Much Improved	1/ 2 (50,0)
		4 = No Change	1/ 2 (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.

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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: 31 March 2021 (DC02)

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=12)	1 = Very Much Improved	5/12 (41,7)
		2 = Much Improved	1/12 (8,3)
		3 = Minimally Improved	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 49 (n=2)	3 = Minimally Improved	1/ 2 (50,0)
		4 = No Change	1/ 2 (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.

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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: 31 March 2021 (DC02)

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=12)	1 = Very Much Improved	6/12 (50,0)
		2 = Much Improved	3/12 (25,0)
		3 = Minimally Improved	2/12 (16,7)
		4 = No Change	1/12 (8,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n=2)	2 = Much Improved	1/ 2 (50,0)
		4 = No Change	1/ 2 (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.

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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: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=9)	1 = Very Much Improved	3/ 9 (33,3)
		2 = Much Improved	3/ 9 (33,3)
		3 = Minimally Improved	2/ 9 (22,2)
		4 = No Change	1/ 9 (11,1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n=3)	1 = Very Much Improved	2/ 3 (66,7)
		3 = Minimally Improved	1/ 3 (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.

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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: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=9)	1 = Very Much Improved	0
		2 = Much Improved	3/ 9 (33,3)
		3 = Minimally Improved	2/ 9 (22,2)
		4 = No Change	3/ 9 (33,3)
		5 = Minimally Worse	1/ 9 (11,1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n=3)	1 = Very Much Improved	1/ 3 (33,3)
		2 = Much Improved	1/ 3 (33,3)
		4 = No Change	1/ 3 (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.

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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: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=9)	1 = Very Much Improved	3/ 9 (33,3)
		2 = Much Improved	2/ 9 (22,2)
		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 49 (n=3)	1 = Very Much Improved	2/ 3 (66,7)
		4 = No Change	1/ 3 (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.

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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: 31 March 2021 (DC02)

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=5)	1 = Very Much Improved	2/ 5 (40,0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	3/ 5 (60,0)
		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.

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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: 31 March 2021 (DC02)

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=6)	1 = Very Much Improved	3/ 6 (50,0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	2/ 6 (33,3)
		5 = Minimally Worse	1/ 6 (16,7)
		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.

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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: 31 March 2021 (DC02)

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=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

[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.

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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: 31 March 2021 (DC02)

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=8)	1 = Very Much Improved	3/ 8 (37,5)
		2 = Much Improved	2/ 8 (25,0)
		3 = Minimally Improved	1/ 8 (12,5)
		4 = No Change	2/ 8 (25,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n=3)	1 = Very Much Improved	1/ 3 (33,3)
		2 = Much Improved	1/ 3 (33,3)
		4 = No Change	1/ 3 (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.

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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: 31 March 2021 (DC02)

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=8)	1 = Very Much Improved	2/ 8 (25,0)
		2 = Much Improved	0
		3 = Minimally Improved	1/ 8 (12,5)
		4 = No Change	4/ 8 (50,0)
		5 = Minimally Worse	1/ 8 (12,5)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n=3)	1 = Very Much Improved	1/ 3 (33,3)
		3 = Minimally Improved	1/ 3 (33,3)
		4 = No Change	1/ 3 (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.

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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: 31 March 2021 (DC02)

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=8)	1 = Very Much Improved	2/ 8 (25,0)
		2 = Much Improved	2/ 8 (25,0)
		3 = Minimally Improved	2/ 8 (25,0)
		4 = No Change	2/ 8 (25,0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n=3)	1 = Very Much Improved	1/ 3 (33,3)
		2 = Much Improved	1/ 3 (33,3)
		4 = No Change	1/ 3 (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.

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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: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=7)	1 = Very Much Improved	2/ 7 (28,6)
		2 = Much Improved	2/ 7 (28,6)
		3 = Minimally Improved	2/ 7 (28,6)
		4 = No Change	1/ 7 (14,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n=2)	1 = Very Much Improved	1/ 2 (50,0)
		3 = Minimally Improved	1/ 2 (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.

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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: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=7)	1 = Very Much Improved	0
		2 = Much Improved	4/ 7 (57,1)
		3 = Minimally Improved	1/ 7 (14,3)
		4 = No Change	2/ 7 (28,6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n=2)	2 = Much Improved	1/ 2 (50,0)
		4 = No Change	1/ 2 (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.

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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: 31 March 2021 (DC02)

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
	Pre-cycle 37 (n=7)	1 = Very Much Improved	3/ 7 (42,9)
		2 = Much Improved	1/ 7 (14,3)
		3 = Minimally Improved	2/ 7 (28,6)
		4 = No Change	1/ 7 (14,3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n=2)	1 = Very Much Improved	1/ 2 (50,0)
		4 = No Change	1/ 2 (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.

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1.16.4.2 Subgruppenanalyse GIC – Elternberichtet (5-7 Jahre)

Table 2.10.1.2.1.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Male (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 6)	1 = Much or Very Much Improved	1 (16.7)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (83.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 7)	1 = Much or Very Much Improved	2 (28.6)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (71.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 7)	1 = Much or Very Much Improved	2 (28.6)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (71.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 7)	1 = Much or Very Much Improved	3 (42.9)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (57.1)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 7)	1 = Much or Very Much Improved	5 (71.4)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (28.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	4 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 5)	1 = Much or Very Much Improved	3 (60.0)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (40.0)
		3 = Much or Very Much Worsened	0
	Overall (n= 8)	1 = Much or Very Much Improved	6 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (75.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n= 7)	1 = Much or Very Much Improved	2 (28.6)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (71.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 7)	1 = Much or Very Much Improved	2 (28.6)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (71.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 7)	1 = Much or Very Much Improved	2 (28.6)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (71.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 7)	1 = Much or Very Much Improved	2 (28.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (57.1)
		3 = Much or Very Much Worsened	1 (14.3)

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 7)	1 = Much or Very Much Improved	3 (42.9)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (57.1)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	3 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 5)	1 = Much or Very Much Improved	2 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (60.0)
		3 = Much or Very Much Worsened	0
	Overall (n= 8)	1 = Much or Very Much Improved	5 (62.5)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (87.5)
		3 = Much or Very Much Worsened	1 (12.5)

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 6)	1 = Much or Very Much Improved	1 (16.7)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (83.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 7)	1 = Much or Very Much Improved	2 (28.6)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (71.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 7)	1 = Much or Very Much Improved	5 (71.4)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (28.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 7)	1 = Much or Very Much Improved	5 (71.4)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (28.6)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 7)	1 = Much or Very Much Improved	5 (71.4)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (28.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	4 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 5)	1 = Much or Very Much Improved	2 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (60.0)
		3 = Much or Very Much Worsened	0
	Overall (n= 8)	1 = Much or Very Much Improved	7 (87.5)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (87.5)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=7) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 6)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	5 (83.3)
		3 = Much or Very Much Worsened	1 (16.7)
	Pre-cycle 5 (n= 6)	1 = Much or Very Much Improved	2 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 7)	1 = Much or Very Much Improved	3 (42.9)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (57.1)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 6)	1 = Much or Very Much Improved	3 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (50.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=7) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 6)	1 = Much or Very Much Improved	3 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 3)	1 = Much or Very Much Improved	1 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 1)	1 = Much or Very Much Improved	1 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n= 7)	1 = Much or Very Much Improved	5 (71.4)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (100)
		3 = Much or Very Much Worsened	1 (14.3)

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=7) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n= 7)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	6 (85.7)
		3 = Much or Very Much Worsened	1 (14.3)
	Pre-cycle 5 (n= 6)	1 = Much or Very Much Improved	2 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 7)	1 = Much or Very Much Improved	2 (28.6)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (71.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 6)	1 = Much or Very Much Improved	3 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (50.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 6)	1 = Much or Very Much Improved	3 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 3)	1 = Much or Very Much Improved	1 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 1)	1 = Much or Very Much Improved	1 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n= 7)	1 = Much or Very Much Improved	5 (71.4)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (100)
		3 = Much or Very Much Worsened	1 (14.3)

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=7) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 5)	1 = Much or Very Much Improved	1 (20.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (80.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 6)	1 = Much or Very Much Improved	1 (16.7)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (83.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 7)	1 = Much or Very Much Improved	4 (57.1)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (42.9)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 6)	1 = Much or Very Much Improved	4 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (33.3)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 6)	1 = Much or Very Much Improved	4 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 3)	1 = Much or Very Much Improved	2 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (33.3)
		3 = Much or Very Much Worsened	0
	Overall (n= 7)	1 = Much or Very Much Improved	6 (85.7)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (85.7)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=10) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 7)	1 = Much or Very Much Improved	1 (14.3)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (71.4)
		3 = Much or Very Much Worsened	1 (14.3)
	Pre-cycle 5 (n= 8)	1 = Much or Very Much Improved	2 (25.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (75.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 9)	1 = Much or Very Much Improved	3 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 9)	1 = Much or Very Much Improved	3 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (66.7)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=10) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 8)	1 = Much or Very Much Improved	5 (62.5)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (37.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 5)	1 = Much or Very Much Improved	1 (20.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (80.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	2 (100)
		3 = Much or Very Much Worsened	0
	Overall (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (88.9)
		3 = Much or Very Much Worsened	1 (11.1)

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=10) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n= 9)	1 = Much or Very Much Improved	1 (11.1)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (77.8)
		3 = Much or Very Much Worsened	1 (11.1)
	Pre-cycle 5 (n= 8)	1 = Much or Very Much Improved	2 (25.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (75.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 9)	1 = Much or Very Much Improved	2 (22.2)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (77.8)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 9)	1 = Much or Very Much Improved	2 (22.2)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (66.7)
		3 = Much or Very Much Worsened	1 (11.1)

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=10) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 8)	1 = Much or Very Much Improved	4 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 5)	1 = Much or Very Much Improved	1 (20.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (80.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	2 (100)
		3 = Much or Very Much Worsened	0
	Overall (n= 9)	1 = Much or Very Much Improved	5 (55.6)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (88.9)
		3 = Much or Very Much Worsened	2 (22.2)

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=10) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 6)	1 = Much or Very Much Improved	1 (16.7)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (83.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 8)	1 = Much or Very Much Improved	1 (12.5)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (87.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 9)	1 = Much or Very Much Improved	7 (77.8)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (22.2)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=10) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 8)	1 = Much or Very Much Improved	6 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (25.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 5)	1 = Much or Very Much Improved	2 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (60.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	2 (100)
		3 = Much or Very Much Worsened	0
	Overall (n= 9)	1 = Much or Very Much Improved	8 (88.9)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (100)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=4) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 3)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	3 (100)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 3)	1 = Much or Very Much Improved	1 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 3)	1 = Much or Very Much Improved	1 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=4) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 3)	1 = Much or Very Much Improved	1 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n= 4)	1 = Much or Very Much Improved	3 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (75.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=4) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n= 3)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	3 (100)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 3)	1 = Much or Very Much Improved	1 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 3)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	3 (100)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=4) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 3)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	3 (100)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n= 4)	1 = Much or Very Much Improved	3 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (100)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=4) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 3)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	3 (100)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 3)	1 = Much or Very Much Improved	1 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 3)	1 = Much or Very Much Improved	2 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=4) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 3)	1 = Much or Very Much Improved	2 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n= 4)	1 = Much or Very Much Improved	3 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (75.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=2) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 2)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	2 (100)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=2) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (100)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=2) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=2) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Overall (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (100)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=2) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.1.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 5-7 - PN status = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=2) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 1)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	1 (100)
		3 = Much or Very Much Worsened	0
	Overall (n= 2)	1 = Much or Very Much Improved	2 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 5 to 7 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.1.3.1 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 6)	1 = Very Much Improved	0
		2 = Much Improved	1 (16.7)
		3 = Minimally Improved	2 (33.3)
		4 = No Change	3 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n= 7)	1 = Very Much Improved	2 (28.6)
		2 = Much Improved	0
		3 = Minimally Improved	1 (14.3)
		4 = No Change	4 (57.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 7)	1 = Very Much Improved	1 (14.3)
		2 = Much Improved	1 (14.3)
		3 = Minimally Improved	2 (28.6)
		4 = No Change	3 (42.9)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.1 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 13 (n= 7)	1 = Very Much Improved	1 (14.3)
		2 = Much Improved	2 (28.6)
		3 = Minimally Improved	0
		4 = No Change	4 (57.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 6)	1 = Very Much Improved	2 (33.3)
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	1 (16.7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 5)	1 = Very Much Improved	1 (20.0)
		2 = Much Improved	2 (40.0)
		3 = Minimally Improved	0
		4 = No Change	2 (40.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.1 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 49 (n= 4)	1 = Very Much Improved	1 (25.0)
		2 = Much Improved	1 (25.0)
		3 = Minimally Improved	0
		4 = No Change	1 (25.0)
		5 = Minimally Worse	1 (25.0)
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n= 7)	1 = Very Much Improved	0
		2 = Much Improved	2 (28.6)
		3 = Minimally Improved	1 (14.3)
		4 = No Change	4 (57.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n= 7)	1 = Very Much Improved	1 (14.3)
		2 = Much Improved	1 (14.3)
		3 = Minimally Improved	1 (14.3)
		4 = No Change	4 (57.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.1 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ^{2} BID (N=7) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 9 (n= 7)	1 = Very Much Improved	2 (28.6)
		2 = Much Improved	0
		3 = Minimally Improved	2 (28.6)
		4 = No Change	3 (42.9)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 7)	1 = Very Much Improved	1 (14.3)
		2 = Much Improved	1 (14.3)
		3 = Minimally Improved	1 (14.3)
		4 = No Change	3 (42.9)
		5 = Minimally Worse	0
		6 = Much Worse	1 (14.3)
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 6)	1 = Very Much Improved	2 (33.3)
		2 = Much Improved	1 (16.7)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	2 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.1 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 37 (n= 5)	1 = Very Much Improved	1 (20.0)
		2 = Much Improved	1 (20.0)
		3 = Minimally Improved	0
		4 = No Change	3 (60.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 4)	1 = Very Much Improved	0
		2 = Much Improved	1 (25.0)
		3 = Minimally Improved	0
		4 = No Change	2 (50.0)
		5 = Minimally Worse	1 (25.0)
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 6)	1 = Very Much Improved	0
		2 = Much Improved	1 (16.7)
		3 = Minimally Improved	4 (66.7)
		4 = No Change	1 (16.7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.1 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 5 (n= 7)	1 = Very Much Improved	0
		2 = Much Improved	2 (28.6)
		3 = Minimally Improved	4 (57.1)
		4 = No Change	1 (14.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 7)	1 = Very Much Improved	2 (28.6)
		2 = Much Improved	3 (42.9)
		3 = Minimally Improved	2 (28.6)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 7)	1 = Very Much Improved	4 (57.1)
		2 = Much Improved	1 (14.3)
		3 = Minimally Improved	1 (14.3)
		4 = No Change	1 (14.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.1 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 6)	1 = Very Much Improved	2 (33.3)
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	2 (33.3)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 5)	1 = Very Much Improved	2 (40.0)
		2 = Much Improved	1 (20.0)
		3 = Minimally Improved	2 (40.0)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 4)	1 = Very Much Improved	1 (25.0)
		2 = Much Improved	0
		3 = Minimally Improved	1 (25.0)
		4 = No Change	1 (25.0)
		5 = Minimally Worse	1 (25.0)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.2 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 6)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	4 (66.7)
		4 = No Change	0
		5 = Minimally Worse	1 (16.7)
		6 = Much Worse	1 (16.7)
		7 = Very Much Worse	0
	Pre-cycle 5 (n= 6)	1 = Very Much Improved	1 (16.7)
		2 = Much Improved	1 (16.7)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	2 (33.3)
		5 = Minimally Worse	1 (16.7)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 7)	1 = Very Much Improved	2 (28.6)
		2 = Much Improved	1 (14.3)
		3 = Minimally Improved	2 (28.6)
		4 = No Change	2 (28.6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.2 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ^{2} BID (N=7) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 13 (n= 6)	1 = Very Much Improved	2 (33.3)
		2 = Much Improved	1 (16.7)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	2 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 6)	1 = Very Much Improved	1 (16.7)
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	2 (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 (33.3)
		2 = Much Improved	0
		3 = Minimally Improved	1 (33.3)
		4 = No Change	1 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.2 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 49 (n= 1)	1 = Very Much Improved	1 (100)
		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
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n= 7)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	3 (42.9)
		4 = No Change	3 (42.9)
		5 = Minimally Worse	0
		6 = Much Worse	1 (14.3)
		7 = Very Much Worse	0
	Pre-cycle 5 (n= 6)	1 = Very Much Improved	1 (16.7)
		2 = Much Improved	1 (16.7)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	1 (16.7)
		5 = Minimally Worse	2 (33.3)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.2 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 9 (n= 7)	1 = Very Much Improved	2 (28.6)
		2 = Much Improved	0
		3 = Minimally Improved	3 (42.9)
		4 = No Change	1 (14.3)
		5 = Minimally Worse	1 (14.3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 6)	1 = Very Much Improved	2 (33.3)
		2 = Much Improved	1 (16.7)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	2 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 6)	1 = Very Much Improved	1 (16.7)
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	0
		4 = No Change	2 (33.3)
		5 = Minimally Worse	1 (16.7)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

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Table 2.10.1.1.3.2 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 37 (n= 3)	1 = Very Much Improved	1 (33.3)
		2 = Much Improved	0
		3 = Minimally Improved	1 (33.3)
		4 = No Change	1 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 1)	1 = Very Much Improved	1 (100)
		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
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 5)	1 = Very Much Improved	0
		2 = Much Improved	1 (20.0)
		3 = Minimally Improved	0
		4 = No Change	2 (40.0)
		5 = Minimally Worse	2 (40.0)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a2.sas Executed: 2023-03-31T13:32

Table 2.10.1.1.3.2 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 5 (n= 6)	1 = Very Much Improved	0
		2 = Much Improved	1 (16.7)
		3 = Minimally Improved	4 (66.7)
		4 = No Change	0
		5 = Minimally Worse	1 (16.7)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 7)	1 = Very Much Improved	1 (14.3)
		2 = Much Improved	3 (42.9)
		3 = Minimally Improved	3 (42.9)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 6)	1 = Very Much Improved	2 (33.3)
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	0
		4 = No Change	1 (16.7)
		5 = Minimally Worse	1 (16.7)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a2.sas Executed: 2023-03-31T13:32

Table 2.10.1.1.3.2 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=7) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 6)	1 = Very Much Improved	2 (33.3)
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	0
		5 = Minimally Worse	1 (16.7)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 3)	1 = Very Much Improved	2 (66.7)
		2 = Much Improved	0
		3 = Minimally Improved	1 (33.3)
		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 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a2.sas Executed: 2023-03-31T13:32

Table 2.10.1.1.3.3 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 7)	1 = Very Much Improved	0
		2 = Much Improved	1 (14.3)
		3 = Minimally Improved	2 (28.6)
		4 = No Change	2 (28.6)
		5 = Minimally Worse	1 (14.3)
		6 = Much Worse	1 (14.3)
		7 = Very Much Worse	0
	Pre-cycle 5 (n= 8)	1 = Very Much Improved	2 (25.0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	5 (62.5)
		5 = Minimally Worse	1 (12.5)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 9)	1 = Very Much Improved	2 (22.2)
		2 = Much Improved	1 (11.1)
		3 = Minimally Improved	2 (22.2)
		4 = No Change	4 (44.4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a3.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.3 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 -
PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 13 (n= 9)	1 = Very Much Improved	2 (22.2)
		2 = Much Improved	1 (11.1)
		3 = Minimally Improved	1 (11.1)
		4 = No Change	5 (55.6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 8)	1 = Very Much Improved	1 (12.5)
		2 = Much Improved	4 (50.0)
		3 = Minimally Improved	1 (12.5)
		4 = No Change	2 (25.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 5)	1 = Very Much Improved	0
		2 = Much Improved	1 (20.0)
		3 = Minimally Improved	1 (20.0)
		4 = No Change	3 (60.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a3.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.3 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 49 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1 (50.0)
		5 = Minimally Worse	1 (50.0)
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n= 9)	1 = Very Much Improved	0
		2 = Much Improved	1 (11.1)
		3 = Minimally Improved	2 (22.2)
		4 = No Change	5 (55.6)
		5 = Minimally Worse	0
		6 = Much Worse	1 (11.1)
		7 = Very Much Worse	0
	Pre-cycle 5 (n= 8)	1 = Very Much Improved	1 (12.5)
		2 = Much Improved	1 (12.5)
		3 = Minimally Improved	0
		4 = No Change	4 (50.0)
		5 = Minimally Worse	2 (25.0)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a3.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.3 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 -
PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 9 (n= 9)	1 = Very Much Improved	2 (22.2)
		2 = Much Improved	0
		3 = Minimally Improved	3 (33.3)
		4 = No Change	3 (33.3)
		5 = Minimally Worse	1 (11.1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 9)	1 = Very Much Improved	2 (22.2)
		2 = Much Improved	0
		3 = Minimally Improved	2 (22.2)
		4 = No Change	4 (44.4)
		5 = Minimally Worse	0
		6 = Much Worse	1 (11.1)
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 8)	1 = Very Much Improved	1 (12.5)
		2 = Much Improved	3 (37.5)
		3 = Minimally Improved	0
		4 = No Change	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 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a3.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.3 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 37 (n= 5)	1 = Very Much Improved	0
		2 = Much Improved	1 (20.0)
		3 = Minimally Improved	1 (20.0)
		4 = No Change	3 (60.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1 (50.0)
		5 = Minimally Worse	1 (50.0)
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 6)	1 = Very Much Improved	0
		2 = Much Improved	1 (16.7)
		3 = Minimally Improved	2 (33.3)
		4 = No Change	2 (33.3)
		5 = Minimally Worse	1 (16.7)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a3.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.3 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=9) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 5 (n= 8)	1 = Very Much Improved	0
		2 = Much Improved	1 (12.5)
		3 = Minimally Improved	6 (75.0)
		4 = No Change	1 (12.5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 9)	1 = Very Much Improved	1 (11.1)
		2 = Much Improved	5 (55.6)
		3 = Minimally Improved	3 (33.3)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 9)	1 = Very Much Improved	4 (44.4)
		2 = Much Improved	3 (33.3)
		3 = Minimally Improved	0
		4 = No Change	1 (11.1)
		5 = Minimally Worse	1 (11.1)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a3.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.3 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 -
PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=9) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 8)	1 = Very Much Improved	2 (25.0)
		2 = Much Improved	4 (50.0)
		3 = Minimally Improved	2 (25.0)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 5)	1 = Very Much Improved	2 (40.0)
		2 = Much Improved	0
		3 = Minimally Improved	3 (60.0)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	1 (50.0)
		4 = No Change	0
		5 = Minimally Worse	1 (50.0)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a3.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.4 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 -
PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=3) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 3)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	2 (66.7)
		4 = No Change	1 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n= 3)	1 = Very Much Improved	0
		2 = Much Improved	1 (33.3)
		3 = Minimally Improved	1 (33.3)
		4 = No Change	1 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 3)	1 = Very Much Improved	0
		2 = Much Improved	1 (33.3)
		3 = Minimally Improved	1 (33.3)
		4 = No Change	1 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a4.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.4 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=3) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 13 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	0
		4 = No Change	1 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	1 (50.0)
		4 = No Change	1 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 1)	1 = Very Much Improved	1 (100)
		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 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a4.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.4 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 -
PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=3) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 49 (n= 1)	1 = Very Much Improved	0
		2 = Much Improved	1 (100)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n= 3)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	1 (33.3)
		4 = No Change	2 (66.7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n= 3)	1 = Very Much Improved	0
		2 = Much Improved	1 (33.3)
		3 = Minimally Improved	1 (33.3)
		4 = No Change	1 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a4.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.4 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 -
PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=3) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 9 (n= 3)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	2 (66.7)
		4 = No Change	1 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	0
		4 = No Change	1 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	1 (50.0)
		4 = No Change	0
		5 = Minimally Worse	1 (50.0)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a4.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.4 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=3) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 37 (n= 1)	1 = Very Much Improved	1 (100)
		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
	Pre-cycle 49 (n= 1)	1 = Very Much Improved	0
		2 = Much Improved	1 (100)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 3)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	1 (33.3)
		4 = No Change	1 (33.3)
		5 = Minimally Worse	1 (33.3)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a4.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.4 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 -
PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=3) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 5 (n= 3)	1 = Very Much Improved	0
		2 = Much Improved	1 (33.3)
		3 = Minimally Improved	1 (33.3)
		4 = No Change	0
		5 = Minimally Worse	1 (33.3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 3)	1 = Very Much Improved	1 (33.3)
		2 = Much Improved	1 (33.3)
		3 = Minimally Improved	1 (33.3)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a4.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.4 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 -
PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=3) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	1 (50.0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 1)	1 = Very Much Improved	1 (100)
		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
	Pre-cycle 49 (n= 1)	1 = Very Much Improved	1 (100)
		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 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a4.sas Executed: 2023-03-31T13:33

Table 2.10.1.1.3.5 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=2) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	2 (100)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	0
		3 = Minimally Improved	1 (50.0)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	0
		3 = Minimally Improved	1 (50.0)
		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 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a5.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.3.5 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=2) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 13 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 2)	1 = Very Much Improved	2 (100)
		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
	Pre-cycle 37 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	1 (50.0)
		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 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a5.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.3.5 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=2) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 49 (n= 2)	1 = Very Much Improved	2 (100)
		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
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	1 (50.0)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	0
		3 = Minimally Improved	1 (50.0)
		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 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a5.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.3.5 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=2) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 9 (n= 2)	1 = Very Much Improved	2 (100)
		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
	Pre-cycle 13 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 2)	1 = Very Much Improved	2 (100)
		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 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a5.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.3.5 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=2) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 37 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	1 (50.0)
		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 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a5.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.3.5 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 -
PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=2) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 5 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	1 (50.0)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	0
		3 = Minimally Improved	1 (50.0)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	0
		3 = Minimally Improved	1 (50.0)
		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 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a5.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.3.5 Distribution of Global Impression of Change parent-report responses over time - Ages 5-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=2) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	0
		3 = Minimally Improved	1 (50.0)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 2)	1 = Very Much Improved	1 (50.0)
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 1)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1 (100)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 5 to 7 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8a5.sas Executed: 2023-03-31T13:34

1.16.4.3 Subgruppenanalyse GIC – Elternberichtet (8-18 Jahre)

Table 2.10.1.2.2.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=14)	1 = Much or Very Much Improved	5 (35.7)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (64.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=19)	1 = Much or Very Much Improved	8 (42.1)
		2 = Minimally Improved, No Change, or Minimally Worse	11 (57.9)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=19)	1 = Much or Very Much Improved	10 (52.6)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (47.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=19)	1 = Much or Very Much Improved	10 (52.6)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (47.4)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req7c1.sas Executed: 2023-04-13T07:22

Table 2.10.1.2.2.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n=14)	1 = Much or Very Much Improved	7 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n=12)	1 = Much or Very Much Improved	6 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	3 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n=20)	1 = Much or Very Much Improved	15 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	14 (70.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req7c1.sas Executed: 2023-04-13T07:22

Table 2.10.1.2.2.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=18)	1 = Much or Very Much Improved	5 (27.8)
		2 = Minimally Improved, No Change, or Minimally Worse	13 (72.2)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=19)	1 = Much or Very Much Improved	8 (42.1)
		2 = Minimally Improved, No Change, or Minimally Worse	11 (57.9)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=19)	1 = Much or Very Much Improved	10 (52.6)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (47.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=19)	1 = Much or Very Much Improved	8 (42.1)
		2 = Minimally Improved, No Change, or Minimally Worse	11 (57.9)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req7c1.sas Executed: 2023-04-13T07:22

Table 2.10.1.2.2.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=21) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n=14)	1 = Much or Very Much Improved	6 (42.9)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (57.1)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n=12)	1 = Much or Very Much Improved	6 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	3 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n=20)	1 = Much or Very Much Improved	14 (70.0)
		2 = Minimally Improved, No Change, or Minimally Worse	15 (75.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req7c1.sas Executed: 2023-04-13T07:22

Table 2.10.1.2.2.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=12)	1 = Much or Very Much Improved	4 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=18)	1 = Much or Very Much Improved	9 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=19)	1 = Much or Very Much Improved	14 (73.7)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (26.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=19)	1 = Much or Very Much Improved	14 (73.7)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (26.3)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req7c1.sas Executed: 2023-04-13T07:22

Table 2.10.1.2.2.1 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Male (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n=14)	1 = Much or Very Much Improved	10 (71.4)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (28.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n=12)	1 = Much or Very Much Improved	10 (83.3)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (16.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Overall (n=20)	1 = Much or Very Much Improved	17 (85.0)
		2 = Minimally Improved, No Change, or Minimally Worse	15 (75.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req7c1.sas Executed: 2023-04-13T07:22

Table 2.10.1.2.2.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=12)	1 = Much or Very Much Improved	3 (25.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (75.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=12)	1 = Much or Very Much Improved	4 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=12)	1 = Much or Very Much Improved	8 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=11)	1 = Much or Very Much Improved	9 (81.8)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (18.2)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req7c2.sas Executed: 2023-04-13T07:01

Table 2.10.1.2.2.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 8)	1 = Much or Very Much Improved	6 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (25.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	2 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (33.3)
		3 = Much or Very Much Worsened	0
	Overall (n=12)	1 = Much or Very Much Improved	9 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (75.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-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 = Much or Very Much Improved	3 (25.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (75.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=12)	1 = Much or Very Much Improved	5 (41.7)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (58.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=12)	1 = Much or Very Much Improved	7 (58.3)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (41.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=11)	1 = Much or Very Much Improved	9 (81.8)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (18.2)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 8)	1 = Much or Very Much Improved	5 (62.5)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (37.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	1 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (33.3)
		3 = Much or Very Much Worsened	1 (33.3)
	Overall (n=12)	1 = Much or Very Much Improved	9 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (75.0)
		3 = Much or Very Much Worsened	1 (8.3)

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=11)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	11 (100)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=12)	1 = Much or Very Much Improved	3 (25.0)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (75.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=12)	1 = Much or Very Much Improved	5 (41.7)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (58.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=11)	1 = Much or Very Much Improved	8 (72.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (27.3)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.2 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 8)	1 = Much or Very Much Improved	7 (87.5)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (12.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	1 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (66.7)
		3 = Much or Very Much Worsened	0
	Overall (n=12)	1 = Much or Very Much Improved	9 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	12 (100)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 8)	1 = Much or Very Much Improved	2 (25.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (75.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	4 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=11)	1 = Much or Very Much Improved	5 (45.5)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (54.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=10)	1 = Much or Very Much Improved	6 (60.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (40.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 6)	1 = Much or Very Much Improved	3 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	4 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 1)	1 = Much or Very Much Improved	1 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n=11)	1 = Much or Very Much Improved	8 (72.7)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (63.6)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-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 = Much or Very Much Improved	3 (30.0)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (70.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	4 (40.0)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (60.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=11)	1 = Much or Very Much Improved	5 (45.5)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (54.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=10)	1 = Much or Very Much Improved	5 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (50.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 6)	1 = Much or Very Much Improved	2 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	4 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 1)	1 = Much or Very Much Improved	1 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n=11)	1 = Much or Very Much Improved	7 (63.6)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (63.6)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-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 = Much or Very Much Improved	1 (20.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (80.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	6 (60.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (40.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=11)	1 = Much or Very Much Improved	8 (72.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (27.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=10)	1 = Much or Very Much Improved	8 (80.0)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (20.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.3 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 6)	1 = Much or Very Much Improved	5 (83.3)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (16.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	6 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 1)	1 = Much or Very Much Improved	1 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n=11)	1 = Much or Very Much Improved	9 (81.8)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (72.7)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 9)	1 = Much or Very Much Improved	3 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	5 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 8)	1 = Much or Very Much Improved	4 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	3 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n=10)	1 = Much or Very Much Improved	8 (80.0)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (80.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Much or Very Much Improved	3 (30.0)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (70.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	5 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	5 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 9)	1 = Much or Very Much Improved	5 (55.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (44.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 9)	1 = Much or Very Much Improved	5 (55.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (44.4)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 8)	1 = Much or Very Much Improved	4 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 3)	1 = Much or Very Much Improved	3 (100)
		2 = Minimally Improved, No Change, or Minimally Worse	0
		3 = Much or Very Much Worsened	0
	Overall (n=10)	1 = Much or Very Much Improved	8 (80.0)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (80.0)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-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 = Much or Very Much Improved	1 (11.1)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (88.9)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	3 (30.0)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (70.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n= 9)	1 = Much or Very Much Improved	6 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n= 9)	1 = Much or Very Much Improved	7 (77.8)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (22.2)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req7c4.sas Executed: 2023-04-13T07:02

Table 2.10.1.2.2.4 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 9)	1 = Much or Very Much Improved	7 (77.8)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (22.2)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 8)	1 = Much or Very Much Improved	6 (75.0)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (25.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Overall (n=10)	1 = Much or Very Much Improved	9 (90.0)
		2 = Minimally Improved, No Change, or Minimally Worse	10 (100)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-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 = Much or Very Much Improved	3 (33.3)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (66.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=11)	1 = Much or Very Much Improved	3 (27.3)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (72.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=11)	1 = Much or Very Much Improved	7 (63.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (36.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=11)	1 = Much or Very Much Improved	7 (63.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (36.4)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=12) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 25 (n= 8)	1 = Much or Very Much Improved	4 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	4 (66.7)
		2 = Minimally Improved, No Change, or Minimally Worse	2 (33.3)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	1 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	0
	Overall (n=11)	1 = Much or Very Much Improved	8 (72.7)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (72.7)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=12) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Much or Very Much Improved	2 (20.0)
		2 = Minimally Improved, No Change, or Minimally Worse	8 (80.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=11)	1 = Much or Very Much Improved	4 (36.4)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (63.6)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=11)	1 = Much or Very Much Improved	7 (63.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (36.4)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=11)	1 = Much or Very Much Improved	7 (63.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (36.4)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=12) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 25 (n= 8)	1 = Much or Very Much Improved	4 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	3 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	3 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	1 (50.0)
		3 = Much or Very Much Worsened	1 (50.0)
	Overall (n=11)	1 = Much or Very Much Improved	8 (72.7)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (81.8)
		3 = Much or Very Much Worsened	1 (9.1)

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-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 = Much or Very Much Improved	2 (22.2)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (77.8)
		3 = Much or Very Much Worsened	0
	Pre-cycle 5 (n=10)	1 = Much or Very Much Improved	3 (30.0)
		2 = Minimally Improved, No Change, or Minimally Worse	7 (70.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 9 (n=11)	1 = Much or Very Much Improved	5 (45.5)
		2 = Minimally Improved, No Change, or Minimally Worse	6 (54.5)
		3 = Much or Very Much Worsened	0
	Pre-cycle 13 (n=11)	1 = Much or Very Much Improved	7 (63.6)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (36.4)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

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Table 2.10.1.2.2.5 Distribution of Global Impression of Change parent-report item responses over time - Patients with much or very much improved or worsened - Ages 8-18 - PN status = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=12) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 8)	1 = Much or Very Much Improved	4 (50.0)
		2 = Minimally Improved, No Change, or Minimally Worse	4 (50.0)
		3 = Much or Very Much Worsened	0
	Pre-cycle 37 (n= 6)	1 = Much or Very Much Improved	5 (83.3)
		2 = Minimally Improved, No Change, or Minimally Worse	1 (16.7)
		3 = Much or Very Much Worsened	0
	Pre-cycle 49 (n= 2)	1 = Much or Very Much Improved	0
		2 = Minimally Improved, No Change, or Minimally Worse	2 (100)
		3 = Much or Very Much Worsened	0
	Overall (n=11)	1 = Much or Very Much Improved	8 (72.7)
		2 = Minimally Improved, No Change, or Minimally Worse	9 (81.8)
		3 = Much or Very Much Worsened	0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 and Worsened category includes patients with much or very much Worsened.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req7c5.sas Executed: 2023-04-13T07:02

Table 2.10.1.1.4.1 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=14)	1 = Very Much Improved	1 (7.1)
		2 = Much Improved	4 (28.6)
		3 = Minimally Improved	3 (21.4)
		4 = No Change	6 (42.9)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=19)	1 = Very Much Improved	3 (15.8)
		2 = Much Improved	5 (26.3)
		3 = Minimally Improved	1 (5.3)
		4 = No Change	10 (52.6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=19)	1 = Very Much Improved	8 (42.1)
		2 = Much Improved	2 (10.5)
		3 = Minimally Improved	4 (21.1)
		4 = No Change	5 (26.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b1.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.4.1 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 13 (n=19)	1 = Very Much Improved	6 (31.6)
		2 = Much Improved	4 (21.1)
		3 = Minimally Improved	1 (5.3)
		4 = No Change	8 (42.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=14)	1 = Very Much Improved	3 (21.4)
		2 = Much Improved	4 (28.6)
		3 = Minimally Improved	1 (7.1)
		4 = No Change	6 (42.9)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=12)	1 = Very Much Improved	4 (33.3)
		2 = Much Improved	2 (16.7)
		3 = Minimally Improved	2 (16.7)
		4 = No Change	4 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b1.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.4.1 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 49 (n= 3)	1 = Very Much Improved	1 (33.3)
		2 = Much Improved	2 (66.7)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=18)	1 = Very Much Improved	2 (11.1)
		2 = Much Improved	3 (16.7)
		3 = Minimally Improved	4 (22.2)
		4 = No Change	9 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=19)	1 = Very Much Improved	2 (10.5)
		2 = Much Improved	6 (31.6)
		3 = Minimally Improved	2 (10.5)
		4 = No Change	8 (42.1)
		5 = Minimally Worse	1 (5.3)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b1.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.4.1 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 9 (n=19)	1 = Very Much Improved	4 (21.1)
		2 = Much Improved	6 (31.6)
		3 = Minimally Improved	1 (5.3)
		4 = No Change	7 (36.8)
		5 = Minimally Worse	1 (5.3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=19)	1 = Very Much Improved	4 (21.1)
		2 = Much Improved	4 (21.1)
		3 = Minimally Improved	3 (15.8)
		4 = No Change	7 (36.8)
		5 = Minimally Worse	1 (5.3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n=14)	1 = Very Much Improved	2 (14.3)
		2 = Much Improved	4 (28.6)
		3 = Minimally Improved	3 (21.4)
		4 = No Change	5 (35.7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b1.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.4.1 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 37 (n=12)	1 = Very Much Improved	2 (16.7)
		2 = Much Improved	4 (33.3)
		3 = Minimally Improved	1 (8.3)
		4 = No Change	5 (41.7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 3)	1 = Very Much Improved	1 (33.3)
		2 = Much Improved	2 (66.7)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=12)	1 = Very Much Improved	0
		2 = Much Improved	4 (33.3)
		3 = Minimally Improved	4 (33.3)
		4 = No Change	3 (25.0)
		5 = Minimally Worse	1 (8.3)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b1.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.4.1 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 5 (n=18)	1 = Very Much Improved	3 (16.7)
		2 = Much Improved	6 (33.3)
		3 = Minimally Improved	5 (27.8)
		4 = No Change	4 (22.2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=19)	1 = Very Much Improved	5 (26.3)
		2 = Much Improved	9 (47.4)
		3 = Minimally Improved	3 (15.8)
		4 = No Change	2 (10.5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=19)	1 = Very Much Improved	6 (31.6)
		2 = Much Improved	8 (42.1)
		3 = Minimally Improved	4 (21.1)
		4 = No Change	1 (5.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b1.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.4.1 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=21) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n=14)	1 = Very Much Improved	6 (42.9)
		2 = Much Improved	4 (28.6)
		3 = Minimally Improved	3 (21.4)
		4 = No Change	1 (7.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n=12)	1 = Very Much Improved	2 (16.7)
		2 = Much Improved	8 (66.7)
		3 = Minimally Improved	1 (8.3)
		4 = No Change	0
		5 = Minimally Worse	1 (8.3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	1 (50.0)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b1.sas Executed: 2023-03-31T13:34

Table 2.10.1.1.4.2 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n=12)	1 = Very Much Improved	1 (8.3)
		2 = Much Improved	2 (16.7)
		3 = Minimally Improved	2 (16.7)
		4 = No Change	7 (58.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=12)	1 = Very Much Improved	2 (16.7)
		2 = Much Improved	2 (16.7)
		3 = Minimally Improved	4 (33.3)
		4 = No Change	4 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=12)	1 = Very Much Improved	3 (25.0)
		2 = Much Improved	5 (41.7)
		3 = Minimally Improved	1 (8.3)
		4 = No Change	3 (25.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b2.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.2 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 13 (n=11)	1 = Very Much Improved	5 (45.5)
		2 = Much Improved	4 (36.4)
		3 = Minimally Improved	1 (9.1)
		4 = No Change	1 (9.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 9)	1 = Very Much Improved	5 (55.6)
		2 = Much Improved	1 (11.1)
		3 = Minimally Improved	1 (11.1)
		4 = No Change	2 (22.2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 8)	1 = Very Much Improved	3 (37.5)
		2 = Much Improved	3 (37.5)
		3 = Minimally Improved	1 (12.5)
		4 = No Change	1 (12.5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

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Table 2.10.1.1.4.2 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 49 (n= 3)	1 = Very Much Improved	1 (33.3)
		2 = Much Improved	1 (33.3)
		3 = Minimally Improved	0
		4 = No Change	1 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=12)	1 = Very Much Improved	0
		2 = Much Improved	3 (25.0)
		3 = Minimally Improved	4 (33.3)
		4 = No Change	5 (41.7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=12)	1 = Very Much Improved	2 (16.7)
		2 = Much Improved	3 (25.0)
		3 = Minimally Improved	4 (33.3)
		4 = No Change	3 (25.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

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Table 2.10.1.1.4.2 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 9 (n=12)	1 = Very Much Improved	0
		2 = Much Improved	7 (58.3)
		3 = Minimally Improved	1 (8.3)
		4 = No Change	4 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=11)	1 = Very Much Improved	3 (27.3)
		2 = Much Improved	6 (54.5)
		3 = Minimally Improved	1 (9.1)
		4 = No Change	1 (9.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 9)	1 = Very Much Improved	5 (55.6)
		2 = Much Improved	1 (11.1)
		3 = Minimally Improved	1 (11.1)
		4 = No Change	2 (22.2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

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Table 2.10.1.1.4.2 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 37 (n= 8)	1 = Very Much Improved	3 (37.5)
		2 = Much Improved	2 (25.0)
		3 = Minimally Improved	2 (25.0)
		4 = No Change	1 (12.5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 3)	1 = Very Much Improved	1 (33.3)
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	1 (33.3)
		7 = Very Much Worse	0
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n=11)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	4 (36.4)
		4 = No Change	7 (63.6)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b2.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.2 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ^{2} BID (N=13) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 5 (n=12)	1 = Very Much Improved	1 (8.3)
		2 = Much Improved	2 (16.7)
		3 = Minimally Improved	4 (33.3)
		4 = No Change	4 (33.3)
		5 = Minimally Worse	1 (8.3)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=12)	1 = Very Much Improved	1 (8.3)
		2 = Much Improved	4 (33.3)
		3 = Minimally Improved	2 (16.7)
		4 = No Change	5 (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 (27.3)
		2 = Much Improved	5 (45.5)
		3 = Minimally Improved	1 (9.1)
		4 = No Change	2 (18.2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b2.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.2 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=13) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 9)	1 = Very Much Improved	3 (33.3)
		2 = Much Improved	3 (33.3)
		3 = Minimally Improved	1 (11.1)
		4 = No Change	2 (22.2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 8)	1 = Very Much Improved	2 (25.0)
		2 = Much Improved	5 (62.5)
		3 = Minimally Improved	1 (12.5)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 3)	1 = Very Much Improved	0
		2 = Much Improved	1 (33.3)
		3 = Minimally Improved	1 (33.3)
		4 = No Change	1 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b2.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.3 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 8)	1 = Very Much Improved	0
		2 = Much Improved	2 (25.0)
		3 = Minimally Improved	0
		4 = No Change	6 (75.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	1 (10.0)
		2 = Much Improved	3 (30.0)
		3 = Minimally Improved	0
		4 = No Change	6 (60.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=11)	1 = Very Much Improved	3 (27.3)
		2 = Much Improved	2 (18.2)
		3 = Minimally Improved	2 (18.2)
		4 = No Change	4 (36.4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b3.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.3 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 13 (n=10)	1 = Very Much Improved	2 (20.0)
		2 = Much Improved	4 (40.0)
		3 = Minimally Improved	0
		4 = No Change	4 (40.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 6)	1 = Very Much Improved	1 (16.7)
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	0
		4 = No Change	3 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 6)	1 = Very Much Improved	2 (33.3)
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	0
		4 = No Change	2 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b3.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.3 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 49 (n= 1)	1 = Very Much Improved	0
		2 = Much Improved	1 (100)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Very Much Improved	0
		2 = Much Improved	3 (30.0)
		3 = Minimally Improved	1 (10.0)
		4 = No Change	6 (60.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	1 (10.0)
		2 = Much Improved	3 (30.0)
		3 = Minimally Improved	2 (20.0)
		4 = No Change	3 (30.0)
		5 = Minimally Worse	1 (10.0)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b3.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.3 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 9 (n=11)	1 = Very Much Improved	1 (9.1)
		2 = Much Improved	4 (36.4)
		3 = Minimally Improved	1 (9.1)
		4 = No Change	4 (36.4)
		5 = Minimally Worse	1 (9.1)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=10)	1 = Very Much Improved	2 (20.0)
		2 = Much Improved	3 (30.0)
		3 = Minimally Improved	2 (20.0)
		4 = No Change	2 (20.0)
		5 = Minimally Worse	1 (10.0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 6)	1 = Very Much Improved	0
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	3 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b3.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.3 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 37 (n= 6)	1 = Very Much Improved	1 (16.7)
		2 = Much Improved	3 (50.0)
		3 = Minimally Improved	0
		4 = No Change	2 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 1)	1 = Very Much Improved	0
		2 = Much Improved	1 (100)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 5)	1 = Very Much Improved	0
		2 = Much Improved	1 (20.0)
		3 = Minimally Improved	2 (40.0)
		4 = No Change	1 (20.0)
		5 = Minimally Worse	1 (20.0)
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

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Table 2.10.1.1.4.3 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ^{2} BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 5 (n=10)	1 = Very Much Improved	2 (20.0)
		2 = Much Improved	4 (40.0)
		3 = Minimally Improved	1 (10.0)
		4 = No Change	2 (20.0)
		5 = Minimally Worse	1 (10.0)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=11)	1 = Very Much Improved	2 (18.2)
		2 = Much Improved	6 (54.5)
		3 = Minimally Improved	1 (9.1)
		4 = No Change	2 (18.2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=10)	1 = Very Much Improved	2 (20.0)
		2 = Much Improved	6 (60.0)
		3 = Minimally Improved	1 (10.0)
		4 = No Change	1 (10.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b3.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.3 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 6)	1 = Very Much Improved	2 (33.3)
		2 = Much Improved	3 (50.0)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 6)	1 = Very Much Improved	1 (16.7)
		2 = Much Improved	5 (83.3)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 1)	1 = Very Much Improved	0
		2 = Much Improved	1 (100)
		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 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b3.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.4 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 -
PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 9)	1 = Very Much Improved	0
		2 = Much Improved	3 (33.3)
		3 = Minimally Improved	3 (33.3)
		4 = No Change	3 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	1 (10.0)
		2 = Much Improved	4 (40.0)
		3 = Minimally Improved	2 (20.0)
		4 = No Change	3 (30.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 9)	1 = Very Much Improved	4 (44.4)
		2 = Much Improved	2 (22.2)
		3 = Minimally Improved	2 (22.2)
		4 = No Change	1 (11.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b4.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.4 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 13 (n= 9)	1 = Very Much Improved	4 (44.4)
		2 = Much Improved	2 (22.2)
		3 = Minimally Improved	1 (11.1)
		4 = No Change	2 (22.2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 9)	1 = Very Much Improved	4 (44.4)
		2 = Much Improved	2 (22.2)
		3 = Minimally Improved	1 (11.1)
		4 = No Change	2 (22.2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 8)	1 = Very Much Improved	3 (37.5)
		2 = Much Improved	1 (12.5)
		3 = Minimally Improved	2 (25.0)
		4 = No Change	2 (25.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b4.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.4 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 -
PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 49 (n= 3)	1 = Very Much Improved	2 (66.7)
		2 = Much Improved	1 (33.3)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Very Much Improved	1 (10.0)
		2 = Much Improved	2 (20.0)
		3 = Minimally Improved	3 (30.0)
		4 = No Change	4 (40.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=10)	1 = Very Much Improved	1 (10.0)
		2 = Much Improved	4 (40.0)
		3 = Minimally Improved	1 (10.0)
		4 = No Change	4 (40.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b4.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.4 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 9 (n= 9)	1 = Very Much Improved	3 (33.3)
		2 = Much Improved	2 (22.2)
		3 = Minimally Improved	0
		4 = No Change	4 (44.4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 9)	1 = Very Much Improved	3 (33.3)
		2 = Much Improved	2 (22.2)
		3 = Minimally Improved	1 (11.1)
		4 = No Change	3 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 9)	1 = Very Much Improved	5 (55.6)
		2 = Much Improved	1 (11.1)
		3 = Minimally Improved	2 (22.2)
		4 = No Change	1 (11.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b4.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.4 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 37 (n= 8)	1 = Very Much Improved	3 (37.5)
		2 = Much Improved	1 (12.5)
		3 = Minimally Improved	1 (12.5)
		4 = No Change	3 (37.5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 3)	1 = Very Much Improved	2 (66.7)
		2 = Much Improved	1 (33.3)
		3 = Minimally Improved	0
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 9)	1 = Very Much Improved	0
		2 = Much Improved	1 (11.1)
		3 = Minimally Improved	2 (22.2)
		4 = No Change	6 (66.7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b4.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.4 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m² BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 5 (n=10)	1 = Very Much Improved	2 (20.0)
		2 = Much Improved	1 (10.0)
		3 = Minimally Improved	5 (50.0)
		4 = No Change	2 (20.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n= 9)	1 = Very Much Improved	3 (33.3)
		2 = Much Improved	3 (33.3)
		3 = Minimally Improved	2 (22.2)
		4 = No Change	1 (11.1)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n= 9)	1 = Very Much Improved	5 (55.6)
		2 = Much Improved	2 (22.2)
		3 = Minimally Improved	2 (22.2)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b4.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.4 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=11) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 9)	1 = Very Much Improved	5 (55.6)
		2 = Much Improved	2 (22.2)
		3 = Minimally Improved	2 (22.2)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 8)	1 = Very Much Improved	2 (25.0)
		2 = Much Improved	4 (50.0)
		3 = Minimally Improved	1 (12.5)
		4 = No Change	0
		5 = Minimally Worse	1 (12.5)
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	1 (50.0)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b4.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.5 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 -
PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ^{2} BID (N=12) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 3 (n= 9)	1 = Very Much Improved	2 (22.2)
		2 = Much Improved	1 (11.1)
		3 = Minimally Improved	2 (22.2)
		4 = No Change	4 (44.4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=11)	1 = Very Much Improved	3 (27.3)
		2 = Much Improved	0
		3 = Minimally Improved	3 (27.3)
		4 = No Change	5 (45.5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=11)	1 = Very Much Improved	4 (36.4)
		2 = Much Improved	3 (27.3)
		3 = Minimally Improved	1 (9.1)
		4 = No Change	3 (27.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b5.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.5 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 -
PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=12) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 13 (n=11)	1 = Very Much Improved	5 (45.5)
		2 = Much Improved	2 (18.2)
		3 = Minimally Improved	1 (9.1)
		4 = No Change	3 (27.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 8)	1 = Very Much Improved	3 (37.5)
		2 = Much Improved	1 (12.5)
		3 = Minimally Improved	1 (12.5)
		4 = No Change	3 (37.5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 6)	1 = Very Much Improved	2 (33.3)
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	1 (16.7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b5.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.5 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=12) [a][b]
Item 1: Tumour Pain, n (%)	Pre-cycle 49 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	1 (50.0)
		3 = Minimally Improved	0
		4 = No Change	1 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
Item 2: Overall Pain, n (%)	Pre-cycle 3 (n=10)	1 = Very Much Improved	1 (10.0)
		2 = Much Improved	1 (10.0)
		3 = Minimally Improved	4 (40.0)
		4 = No Change	4 (40.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 5 (n=11)	1 = Very Much Improved	2 (18.2)
		2 = Much Improved	2 (18.2)
		3 = Minimally Improved	3 (27.3)
		4 = No Change	4 (36.4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b5.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.5 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=12) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 9 (n=11)	1 = Very Much Improved	0
		2 = Much Improved	7 (63.6)
		3 = Minimally Improved	1 (9.1)
		4 = No Change	3 (27.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=11)	1 = Very Much Improved	2 (18.2)
		2 = Much Improved	5 (45.5)
		3 = Minimally Improved	1 (9.1)
		4 = No Change	3 (27.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 25 (n= 8)	1 = Very Much Improved	2 (25.0)
		2 = Much Improved	2 (25.0)
		3 = Minimally Improved	1 (12.5)
		4 = No Change	3 (37.5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b5.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.5 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=12) [a][b]
Item 2: Overall Pain, n (%)	Pre-cycle 37 (n= 6)	1 = Very Much Improved	1 (16.7)
		2 = Much Improved	2 (33.3)
		3 = Minimally Improved	2 (33.3)
		4 = No Change	1 (16.7)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	0
		4 = No Change	1 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	1 (50.0)
		7 = Very Much Worse	0
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 3 (n= 9)	1 = Very Much Improved	0
		2 = Much Improved	2 (22.2)
		3 = Minimally Improved	4 (44.4)
		4 = No Change	3 (33.3)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b5.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.5 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ^{2} BID (N=12) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 5 (n=10)	1 = Very Much Improved	0
		2 = Much Improved	3 (30.0)
		3 = Minimally Improved	3 (30.0)
		4 = No Change	4 (40.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 9 (n=11)	1 = Very Much Improved	1 (9.1)
		2 = Much Improved	4 (36.4)
		3 = Minimally Improved	2 (18.2)
		4 = No Change	4 (36.4)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 13 (n=11)	1 = Very Much Improved	2 (18.2)
		2 = Much Improved	5 (45.5)
		3 = Minimally Improved	2 (18.2)
		4 = No Change	2 (18.2)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b5.sas Executed: 2023-03-31T13:35

Table 2.10.1.1.4.5 Distribution of Global Impression of Change parent-report responses over time - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

GIC parent-report	Time point	Response category	Selumetinib 25 mg/m ² BID (N=12) [a][b]
Item 3: Tumour-related morbidity, n (%)	Pre-cycle 25 (n= 8)	1 = Very Much Improved	2 (25.0)
		2 = Much Improved	2 (25.0)
		3 = Minimally Improved	1 (12.5)
		4 = No Change	3 (37.5)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 37 (n= 6)	1 = Very Much Improved	1 (16.7)
		2 = Much Improved	4 (66.7)
		3 = Minimally Improved	1 (16.7)
		4 = No Change	0
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0
	Pre-cycle 49 (n= 2)	1 = Very Much Improved	0
		2 = Much Improved	0
		3 = Minimally Improved	1 (50.0)
		4 = No Change	1 (50.0)
		5 = Minimally Worse	0
		6 = Much Worse	0
		7 = Very Much Worse	0

[a] Parents or legal guardians of children 8 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.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req8b5.sas Executed: 2023-03-31T13:35

2 Endpunktkategorie Gesundheitsbezogene Lebensqualität

2.1 Endpunkt Pediatric Quality of Life Inventory (PedsQL)

2.1.1 Rücklaufquoten für den PedsQL – Elternberichtet (8–18 Jahre)

Tabelle 11: Rücklaufquoten für „PedsQL – elternberichtet (8–18 Jahre)“ aus der Studie **SPRINT** – weitere Untersuchungen

Studie	**Selumetinib 25 mg/m² BID**		
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Alle Patienten im Alter von 8–18 Jahren (FAS) N = 34**		
	Erwartete Antworten, N*	**Alle Fragen beantwortet, n/N* (%)[b]**	**≥ eine Frage beantwortet, n (%)**
PedsQL – elternberichtet (8–18 Jahre)			
Baseline	34	28 (82,4)	34 (100,0)
Zyklus 3	32	25 (78,1)	32 (100,0)
Zyklus 5	32	22 (68,8)	32 (100,0)
Zyklus 9	30	24 (80,0)	30 (100,0)
Zyklus 13	30	26 (86,7)	30 (100,0)
Zyklus 25	23	19 (82,6)	23 (100,0)
Zyklus 37	20	14 (70,0)	19 (95,0)
Zyklus 49	19	15 (78,9)	18 (94,7)

BID: Zweimal täglich; FAS: Full Analysis Set; n: Patienten mit Antwort; N*: Patienten mit erwarteter Antwort; PedsQL: Pediatric Quality of Life Inventory

a: Patienten, die in der vergangenen Woche nicht in der Schule waren (z. B. in den Sommerferien), wurden angewiesen, die Items des Unterskala Schulische Funktionsskala nicht auszufüllen.

Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 5. Stand: 19.04.2023. 2023.

2.1.2 PedsQL Veränderung gegenüber Baseline – Elternberichtet (8–18 Jahre)

Tabelle 12: Ergebnisse für den Endpunkt „PedsQL“ – Elternberichtet (8–18 Jahre) – Veränderung gegenüber Baseline

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Elternberichtet Patienten im Alter von 8–18 Jahren (FAS) N = 34**	
	Absoluter Wert (transformierte Skala) N* Mittelwert ± s Median Min–Max	**Veränderung gegenüber Baseline (transformierte Skala)** N* Mittelwert ± s Median Min–Max
Gesamtscore		
Baseline	34 60,68 ± 19,431 60,33 27,2–98,9	–
Zyklus 3	31 68,86 ± 13,631 69,57 42,4–97,2	31 9,22 ± 13,356 9,18 -17,4–43,7
Zyklus 5	32 68,87 ± 15,412 70,65 30,6–94,6	32 9,32 ± 12,795 9,78 -15,6–45,7
Zyklus 9	32 69,41 ± 17,351 70,65 39,1–98,9	32 9,86 ± 14,183 10,87 -20,7–37,5
Zyklus 13	30 71,79 ± 16,495 75,00 39,1–98,9	30 12,30 ± 15,421 8,82 -10,9–43,2
Zyklus 25	23 77,08 ± 15,895 78,26 38,0–100,0	23 15,50 ± 17,444 17,39 -22,8–53,3
Zyklus 37	20 76,44 ± 14,970 78,56 39,1–98,9	20 15,26 ± 15,676 15,02 -5,4–59,7
Zyklus 49	18 77,82 ± 19,677 83,15 31,5–98,9	18 16,77 ± 19,308 11,75 -6,8–62,8
Physische Funktionsskala		
Baseline	34 62,13 ± 24,855 62,50 9,4–100,0	–
Zyklus 3	31 68,85 ± 20,830 71,88 18,8–100,0	31 8,67 ± 15,619 6,25 -31,3–43,8
Zyklus 5	32 65,63 ± 20,407 67,19 21,9–93,8	32 5,47 ± 17,463 4,69 -25,0–75,0
Zyklus 9	32 69,87 ± 24,045 75,00 12,5–100,0	32 9,71 ± 22,162 12,50 -71,9–43,8
Zyklus 13	30 71,98 ± 21,782 76,56 18,8–100,0	30 11,67 ± 15,699 9,38 -12,5–46,9
Zyklus 25	23 82,74 ± 16,070 87,50 50,0–100,0	23 19,16 ± 17,885 18,75 -21,9–71,9

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT **Phase II, Stratum 1** **Datenschnitt: 31. März 2021**	**Elternberichtet** **Patienten im Alter von 8–18 Jahren (FAS)** **N = 34**	
	Absoluter Wert (transformierte Skala) N* Mittelwert ± s Median Min–Max	**Veränderung gegenüber Baseline (transformierte Skala)** N* Mittelwert ± s Median Min–Max
Zyklus 37	20 78,91 ± 15,963 79,69 50,0–100,0	20 16,41 ± 15,898 15,63 -18,8–56,3
Zyklus 49	18 80,90 ± 23,210 90,63 28,1–100,0	18 18,06 ± 25,059 10,94 -21,9–68,8
Emotionale Funktionsskala		
Baseline	34 66,18 ± 20,782 67,50 25,0–100,0	–
Zyklus 3	32 77,19 ± 15,551 77,50 50,0–100,0	32 11,72 ± 18,431 10,00 -20,0–50,0
Zyklus 5	32 77,50 ± 17,689 75,00 35,0–100,0	32 12,03 ± 18,266 15,00 -35,0–40,0
Zyklus 9	32 76,72 ± 19,411 77,50 25,0–100,0	32 11,25 ± 21,813 12,50 -40,0–50,0
Zyklus 13	30 82,83 ± 16,593 85,00 40,0–100,0	30 17,67 ± 22,733 15,00 -25,0–70,0
Zyklus 25	23 83,48 ± 18,856 90,00 45,0–100,0	23 17,39 ± 25,534 15,00 -25,0–55,0
Zyklus 37	20 81,75 ± 16,406 85,00 45,0–100,0	20 16,75 ± 23,015 12,50 -15,0–60,0
Zyklus 49	18 82,50 ± 19,648 87,50 40,0–100,0	18 18,89 ± 21,663 15,00 -15,0–65,0
Soziale Funktionsskala		
Baseline	34 55,37 ± 24,773 50,00 15,0–100,0	–
Zyklus 3	31 65,65 ± 20,361 65,00 15,0–100,0	31 10,24 ± 15,973 15,00 -30,0–35,0
Zyklus 5	32 68,91 ± 21,914 75,00 15,0–100,0	32 14,45 ± 22,448 15,00 -25,0–80,0
Zyklus 9	32 65,63 ± 24,388 70,00 20,0–100,0	32 11,17 ± 18,740 10,00 -20,0–55,0
Zyklus 13	30 65,83 ± 25,226 60,00 20,0–100,0	30 11,42 ± 22,550 5,00 -30,0–65,0

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT **Phase II, Stratum 1** **Datenschnitt: 31. März 2021**	**Elternberichtet** **Patienten im Alter von 8–18 Jahren (FAS)** **N = 34**	
	Absoluter Wert (transformierte Skala) N* Mittelwert ± s Median Min–Max	**Veränderung gegenüber Baseline (transformierte Skala)** N* Mittelwert ± s Median Min–Max
Zyklus 25	23 68,91 ± 24,493 70,00 25,0–100,0	23 11,63 ± 23,301 10,00 -45,0–60,0
Zyklus 37	20 69,63 ± 23,707 72,50 10,0–100,0	20 11,50 ± 23,472 5,00 -25,0–70,0
Zyklus 49	18 74,44 ± 29,048 85,00 10,0–100,0	18 15,83 ± 28,812 12,50 -30,0–70,0
Schulische Funktionsskala[b]		
Baseline	29 59,14 ± 22,403 65,00 15,0–95,0	–
Zyklus 3	25 62,40 ± 17,507 60,00 25,0–95,0	20 5,75 ± 23,802 5,00 -40,0–60,0
Zyklus 5	22 65,23 ± 16,653 65,00 40,0–100,0	17 5,29 ± 17,895 10,00 -30,0–35,0
Zyklus 9	27 63,52 ± 21,295 60,00 15,0–100,0	23 6,30 ± 17,137 10,00 -45,0–30,0
Zyklus 13	26 65,58 ± 21,509 72,50 20,0–100,0	24 6,25 ± 21,682 2,50 -45,0–45,0
Zyklus 25	19 69,21 ± 22,315 70,00 20,0–100,0	16 8,75 ± 24,866 5,00 -40,0–60,0
Zyklus 37	16 70,94 ± 23,110 70,00 20,0–100,0	13 7,31 ± 17,632 10,00 -30,0–25,0
Zyklus 49	15 70,33 ± 22,715 75,00 20,0–100,0	11 6,82 ± 11,241 10,00 -15,0–20,0

BID: Zweimal täglich; FAS: Full Analysis Set; PN: Plexiformes Neurofibrom; PedsQL: Pediatric Quality of Life Inventory; s: Standardabweichung
N*: Anzahl der in die Analyse mit eingeschlossenen Patienten. Patienten mit vorhandenen Werten bei der jeweiligen Visite gingen in die Analyse mit ein
a: Patienten, die in der vergangenen Woche nicht in der Schule waren (z. B. in den Sommerferien), wurden angewiesen, die Items des Unterskala Schulische Funktionsskala nicht auszufüllen.
Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 5. Stand: 19.04.2023. 2023.

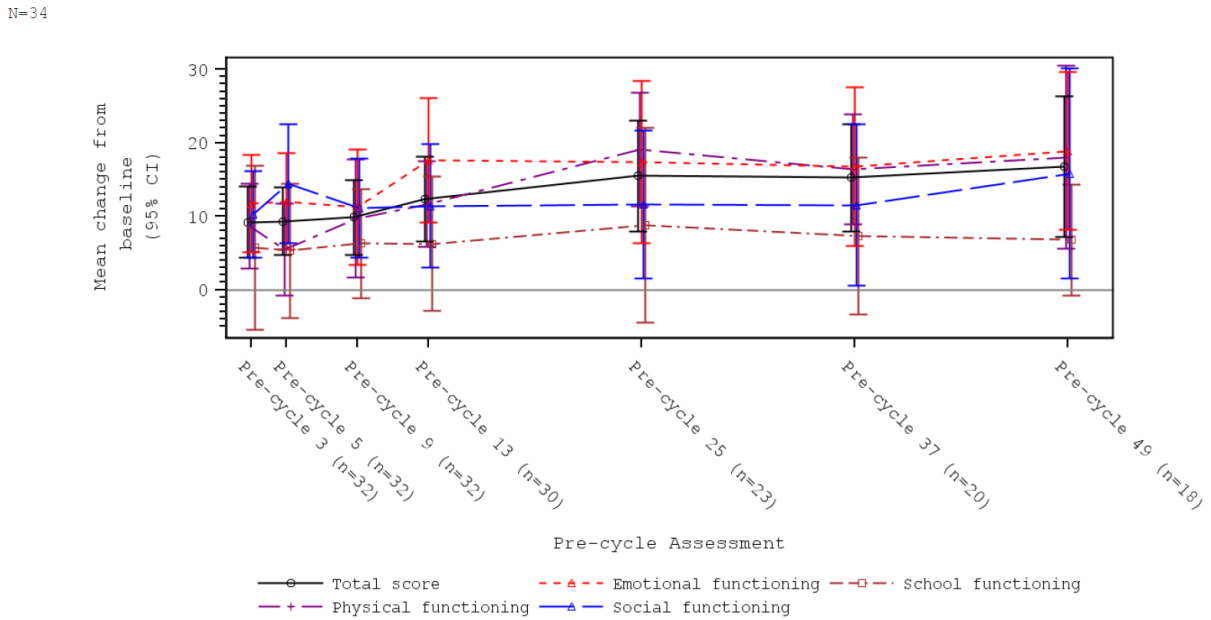

Abbildung 10: PedsQL – elternberichtet (8–18 Jahre) – Mittlere Veränderung gegenüber Baseline im Studienverlauf

Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 5. Stand: 19.04.2023. 2023.

2.1.3 PedsQL MMRM Analyse – Elternberichtet (8-18 Jahre)

Tabelle 13: Ergebnisse für den Endpunkt „PedsQL“ – MMRM (elternberichtet: 8–18 Jahre) aus der Studie **SPRINT** – weitere Untersuchungen

Studie	**Selumetinib 25 mg/m² BID**				
SPRINT Phase-II, Stratum 1 **Datenschnitt: 29. Juni 2018**	**Alle Patienten im Alter von 8–18 Jahren (FAS)** **N = 34**				
	N*	**adjustierter Mittelwert der Veränderung gegenüber Baseline**	**SE**	**[95 %-KI]**	**p-Wert**
PedsQL elternberichtet (8–18 Jahre) - MMRM					
Zyklus 3	31	0,36	0,070	[0,22; 0,50]	< 0,001
Zyklus 5	32	0,36	0,074	[0,21; 0,52]	< 0,001
Zyklus 9	32	0,39	0,089	[0,21; 0,57]	< 0,001
Zyklus 13	30	0,48	0,093	[0,29; 0,67]	< 0,001
Zyklus 25	23	0,62	0,114	[0,38; 0,85]	< 0,001
Zyklus 37	20	0,73	0,112	[0,49; 0,97]	< 0,001
Zyklus 49	18	0,52	0,159	[0,19; 0,85]	0,004

BID: Zweimal täglich; FAS: Full Analysis Set; KI: Konfidenzintervall; MMRM: Mixed Model Repeated Measures; PedsQL: Pediatric Quality of Life Inventory; PN: Plexiformes Neurofibrom; SE: Standardfehler

N*: in die Analyse eingeschlossene Patienten. Die Analyse wird bis zu dem Zyklus, zu dem noch für mindestens 10 Patienten beobachtete Werte vorliegen, durchgeführt

Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 5. Stand: 19.04.2023. 2023.

2.1.4 PedsQL Responderanalyse – Elternberichtet (8-18 Jahre)

Tabelle 14: Ergebnisse aus **SPRINT** für „PedsQL“ – elternberichtet (8–18 Jahre) – Responderanalysen

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Verbesserung ≥ 15 Punkte n/N* (%[a]) [95 %-KI[b]]**	**Verschlechterung ≥ 15 Punkte n/N* (%[a]) [95 %-KI[b]]**
Elternberichtet (8–18 Jahre)		
Zyklus 3		
Gesamtscore	12/31 (38,7) [21,8; 57,8]	1/31 (3,2) [0,1; 16,7]
Physische Funktionsskala	9/31 (29,0) [14,2; 48,0]	1/31 (3,2) [0,1; 16,7]
Emotionale Funktionsskala	14/32 (43,8) [26,4; 62,3]	4/32 (12,5) [3,5; 29,0]
Soziale Funktionsskala	16/31 (51,6) [33,1; 69,8]	2/31 (6,5) [0,8; 21,4]
Schulische Funktionsskala	7/20 (35,0) [15,4; 59,2]	4/20 (20,0) [5,7; 43,7]
Zyklus 5		
Gesamtscore	9/32 (28,1) [13,7; 46,7]	1/32 (3,1) [0,1; 16,2]
Physische Funktionsskala	7/32 (21,9) [9,3; 40,0]	2/32 (6,3) [0,8; 20,8]
Emotionale Funktionsskala	17/32 (53,1) [34,7; 70,9]	4/32 (12,5) [3,5; 29,0]
Soziale Funktionsskala	17/32 (53,1) [34,7; 70,9]	3/32 (9,4) [2,0; 25,0]
Schulische Funktionsskala	6/17 (35,3) [14,2; 61,7]	3/17 (17,6) [3,8; 43,4]
Zyklus 9		
Gesamtscore	11/32 (34,4) [18,6; 53,2]	2/32 (6,3) [0,8; 20,8]
Physische Funktionsskala	14/32 (43,8) [26,4; 62,3]	3/32 (9,4) [2,0; 25,0]
Emotionale Funktionsskala	16/32 (50,0) [31,9; 68,1]	4/32 (12,5) [3,5; 29,0]
Soziale Funktionsskala	14/32 (43,8) [26,4; 62,3]	3/32 (9,4) [2,0; 25,0]
Schulische Funktionsskala	8/23 (34,8) [16,4; 57,3]	3/23 (13,0) [2,8; 33,6]
Zyklus 13		
Gesamtscore	13/30 (43,3) [25,5; 62,6]	0/30 (0,0) [0,0; 11,6]
Physische Funktionsskala	14/30 (46,7) [28,3; 65,7]	0/30 (0,0) [0,0; 11,6]
Emotionale Funktionsskala	17/30 (56,7) [37,4; 74,5]	3/30 (10,0) [2,1; 26,5]
Soziale Funktionsskala	11/30 (36,7) [19,9; 56,1]	3/30 (10,0) [2,1; 26,5]
Schulische Funktionsskala	8/24 (33,3) [15,6; 55,3]	4/24 (16,7) [4,7; 37,4]
Zyklus 25		
Gesamtscore	13/23 (56,5) [34,5; 76,8]	1/23 (4,3) [0,1; 21,9]
Physische Funktionsskala	15/23 (65,2) [42,7; 83,6]	1/23 (4,3) [0,1; 21,9]
Emotionale Funktionsskala	13/23 (56,5) [34,5; 76,8]	3/23 (13,0) [2,8; 33,6]
Soziale Funktionsskala	9/23 (39,1) [19,7; 61,5]	1/23 (4,3) [0,1; 21,9]
Schulische Funktionsskala	4/16 (25,0) [7,3; 52,4]	3/16 (18,8) [4,0; 45,6]
Zyklus 37		
Gesamtscore	10/20 (50,0) [27,2; 72,8]	0/20 (0,0) [0,0; 16,8]
Physische Funktionsskala	13/20 (65,0) [40,8; 84,6]	1/20 (5,0) [0,1; 24,9]
Emotionale Funktionsskala	10/20 (50,0) [27,2; 72,8]	1/20 (5,0) [0,1; 24,9]
Soziale Funktionsskala	9/20 (45,0) [23,1; 68,5]	3/20 (15,0) [3,2; 37,9]
Schulische Funktionsskala	6/13 (46,2) [19,2; 74,9]	2/13 (15,4) [1,9; 45,4]
Zyklus 49		

Studie	**Selumetinib 25 mg/m² BID**	
SPRINT Phase II, Stratum 1 Datenschnitt: 31. März 2021	**Verbesserung ≥ 15 Punkte n/N* (%[a]) [95 %-KI[b]]**	**Verschlechterung ≥ 15 Punkte n/N* (%[a]) [95 %-KI[b]]**
Gesamtscore	8/18 (44,4) [21,5; 69,2]	0/18 (0,0) [0,0; 18,5]
Physische Funktionsskala	8/18 (44,4) [21,5; 69,2]	1/18 (5,6) [0,1; 27,3]
Emotionale Funktionsskala	11/18 (61,1) [35,7; 82,7]	1/18 (5,6) [0,1; 27,3]
Soziale Funktionsskala	9/18 (50,0) [26,0; 74,0]	2/18 (11,1) [1,4; 34,7]
Schulische Funktionsskala	5/11 (45,5) [16,7; 76,6]	1/11 (9,1) [0,2; 41,3]
Zyklus 61		
Gesamtscore	2/3 (66,7) [9,4; 99,2]	0/3 (0,0) [0,0; 70,8]
Physische Funktionsskala	2/3 (66,7) [9,4; 99,2]	0/3 (0,0) [0,0; 70,8]
Emotionale Funktionsskala	3/3 (100,0) [29,2; 100,0]	0/3 (0,0) [0,0; 70,8]
Soziale Funktionsskala	2/3 (66,7) [9,4; 99,2]	0/3 (0,0) [0,0; 70,8]
Schulische Funktionsskala	1/2 (50,0) [n. b.; n. b.]	0/2 (0,0) [n. b.; n. b.]
Gesamt		
Gesamtscore	23/32 (71,9) [53,3; 86,3]	3/32 (9,4) [2,0; 25,0]
Physische Funktionsskala	25/32 (78,1) [60,0; 90,7]	6/32 (18,8) [7,2; 36,4]
Emotionale Funktionsskala	26/32 (81,3) [63,6; 92,8]	9/32 (28,1) [13,7; 46,7]
Soziale Funktionsskala	22/32 (68,8) [50,0; 83,9]	11/32 (34,4) [18,6; 53,2]
Schulische Funktionsskala	19/27 (70,4) [49,8; 86,2]	9/27 (33,3) [16,5; 54,0]

Die Abkürzungen sind im Abkürzungsverzeichnis aufgeführt.

a: Die Prozentsätze basieren auf der Anzahl der Patienten mit einem vorhandenen Wert zu dem jeweiligen Zeitpunkt.

b: Konfidenzintervalle wurden mit der Clopper-Pearson-Methode für binomiale Verteilungen berechnet.

Quelle: Astrazeneca. Studie SPRINT - Post hoc-Analysen zum Datenschnitt vom 31.03.2021 - Batch 8. Stand: 02.06.2023. 2023.

2.1.5 Subgruppenanalysen zum PedsQL

2.1.5.1 Subgruppenanalysen zum PedsQL – Selbstberichtet (8-18 Jahre)

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: 31 March 2021 (DC02)

		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=12)	90,22	9,442	93,06	69,6	100,0	42,9	12	8,77	12,979	6,16	-8,2	38,0	42,9
	Pre-cycle 49 (n=13)	90,78	9,345	93,48	67,4	100,0	38,1	12	11,28	16,112	5,43	-1,1	46,0	42,9
	Pre-cycle 61 (n=3)	88,04	8,627	91,30	78,3	94,6	85,7	3	13,51	14,356	8,70	2,2	29,6	85,7
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=12)	3,61	0,378	3,72	2,8	4,0	42,9	12	0,35	0,519	0,25	-0,3	1,5	42,9
	Pre-cycle 49 (n=13)	3,63	0,374	3,74	2,7	4,0	38,1	12	0,45	0,644	0,22	0,0	1,8	42,9
	Pre-cycle 61 (n=3)	3,52	0,345	3,65	3,1	3,8	85,7	3	0,54	0,574	0,35	0,1	1,2	85,7

[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.

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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: 31 March 2021 (DC02)

		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=12)	91,89	10,680	96,65	62,5	100,0	42,9	12	8,82	21,265	1,56	-12,5	56,3	42,9
	Pre-cycle 49 (n=13)	88,36	14,216	90,63	56,3	100,0	38,1	12	7,96	25,410	-0,67	-15,6	68,8	42,9
	Pre-cycle 61 (n=3)	89,58	4,774	90,63	84,4	93,8	85,7	3	13,54	26,208	0,00	-3,1	43,8	85,7
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=12)	3,68	0,427	3,87	2,5	4,0	42,9	12	0,35	0,851	0,06	-0,5	2,3	42,9
	Pre-cycle 49 (n=13)	3,53	0,569	3,63	2,3	4,0	38,1	12	0,32	1,016	-0,03	-0,6	2,8	42,9
	Pre-cycle 61 (n=3)	3,58	0,191	3,63	3,4	3,8	85,7	3	0,54	1,048	0,00	-0,1	1,8	85,7

[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.

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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: 31 March 2021 (DC02)

		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=12)	93,33	10,075	100,00	70,0	100,0	42,9	12	12,08	20,721	15,00	-30,0	55,0	42,9
	Pre-cycle 49 (n=13)	93,46	11,616	100,00	60,0	100,0	38,1	12	15,00	18,829	12,50	-5,0	55,0	42,9
	Pre-cycle 61 (n=3)	88,33	16,073	95,00	70,0	100,0	85,7	3	16,67	7,638	15,00	10,0	25,0	85,7
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=12)	3,73	0,403	4,00	2,8	4,0	42,9	12	0,48	0,829	0,60	-1,2	2,2	42,9
	Pre-cycle 49 (n=13)	3,74	0,465	4,00	2,4	4,0	38,1	12	0,60	0,753	0,50	-0,2	2,2	42,9
	Pre-cycle 61 (n=3)	3,53	0,643	3,80	2,8	4,0	85,7	3	0,67	0,306	0,60	0,4	1,0	85,7

[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.

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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: 31 March 2021 (DC02)

		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=12)	88,33	16,143	95,00	50,0	100,0	42,9	12	0,42	13,561	2,50	-30,0	15,0	42,9
	Pre-cycle 49 (n=13)	93,85	10,238	100,00	70,0	100,0	38,1	12	7,92	12,332	7,50	-10,0	35,0	42,9
	Pre-cycle 61 (n=3)	90,00	8,660	85,00	85,0	100,0	85,7	3	3,33	15,275	0,00	-10,0	20,0	85,7
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=12)	3,53	0,646	3,80	2,0	4,0	42,9	12	0,02	0,542	0,10	-1,2	0,6	42,9
	Pre-cycle 49 (n=13)	3,75	0,410	4,00	2,8	4,0	38,1	12	0,32	0,493	0,30	-0,4	1,4	42,9
	Pre-cycle 61 (n=3)	3,60	0,346	3,40	3,4	4,0	85,7	3	0,13	0,611	0,00	-0,4	0,8	85,7

[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.

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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: 31 March 2021 (DC02)

		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=8)	83,13	13,076	77,50	70,0	100,0	61,9	7	8,57	11,443	10,00	-10,0	25,0	66,7
	Pre-cycle 49 (n=10)	89,00	9,369	90,00	70,0	100,0	52,4	7	10,00	13,844	10,00	-10,0	35,0	66,7
	Pre-cycle 61 (n=3)	83,33	11,547	90,00	70,0	90,0	85,7	2	NC	NC	NC	5,0	35,0	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=8)	3,33	0,523	3,10	2,8	4,0	61,9	7	0,34	0,458	0,40	-0,4	1,0	66,7
	Pre-cycle 49 (n=10)	3,56	0,375	3,60	2,8	4,0	52,4	7	0,40	0,554	0,40	-0,4	1,4	66,7
	Pre-cycle 61 (n=3)	3,33	0,462	3,60	2,8	3,6	85,7	2	NC	NC	NC	0,2	1,4	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=8)	81,97	14,289	84,24	51,1	96,7	38,5	8	12,05	16,141	9,99	-9,8	35,9	38,5
	Pre-cycle 49 (n=7)	79,35	16,886	84,78	50,0	96,7	46,2	7	3,63	17,190	0,00	-18,5	30,4	46,2
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
	Pre-cycle 37 (n=8)	3,28	0,572	3,37	2,0	3,9	38,5	8	0,48	0,646	0,40	-0,4	1,4	38,5
	Pre-cycle 49 (n=7)	3,17	0,675	3,39	2,0	3,9	46,2	7	0,15	0,688	0,00	-0,7	1,2	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=8)	83,98	17,070	93,75	62,5	100,0	38,5	8	13,67	19,830	12,50	-18,8	46,9	38,5
	Pre-cycle 49 (n=7)	80,80	16,181	78,13	59,4	100,0	46,2	7	6,25	13,975	6,25	-12,5	28,1	46,2
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
	Pre-cycle 37 (n=8)	3,36	0,683	3,75	2,5	4,0	38,5	8	0,55	0,793	0,50	-0,8	1,9	38,5
	Pre-cycle 49 (n=7)	3,23	0,647	3,13	2,4	4,0	46,2	7	0,25	0,559	0,25	-0,5	1,1	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=8)	84,38	19,168	90,00	50,0	100,0	38,5	8	8,13	13,871	5,00	-10,0	35,0	38,5
	Pre-cycle 49 (n=7)	79,29	26,049	90,00	35,0	100,0	46,2	7	-0,71	19,881	0,00	-35,0	30,0	46,2
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
	Pre-cycle 37 (n=8)	3,38	0,767	3,60	2,0	4,0	38,5	8	0,33	0,555	0,20	-0,4	1,4	38,5
	Pre-cycle 49 (n=7)	3,17	1,042	3,60	1,4	4,0	46,2	7	-0,03	0,795	0,00	-1,4	1,2	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=8)	83,75	16,637	90,00	45,0	100,0	38,5	8	10,63	20,777	5,00	-15,0	55,0	38,5
	Pre-cycle 49 (n=7)	83,57	17,252	90,00	55,0	100,0	46,2	7	2,14	18,898	0,00	-20,0	30,0	46,2
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
	Pre-cycle 37 (n=8)	3,35	0,665	3,60	1,8	4,0	38,5	8	0,43	0,831	0,20	-0,6	2,2	38,5
	Pre-cycle 49 (n=7)	3,34	0,690	3,60	2,2	4,0	46,2	7	0,09	0,756	0,00	-0,8	1,2	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	72,14	20,988	80,00	30,0	90,0	46,2	6	9,17	15,626	15,00	-15,0	25,0	53,8
	Pre-cycle 49 (n=7)	72,86	21,381	75,00	30,0	95,0	46,2	6	1,67	22,286	0,00	-25,0	35,0	53,8
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
	Pre-cycle 37 (n=7)	2,89	0,840	3,20	1,2	3,6	46,2	6	0,37	0,625	0,60	-0,6	1,0	53,8
	Pre-cycle 49 (n=7)	2,91	0,855	3,00	1,2	3,8	46,2	6	0,07	0,891	0,00	-1,0	1,4	53,8

[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.

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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: 31 March 2021 (DC02)

		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=6)	89,32	8,119	92,16	73,9	96,7	45,5	6	5,04	11,103	3,12	-8,2	25,3	45,5
	Pre-cycle 49 (n=7)	91,06	10,836	94,57	67,4	100,0	36,4	6	10,73	17,528	5,43	-1,1	46,0	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	78,3	94,6	81,8	2	NC	NC	NC	8,7	29,6	81,8
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=6)	3,57	0,325	3,69	3,0	3,9	45,5	6	0,20	0,444	0,12	-0,3	1,0	45,5
	Pre-cycle 49 (n=7)	3,64	0,433	3,78	2,7	4,0	36,4	6	0,43	0,701	0,22	0,0	1,8	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	3,1	3,8	81,8	2	NC	NC	NC	0,3	1,2	81,8

[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.

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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: 31 March 2021 (DC02)

		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=6)	94,20	6,646	96,65	84,4	100,0	45,5	6	8,78	20,373	3,13	-12,5	46,9	45,5
	Pre-cycle 49 (n=7)	89,29	15,187	90,63	56,3	100,0	36,4	6	9,38	21,287	0,00	-6,3	50,0	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	84,4	93,8	81,8	2	NC	NC	NC	-3,1	43,8	81,8
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=6)	3,77	0,266	3,87	3,4	4,0	45,5	6	0,35	0,815	0,13	-0,5	1,9	45,5
	Pre-cycle 49 (n=7)	3,57	0,607	3,63	2,3	4,0	36,4	6	0,38	0,851	0,00	-0,3	2,0	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	3,4	3,8	81,8	2	NC	NC	NC	-0,1	1,8	81,8

[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.

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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: 31 March 2021 (DC02)

		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=6)	91,67	8,165	92,50	80,0	100,0	45,5	6	9,17	13,934	2,50	0,0	35,0	45,5
	Pre-cycle 49 (n=7)	90,71	15,392	100,00	60,0	100,0	36,4	6	13,33	18,886	7,50	0,0	50,0	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	70,0	95,0	81,8	2	NC	NC	NC	10,0	25,0	81,8
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=6)	3,67	0,327	3,70	3,2	4,0	45,5	6	0,37	0,557	0,10	0,0	1,4	45,5
	Pre-cycle 49 (n=7)	3,63	0,616	4,00	2,4	4,0	36,4	6	0,53	0,755	0,30	0,0	2,0	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	2,8	3,8	81,8	2	NC	NC	NC	0,4	1,0	81,8

[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.

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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: 31 March 2021 (DC02)

		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=6)	82,50	19,937	95,00	50,0	95,0	45,5	6	-9,17	12,007	-5,00	-30,0	5,0	45,5
	Pre-cycle 49 (n=7)	93,57	11,073	100,00	70,0	100,0	36,4	6	5,83	15,626	0,00	-10,0	35,0	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	85,0	100,0	81,8	2	NC	NC	NC	0,0	20,0	81,8
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=6)	3,30	0,797	3,80	2,0	3,8	45,5	6	-0,37	0,480	-0,20	-1,2	0,2	45,5
	Pre-cycle 49 (n=7)	3,74	0,443	4,00	2,8	4,0	36,4	6	0,23	0,625	0,00	-0,4	1,4	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	3,4	4,0	81,8	2	NC	NC	NC	0,0	0,8	81,8

[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.

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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: 31 March 2021 (DC02)

		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=3)	81,67	16,073	75,00	70,0	100,0	72,7	2	NC	NC	NC	-10,0	10,0	81,8
	Pre-cycle 49 (n=6)	90,83	8,612	92,50	75,0	100,0	45,5	3	11,67	22,546	10,00	-10,0	35,0	72,7
	Pre-cycle 61 (n=2)	NC	NC	NC	70,0	90,0	81,8	1	NC	NC	NC	35,0	35,0	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=3)	3,27	0,643	3,00	2,8	4,0	72,7	2	NC	NC	NC	-0,4	0,4	81,8
	Pre-cycle 49 (n=6)	3,63	0,344	3,70	3,0	4,0	45,5	3	0,47	0,902	0,40	-0,4	1,4	72,7
	Pre-cycle 61 (n=2)	NC	NC	NC	2,8	3,6	81,8	1	NC	NC	NC	1,4	1,4	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.

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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: 31 March 2021 (DC02)

		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=7)	95,08	4,055	96,74	88,0	100,0	36,4	7	16,20	14,782	7,61	0,0	38,0	36,4
	Pre-cycle 49 (n=8)	89,89	10,270	93,48	65,2	96,7	27,3	8	10,41	19,113	5,29	-18,5	43,5	27,3
	Pre-cycle 61 (n=1)	NC	NC	NC	91,3	91,3	90,9	1	NC	NC	NC	2,2	2,2	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=7)	3,80	0,162	3,87	3,5	4,0	36,4	7	0,65	0,591	0,30	0,0	1,5	36,4
	Pre-cycle 49 (n=8)	3,60	0,411	3,74	2,6	3,9	27,3	8	0,42	0,765	0,21	-0,7	1,7	27,3
	Pre-cycle 61 (n=1)	NC	NC	NC	3,7	3,7	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.

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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: 31 March 2021 (DC02)

		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=7)	95,98	4,313	96,88	87,5	100,0	36,4	7	15,18	21,074	6,25	0,0	56,3	36,4
	Pre-cycle 49 (n=8)	91,63	6,719	93,75	78,1	100,0	27,3	8	10,77	26,016	-0,67	-9,4	68,8	27,3
	Pre-cycle 61 (n=1)	NC	NC	NC	90,6	90,6	90,9	1	NC	NC	NC	0,0	0,0	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=7)	3,84	0,173	3,88	3,5	4,0	36,4	7	0,61	0,843	0,25	0,0	2,3	36,4
	Pre-cycle 49 (n=8)	3,67	0,269	3,75	3,1	4,0	27,3	8	0,43	1,041	-0,03	-0,4	2,8	27,3
	Pre-cycle 61 (n=1)	NC	NC	NC	3,6	3,6	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.

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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: 31 March 2021 (DC02)

		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=7)	98,57	3,780	100,00	90,0	100,0	36,4	7	22,14	17,762	15,00	0,0	55,0	36,4
	Pre-cycle 49 (n=8)	88,13	22,190	97,50	35,0	100,0	27,3	8	12,50	25,635	15,00	-35,0	55,0	27,3
	Pre-cycle 61 (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=7)	3,94	0,151	4,00	3,6	4,0	36,4	7	0,89	0,710	0,60	0,0	2,2	36,4
	Pre-cycle 49 (n=8)	3,53	0,888	3,90	1,4	4,0	27,3	8	0,50	1,025	0,60	-1,4	2,2	27,3
	Pre-cycle 61 (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.

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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: 31 March 2021 (DC02)

		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=7)	96,43	5,563	100,00	85,0	100,0	36,4	7	10,71	7,868	15,00	0,0	20,0	36,4
	Pre-cycle 49 (n=8)	95,00	8,864	100,00	75,0	100,0	27,3	8	8,13	15,797	12,50	-20,0	30,0	27,3
	Pre-cycle 61 (n=1)	NC	NC	NC	85,0	85,0	90,9	1	NC	NC	NC	-10,0	-10,0	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=7)	3,86	0,223	4,00	3,4	4,0	36,4	7	0,43	0,315	0,60	0,0	0,8	36,4
	Pre-cycle 49 (n=8)	3,80	0,355	4,00	3,0	4,0	27,3	8	0,33	0,632	0,50	-0,8	1,2	27,3
	Pre-cycle 61 (n=1)	NC	NC	NC	3,4	3,4	90,9	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.

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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: 31 March 2021 (DC02)

		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=5)	86,00	11,937	85,00	70,0	100,0	54,5	5	4,00	12,450	5,00	-15,0	15,0	54,5
	Pre-cycle 49 (n=7)	82,14	11,852	90,00	65,0	95,0	36,4	7	5,00	19,149	10,00	-25,0	35,0	36,4
	Pre-cycle 61 (n=1)	NC	NC	NC	90,0	90,0	90,9	1	NC	NC	NC	5,0	5,0	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=5)	3,44	0,477	3,40	2,8	4,0	54,5	5	0,16	0,498	0,20	-0,6	0,6	54,5
	Pre-cycle 49 (n=7)	3,29	0,474	3,60	2,6	3,8	36,4	7	0,20	0,766	0,40	-1,0	1,4	36,4
	Pre-cycle 61 (n=1)	NC	NC	NC	3,6	3,6	90,9	1	NC	NC	NC	0,2	0,2	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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	76,71	13,399	80,43	51,1	91,3	41,7	7	8,29	15,078	7,61	-9,8	35,9	41,7
	Pre-cycle 49 (n=5)	75,81	16,608	76,09	50,0	94,6	58,3	5	2,63	11,864	0,00	-14,1	16,7	58,3
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
	Pre-cycle 37 (n=7)	3,07	0,536	3,22	2,0	3,7	41,7	7	0,33	0,603	0,30	-0,4	1,4	41,7
	Pre-cycle 49 (n=5)	3,03	0,664	3,04	2,0	3,8	58,3	5	0,11	0,475	0,00	-0,6	0,7	58,3

[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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	76,79	16,911	65,63	62,5	96,9	41,7	7	8,04	21,939	6,25	-18,8	46,9	41,7
	Pre-cycle 49 (n=5)	71,25	16,887	65,63	59,4	100,0	58,3	5	-0,63	14,557	-3,13	-15,6	18,8	58,3
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
	Pre-cycle 37 (n=7)	3,07	0,676	2,63	2,5	3,9	41,7	7	0,32	0,878	0,25	-0,8	1,9	41,7
	Pre-cycle 49 (n=5)	2,85	0,675	2,63	2,4	4,0	58,3	5	-0,03	0,582	-0,13	-0,6	0,8	58,3

[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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	79,29	19,670	85,00	50,0	100,0	41,7	7	0,00	16,073	5,00	-30,0	20,0	41,7
	Pre-cycle 49 (n=5)	86,00	20,433	95,00	50,0	100,0	58,3	5	-1,00	8,216	-5,00	-10,0	10,0	58,3
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
	Pre-cycle 37 (n=7)	3,17	0,787	3,40	2,0	4,0	41,7	7	0,00	0,643	0,20	-1,2	0,8	41,7
	Pre-cycle 49 (n=5)	3,44	0,817	3,80	2,0	4,0	58,3	5	-0,04	0,329	-0,20	-0,4	0,4	58,3

[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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	80,00	16,583	90,00	45,0	90,0	41,7	7	10,00	21,794	5,00	-15,0	55,0	41,7
	Pre-cycle 49 (n=5)	78,00	17,536	75,00	55,0	100,0	58,3	5	2,00	14,832	5,00	-20,0	15,0	58,3
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
	Pre-cycle 37 (n=7)	3,20	0,663	3,60	1,8	3,6	41,7	7	0,40	0,872	0,20	-0,6	2,2	41,7
	Pre-cycle 49 (n=5)	3,12	0,701	3,00	2,2	4,0	58,3	5	0,08	0,593	0,20	-0,8	0,6	58,3

[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.

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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: 31 March 2021 (DC02)

		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
	Pre-cycle 37 (n=7)	70,71	20,295	75,00	30,0	90,0	41,7	6	15,83	11,143	17,50	-5,0	25,0	50,0
	Pre-cycle 49 (n=4)	70,00	27,988	77,50	30,0	95,0	66,7	3	3,33	16,073	10,00	-15,0	15,0	75,0
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
	Pre-cycle 37 (n=7)	2,83	0,812	3,00	1,2	3,6	41,7	6	0,63	0,446	0,70	-0,2	1,0	50,0
	Pre-cycle 49 (n=4)	2,80	1,120	3,10	1,2	3,8	66,7	3	0,13	0,643	0,40	-0,6	0,6	75,0

[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.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	5.3	0.1, 26.0
		No improvement or deterioration	15	78.9	54.4, 93.9
	Pre-cycle 5 (N=19)	Categories of change [d]			
		Improvement	4	21.1	6.1, 45.6
		Deterioration	1	5.3	0.1, 26.0
		No improvement or deterioration	14	73.7	48.8, 90.9
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	5	26.3	9.1, 51.2
		Deterioration	2	10.5	1.3, 33.1
		No improvement or deterioration	12	63.2	38.4, 83.7
	Pre-cycle 13 (N=18)	Categories of change [d]			
		Improvement	4	22.2	6.4, 47.6
		Deterioration	2	11.1	1.4, 34.7
		No improvement or deterioration	12	66.7	41.0, 86.7

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	4	28.6	8.4, 58.1
		Deterioration	0	0	0, 23.2
		No improvement or deterioration	10	71.4	41.9, 91.6
	Pre-cycle 37 (N=12)	Categories of change [d]			
		Improvement	3	25.0	5.5, 57.2
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	9	75.0	42.8, 94.5
	Pre-cycle 49 (N=12)	Categories of change [d]			
		Improvement	2	16.7	2.1, 48.4
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	10	83.3	51.6, 97.9
	Pre-cycle 61 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=19)	Categories of change [d]			
		Improvement	8	42.1	20.3, 66.5
		Deterioration	4	21.1	6.1, 45.6
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	2	10.5	1.3, 33.1
		No improvement or deterioration	14	73.7	48.8, 90.9
	Pre-cycle 5 (N=19)	Categories of change [d]			
		Improvement	4	21.1	6.1, 45.6
		Deterioration	2	10.5	1.3, 33.1
		No improvement or deterioration	13	68.4	43.4, 87.4
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	2	10.5	1.3, 33.1
		Deterioration	3	15.8	3.4, 39.6
		No improvement or deterioration	14	73.7	48.8, 90.9
	Pre-cycle 13 (N=18)	Categories of change [d]			
		Improvement	6	33.3	13.3, 59.0
		Deterioration	1	5.6	0.1, 27.3
		No improvement or deterioration	11	61.1	35.7, 82.7

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	4	28.6	8.4, 58.1
		Deterioration	1	7.1	0.2, 33.9
		No improvement or deterioration	9	64.3	35.1, 87.2
	Pre-cycle 37 (N=12)	Categories of change [d]			
		Improvement	2	16.7	2.1, 48.4
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	10	83.3	51.6, 97.9
	Pre-cycle 49 (N=12)	Categories of change [d]			
		Improvement	3	25.0	5.5, 57.2
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	8	66.7	34.9, 90.1
	Pre-cycle 61 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Overall (N=19)	Categories of change [d]			
		Improvement	8	42.1	20.3, 66.5
		Deterioration	5	26.3	9.1, 51.2
		No improvement or deterioration	6	31.6	12.6, 56.6

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	5.3	0.1, 26.0
		No improvement or deterioration	11	57.9	33.5, 79.7
	Pre-cycle 5 (N=19)	Categories of change [d]			
		Improvement	7	36.8	16.3, 61.6
		Deterioration	2	10.5	1.3, 33.1
		No improvement or deterioration	10	52.6	28.9, 75.6
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	7	36.8	16.3, 61.6
		Deterioration	3	15.8	3.4, 39.6
		No improvement or deterioration	9	47.4	24.4, 71.1
	Pre-cycle 13 (N=18)	Categories of change [d]			
		Improvement	8	44.4	21.5, 69.2
		Deterioration	4	22.2	6.4, 47.6
		No improvement or deterioration	6	33.3	13.3, 59.0

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	6	42.9	17.7, 71.1
		Deterioration	1	7.1	0.2, 33.9
		No improvement or deterioration	7	50.0	23.0, 77.0
	Pre-cycle 37 (N=12)	Categories of change [d]			
		Improvement	7	58.3	27.7, 84.8
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	4	33.3	9.9, 65.1
	Pre-cycle 49 (N=12)	Categories of change [d]			
		Improvement	6	50.0	21.1, 78.9
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	6	50.0	21.1, 78.9
	Pre-cycle 61 (N=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Overall (N=19)	Categories of change [d]			
		Improvement	12	63.2	38.4, 83.7
		Deterioration	6	31.6	12.6, 56.6
		No improvement or deterioration	2	10.5	1.3, 33.1

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	4	21.1	6.1, 45.6
		No improvement or deterioration	8	42.1	20.3, 66.5
	Pre-cycle 5 (N=19)	Categories of change [d]			
		Improvement	7	36.8	16.3, 61.6
		Deterioration	2	10.5	1.3, 33.1
		No improvement or deterioration	10	52.6	28.9, 75.6
	Pre-cycle 9 (N=19)	Categories of change [d]			
		Improvement	4	21.1	6.1, 45.6
		Deterioration	2	10.5	1.3, 33.1
		No improvement or deterioration	13	68.4	43.4, 87.4
	Pre-cycle 13 (N=18)	Categories of change [d]			
		Improvement	5	27.8	9.7, 53.5
		Deterioration	3	16.7	3.6, 41.4
		No improvement or deterioration	10	55.6	30.8, 78.5

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	5	35.7	12.8, 64.9
		Deterioration	1	7.1	0.2, 33.9
		No improvement or deterioration	8	57.1	28.9, 82.3
	Pre-cycle 37 (N=12)	Categories of change [d]			
		Improvement	3	25.0	5.5, 57.2
		Deterioration	2	16.7	2.1, 48.4
		No improvement or deterioration	7	58.3	27.7, 84.8
	Pre-cycle 49 (N=12)	Categories of change [d]			
		Improvement	4	33.3	9.9, 65.1
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	8	66.7	34.9, 90.1
	Pre-cycle 61 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Overall (N=19)	Categories of change [d]			
		Improvement	11	57.9	33.5, 79.7
		Deterioration	9	47.4	24.4, 71.1
		No improvement or deterioration	3	15.8	3.4, 39.6

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	3	20.0	4.3, 48.1
		No improvement or deterioration	7	46.7	21.3, 73.4
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 9 (N=13)	Categories of change [d]			
		Improvement	4	30.8	9.1, 61.4
		Deterioration	1	7.7	0.2, 36.0
		No improvement or deterioration	8	61.5	31.6, 86.1
	Pre-cycle 13 (N=13)	Categories of change [d]			
		Improvement	3	23.1	5.0, 53.8
		Deterioration	2	15.4	1.9, 45.4
		No improvement or deterioration	8	61.5	31.6, 86.1

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 49 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 61 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.1 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Overall (N=16)	Categories of change [d]			
		Improvement	11	68.8	41.3, 89.0
		Deterioration	6	37.5	15.2, 64.6
		No improvement or deterioration	2	12.5	1.6, 38.3

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.2 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	9	75.0	42.8, 94.5
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	2	16.7	2.1, 48.4
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	10	83.3	51.6, 97.9
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	4	33.3	9.9, 65.1
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	7	58.3	27.7, 84.8
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	3	27.3	6.0, 61.0
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.2 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 37 (N=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	5	62.5	24.5, 91.5
	Pre-cycle 49 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	4	57.1	18.4, 90.1
	Overall (N=12)	Categories of change [d]			
		Improvement	5	41.7	15.2, 72.3
		Deterioration	3	25.0	5.5, 57.2
		No improvement or deterioration	4	33.3	9.9, 65.1

[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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.2 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	6	50.0	21.1, 78.9
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	4	33.3	9.9, 65.1
		Deterioration	3	25.0	5.5, 57.2
		No improvement or deterioration	5	41.7	15.2, 72.3
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	2	16.7	2.1, 48.4
		Deterioration	2	16.7	2.1, 48.4
		No improvement or deterioration	8	66.7	34.9, 90.1
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	3	27.3	6.0, 61.0
		No improvement or deterioration	4	36.4	10.9, 69.2

[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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.2 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 37 (N=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 49 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Overall (N=12)	Categories of change [d]			
		Improvement	5	41.7	15.2, 72.3
		Deterioration	3	25.0	5.5, 57.2
		No improvement or deterioration	4	33.3	9.9, 65.1

[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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.2 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	7	58.3	27.7, 84.8
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	3	25.0	5.5, 57.2
		Deterioration	2	16.7	2.1, 48.4
		No improvement or deterioration	7	58.3	27.7, 84.8
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	3	25.0	5.5, 57.2
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	8	66.7	34.9, 90.1
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	3	27.3	6.0, 61.0
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.2 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	1	11.1	0.3, 48.2
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 37 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	6	75.0	34.9, 96.8
	Pre-cycle 49 (N=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	5	71.4	29.0, 96.3
	Overall (N=12)	Categories of change [d]			
		Improvement	5	41.7	15.2, 72.3
		Deterioration	4	33.3	9.9, 65.1
		No improvement or deterioration	4	33.3	9.9, 65.1

[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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.2 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	8	72.7	39.0, 94.0
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	2	16.7	2.1, 48.4
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	10	83.3	51.6, 97.9
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	4	33.3	9.9, 65.1
		Deterioration	3	25.0	5.5, 57.2
		No improvement or deterioration	5	41.7	15.2, 72.3
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.2 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 37 (N=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	4	50.0	15.7, 84.3
	Pre-cycle 49 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	2	28.6	3.7, 71.0
	Overall (N=12)	Categories of change [d]			
		Improvement	6	50.0	21.1, 78.9
		Deterioration	4	33.3	9.9, 65.1
		No improvement or deterioration	3	25.0	5.5, 57.2

[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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.2 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 5 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.2 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	2	33.3	4.3, 77.7
	Overall (N=11)	Categories of change [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	4	36.4	10.9, 69.2
		No improvement or deterioration	2	18.2	2.3, 51.8

[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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	3	27.3	6.0, 61.0
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	3	27.3	6.0, 61.0
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 61 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	3	27.3	6.0, 61.0
		No improvement or deterioration	4	36.4	10.9, 69.2

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	3	27.3	6.0, 61.0
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	6	54.5	23.4, 83.3
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	1	9.1	0.2, 41.3
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	8	72.7	39.0, 94.0
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 61 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Overall (N=11)	Categories of change [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	3	27.3	6.0, 61.0
		No improvement or deterioration	3	27.3	6.0, 61.0

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	1	9.1	0.2, 41.3
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	9	81.8	48.2, 97.7
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	3	30.0	6.7, 65.2
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 61 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Overall (N=11)	Categories of change [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	4	36.4	10.9, 69.2
		No improvement or deterioration	2	18.2	2.3, 51.8

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	3	27.3	6.0, 61.0
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	3	27.3	6.0, 61.0
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45.9
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	6	100	54.1, 100
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45.9
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6
	Pre-cycle 61 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Overall (N=11)	Categories of change [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	6	54.5	23.4, 83.3
		No improvement or deterioration	2	18.2	2.3, 51.8

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 5 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	4	50.0	15.7, 84.3
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	2	33.3	4.3, 77.7

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 49 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.3 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Overall (N=9)	Categories of change [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	4	44.4	13.7, 78.8
		No improvement or deterioration	1	11.1	0.3, 48.2

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	9	90.0	55.5, 99.7
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	7	77.8	40.0, 97.2

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 49 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	5	62.5	24.5, 91.5
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	7	70.0	34.8, 93.3
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	7	77.8	40.0, 97.2
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 49 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	6	75.0	34.9, 96.8
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Overall (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	3	30.0	6.7, 65.2
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	7	70.0	34.8, 93.3
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	3	30.0	6.7, 65.2
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	6	66.7	29.9, 92.5
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	3	33.3	7.5, 70.1

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	6	85.7	42.1, 99.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	1	14.3	0.4, 57.9
	Pre-cycle 49 (N=8)	Categories of change [d]			
		Improvement	5	62.5	24.5, 91.5
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	2	25.0	3.2, 65.1
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Overall (N=10)	Categories of change [d]			
		Improvement	8	80.0	44.4, 97.5
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	1	10.0	0.3, 44.5

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	7	70.0	34.8, 93.3
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 49 (N=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Overall (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	4	40.0	12.2, 73.8
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	6	75.0	34.9, 96.8
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	5	62.5	24.5, 91.5
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	7	77.8	40.0, 97.2

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	4	50.0	15.7, 84.3
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 49 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.4 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Overall (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	4	40.0	12.2, 73.8
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.1.5 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	1	10.0	0.3, 44.5
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	9	90.0	55.5, 99.7
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.5 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	5	62.5	24.5, 91.5
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Overall (N=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	3	30.0	6.7, 65.2

[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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.5 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	3	30.0	6.7, 65.2
		No improvement or deterioration	4	40.0	12.2, 73.8
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30.8
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	3	30.0	6.7, 65.2
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.5 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	3	60.0	14.7, 94.7
	Overall (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	4	40.0	12.2, 73.8
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.5 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	0	0	0, 30.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	9	90.0	55.5, 99.7
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	3	30.0	6.7, 65.2
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.5 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	4	50.0	15.7, 84.3
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	0	0	0, 52.2
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	5	100	47.8, 100
	Overall (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	5	50.0	18.7, 81.3
		No improvement or deterioration	3	30.0	6.7, 65.2

[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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.5 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.5 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Overall (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	3	30.0	6.7, 65.2
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.5 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 9 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 13 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.1.5 PedsQL self-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	5	83.3	35.9, 99.6
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 49 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Overall (N=8)	Categories of change [d]			
		Improvement	6	75.0	34.9, 96.8
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	1	12.5	0.3, 52.7

[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 are based on a clinically meaningful threshold (CMT) of 15.

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2.1.5.2 Subgruppenanalysen zum PedsQL – Elternberichtet (3-7 Jahre)

Table 2.12.3.2.1.1 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - Gender = Male
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=9) [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=9)	68,91	13,014	67,39	48,8	84,8	0,0							
	Pre-cycle 3 (n=9)	74,50	18,240	70,65	50,0	100,0	0,0	9	5,59	14,925	9,78	-21,7	30,4	0,0
	Pre-cycle 5 (n=9)	77,79	14,708	81,25	46,7	94,4	0,0	9	8,88	8,424	9,66	-7,6	20,2	0,0
	Pre-cycle 9 (n=9)	76,42	17,444	85,87	51,1	95,7	0,0	9	7,51	15,352	7,14	-23,9	27,2	0,0
	Pre-cycle 13 (n=9)	78,33	14,616	83,70	53,3	94,6	0,0	9	9,42	13,581	13,10	-8,7	32,6	0,0
	Pre-cycle 25 (n=7)	72,08	16,048	66,30	54,3	94,6	22,2	7	2,56	19,303	6,52	-29,0	26,0	22,2
	Pre-cycle 37 (n=6)	77,84	11,316	77,72	63,0	95,7	33,3	6	7,97	16,999	15,58	-20,3	21,7	33,3
	Pre-cycle 49 (n=5)	72,39	17,024	63,04	57,6	96,7	44,4	5	4,64	24,061	8,70	-25,7	29,3	44,4
	Pre-cycle 61 (n=1)	NC	NC	NC	59,8	59,8	88,9	1	NC	NC	NC	-23,6	-23,6	88,9
Raw Total Score	Baseline (n=9)	2,76	0,521	2,70	2,0	3,4	0,0							
	Pre-cycle 3 (n=9)	2,98	0,730	2,83	2,0	4,0	0,0	9	0,22	0,597	0,39	-0,9	1,2	0,0
	Pre-cycle 5 (n=9)	3,11	0,588	3,25	1,9	3,8	0,0	9	0,36	0,337	0,39	-0,3	0,8	0,0
	Pre-cycle 9 (n=9)	3,06	0,698	3,43	2,0	3,8	0,0	9	0,30	0,614	0,29	-1,0	1,1	0,0
	Pre-cycle 13 (n=9)	3,13	0,585	3,35	2,1	3,8	0,0	9	0,38	0,543	0,52	-0,3	1,3	0,0
	Pre-cycle 25 (n=7)	2,88	0,642	2,65	2,2	3,8	22,2	7	0,10	0,772	0,26	-1,2	1,0	22,2
	Pre-cycle 37 (n=6)	3,11	0,453	3,11	2,5	3,8	33,3	6	0,32	0,680	0,62	-0,8	0,9	33,3
	Pre-cycle 49 (n=5)	2,90	0,681	2,52	2,3	3,9	44,4	5	0,19	0,962	0,35	-1,0	1,2	44,4
	Pre-cycle 61 (n=1)	NC	NC	NC	2,4	2,4	88,9	1	NC	NC	NC	-0,9	-0,9	88,9

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.1 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - Gender = Male
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=9) [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=9)	65,97	25,216	71,88	25,0	90,6	0,0							
	Pre-cycle 3 (n=9)	76,04	24,557	78,13	18,8	100,0	0,0	9	10,07	18,207	9,38	-18,8	43,8	0,0
	Pre-cycle 5 (n=9)	81,25	25,722	93,75	25,0	100,0	0,0	9	15,28	11,635	12,50	0,0	40,6	0,0
	Pre-cycle 9 (n=9)	73,96	25,864	78,13	25,0	100,0	0,0	9	7,99	19,271	9,38	-21,9	43,8	0,0
	Pre-cycle 13 (n=9)	75,69	24,891	78,13	18,8	100,0	0,0	9	9,72	20,578	9,38	-12,5	53,1	0,0
	Pre-cycle 25 (n=7)	68,30	34,865	81,25	0,0	100,0	22,2	7	2,68	32,597	-6,25	-31,3	65,6	22,2
	Pre-cycle 37 (n=6)	75,52	24,400	82,81	34,4	96,9	33,3	6	10,42	25,744	9,38	-25,0	50,0	33,3
	Pre-cycle 49 (n=5)	69,38	34,332	75,00	15,6	100,0	44,4	5	5,63	35,726	-9,38	-25,0	65,6	44,4
	Pre-cycle 61 (n=1)	NC	NC	NC	53,1	53,1	88,9	1	NC	NC	NC	-31,3	-31,3	88,9
Raw Physical functioning	Baseline (n=9)	2,64	1,009	2,88	1,0	3,6	0,0							
	Pre-cycle 3 (n=9)	3,04	0,982	3,13	0,8	4,0	0,0	9	0,40	0,728	0,38	-0,8	1,8	0,0
	Pre-cycle 5 (n=9)	3,25	1,029	3,75	1,0	4,0	0,0	9	0,61	0,465	0,50	0,0	1,6	0,0
	Pre-cycle 9 (n=9)	2,96	1,035	3,13	1,0	4,0	0,0	9	0,32	0,771	0,38	-0,9	1,8	0,0
	Pre-cycle 13 (n=9)	3,03	0,996	3,13	0,8	4,0	0,0	9	0,39	0,823	0,38	-0,5	2,1	0,0
	Pre-cycle 25 (n=7)	2,73	1,395	3,25	0,0	4,0	22,2	7	0,11	1,304	-0,25	-1,3	2,6	22,2
	Pre-cycle 37 (n=6)	3,02	0,976	3,31	1,4	3,9	33,3	6	0,42	1,030	0,38	-1,0	2,0	33,3
	Pre-cycle 49 (n=5)	2,78	1,373	3,00	0,6	4,0	44,4	5	0,23	1,429	-0,38	-1,0	2,6	44,4
	Pre-cycle 61 (n=1)	NC	NC	NC	2,1	2,1	88,9	1	NC	NC	NC	-1,3	-1,3	88,9

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.1 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - Gender = Male (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=9) [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=9)	74,44	17,401	75,00	50,0	100,0	0,0							
	Pre-cycle 3 (n=9)	80,00	21,065	85,00	50,0	100,0	0,0	9	5,56	17,756	10,00	-35,0	25,0	0,0
	Pre-cycle 5 (n=9)	79,44	16,094	80,00	55,0	100,0	0,0	9	5,00	13,229	5,00	-25,0	20,0	0,0
	Pre-cycle 9 (n=9)	88,89	13,176	95,00	65,0	100,0	0,0	9	14,44	15,092	15,00	0,0	50,0	0,0
	Pre-cycle 13 (n=9)	87,78	9,391	90,00	70,0	100,0	0,0	9	13,33	12,990	15,00	-5,0	30,0	0,0
	Pre-cycle 25 (n=7)	80,71	18,803	90,00	55,0	100,0	22,2	7	7,14	16,797	0,00	-5,0	40,0	22,2
	Pre-cycle 37 (n=6)	83,33	17,795	87,50	55,0	100,0	33,3	6	6,67	16,931	-2,50	-5,0	35,0	33,3
	Pre-cycle 49 (n=5)	85,00	17,678	90,00	55,0	100,0	44,4	5	9,00	21,036	0,00	-5,0	45,0	44,4
	Pre-cycle 61 (n=1)	NC	NC	NC	75,0	75,0	88,9	1	NC	NC	NC	0,0	0,0	88,9
Raw Emotional functioning	Baseline (n=9)	2,98	0,696	3,00	2,0	4,0	0,0							
	Pre-cycle 3 (n=9)	3,20	0,843	3,40	2,0	4,0	0,0	9	0,22	0,710	0,40	-1,4	1,0	0,0
	Pre-cycle 5 (n=9)	3,18	0,644	3,20	2,2	4,0	0,0	9	0,20	0,529	0,20	-1,0	0,8	0,0
	Pre-cycle 9 (n=9)	3,56	0,527	3,80	2,6	4,0	0,0	9	0,58	0,604	0,60	0,0	2,0	0,0
	Pre-cycle 13 (n=9)	3,51	0,376	3,60	2,8	4,0	0,0	9	0,53	0,520	0,60	-0,2	1,2	0,0
	Pre-cycle 25 (n=7)	3,23	0,752	3,60	2,2	4,0	22,2	7	0,29	0,672	0,00	-0,2	1,6	22,2
	Pre-cycle 37 (n=6)	3,33	0,712	3,50	2,2	4,0	33,3	6	0,27	0,677	-0,10	-0,2	1,4	33,3
	Pre-cycle 49 (n=5)	3,40	0,707	3,60	2,2	4,0	44,4	5	0,36	0,841	0,00	-0,2	1,8	44,4
	Pre-cycle 61 (n=1)	NC	NC	NC	3,0	3,0	88,9	1	NC	NC	NC	0,0	0,0	88,9

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.1 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - Gender = Male
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=9) [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=9)	70,56	17,931	70,00	50,0	100,0	0,0							
	Pre-cycle 3 (n=9)	72,78	25,753	75,00	30,0	100,0	0,0	9	2,22	21,667	5,00	-40,0	25,0	0,0
	Pre-cycle 5 (n=9)	74,44	15,501	80,00	45,0	100,0	0,0	9	3,89	13,642	0,00	-15,0	25,0	0,0
	Pre-cycle 9 (n=9)	73,89	20,429	75,00	30,0	100,0	0,0	9	3,33	22,079	0,00	-40,0	35,0	0,0
	Pre-cycle 13 (n=9)	80,00	18,875	85,00	50,0	100,0	0,0	9	9,44	20,531	5,00	-20,0	45,0	0,0
	Pre-cycle 25 (n=7)	70,71	18,127	70,00	55,0	100,0	22,2	7	0,00	24,664	-5,00	-30,0	45,0	22,2
	Pre-cycle 37 (n=6)	76,67	15,384	77,50	60,0	100,0	33,3	6	5,83	24,782	-2,50	-20,0	45,0	33,3
	Pre-cycle 49 (n=5)	76,00	18,166	85,00	50,0	95,0	44,4	5	10,00	37,914	30,00	-50,0	40,0	44,4
	Pre-cycle 61 (n=1)	NC	NC	NC	60,0	60,0	88,9	1	NC	NC	NC	-40,0	-40,0	88,9
Raw Social functioning	Baseline (n=9)	2,82	0,717	2,80	2,0	4,0	0,0							
	Pre-cycle 3 (n=9)	2,91	1,030	3,00	1,2	4,0	0,0	9	0,09	0,867	0,20	-1,6	1,0	0,0
	Pre-cycle 5 (n=9)	2,98	0,620	3,20	1,8	4,0	0,0	9	0,16	0,546	0,00	-0,6	1,0	0,0
	Pre-cycle 9 (n=9)	2,96	0,817	3,00	1,2	4,0	0,0	9	0,13	0,883	0,00	-1,6	1,4	0,0
	Pre-cycle 13 (n=9)	3,20	0,755	3,40	2,0	4,0	0,0	9	0,38	0,821	0,20	-0,8	1,8	0,0
	Pre-cycle 25 (n=7)	2,83	0,725	2,80	2,2	4,0	22,2	7	0,00	0,987	-0,20	-1,2	1,8	22,2
	Pre-cycle 37 (n=6)	3,07	0,615	3,10	2,4	4,0	33,3	6	0,23	0,991	-0,10	-0,8	1,8	33,3
	Pre-cycle 49 (n=5)	3,04	0,727	3,40	2,0	3,8	44,4	5	0,40	1,517	1,20	-2,0	1,6	44,4
	Pre-cycle 61 (n=1)	NC	NC	NC	2,4	2,4	88,9	1	NC	NC	NC	-1,6	-1,6	88,9

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.1 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - Gender = Male
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=9) [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=9)	63,89	22,298	70,00	8,3	80,0	0,0							
	Pre-cycle 3 (n=8)	66,88	23,290	57,50	45,0	100,0	11,1	8	-3,96	22,235	-5,00	-30,0	33,3	11,1
	Pre-cycle 5 (n=6)	68,06	24,820	72,50	30,0	100,0	33,3	6	11,39	24,842	8,33	-25,0	41,7	33,3
	Pre-cycle 9 (n=8)	68,75	23,734	73,33	33,3	95,0	11,1	8	6,25	20,310	12,50	-40,0	25,0	11,1
	Pre-cycle 13 (n=8)	67,29	20,392	67,50	33,3	95,0	11,1	8	3,54	17,603	4,17	-25,0	25,0	11,1
	Pre-cycle 25 (n=5)	65,00	27,839	60,00	25,0	100,0	44,4	5	-5,33	27,699	-15,00	-41,7	25,0	44,4
	Pre-cycle 37 (n=5)	76,00	22,472	75,00	45,0	100,0	44,4	5	6,67	23,834	0,00	-21,7	40,0	44,4
	Pre-cycle 49 (n=5)	61,00	27,928	50,00	35,0	100,0	44,4	5	-5,33	32,922	-20,00	-35,0	35,0	44,4
	Pre-cycle 61 (n=1)	NC	NC	NC	55,0	55,0	88,9	1	NC	NC	NC	-11,7	-11,7	88,9
Raw School functioning score	Baseline (n=9)	2,56	0,892	2,80	0,3	3,2	0,0							
	Pre-cycle 3 (n=8)	2,68	0,932	2,30	1,8	4,0	11,1	8	-0,16	0,889	-0,20	-1,2	1,3	11,1
	Pre-cycle 5 (n=6)	2,72	0,993	2,90	1,2	4,0	33,3	6	0,46	0,994	0,33	-1,0	1,7	33,3
	Pre-cycle 9 (n=8)	2,75	0,949	2,93	1,3	3,8	11,1	8	0,25	0,812	0,50	-1,6	1,0	11,1
	Pre-cycle 13 (n=8)	2,69	0,816	2,70	1,3	3,8	11,1	8	0,14	0,704	0,17	-1,0	1,0	11,1
	Pre-cycle 25 (n=5)	2,60	1,114	2,40	1,0	4,0	44,4	5	-0,21	1,108	-0,60	-1,7	1,0	44,4
	Pre-cycle 37 (n=5)	3,04	0,899	3,00	1,8	4,0	44,4	5	0,27	0,953	0,00	-0,9	1,6	44,4
	Pre-cycle 49 (n=5)	2,44	1,117	2,00	1,4	4,0	44,4	5	-0,21	1,317	-0,80	-1,4	1,4	44,4
	Pre-cycle 61 (n=1)	NC	NC	NC	2,2	2,2	88,9	1	NC	NC	NC	-0,5	-0,5	88,9

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.2 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - Gender = Female
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [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=7)	50,90	19,764	50,00	20,7	79,3	0,0							
	Pre-cycle 3 (n=7)	60,25	19,208	55,43	39,1	94,6	0,0	7	9,35	18,693	5,43	-17,4	36,1	0,0
	Pre-cycle 5 (n=6)	54,53	23,083	57,61	25,0	84,8	14,3	6	7,11	24,028	4,89	-19,6	45,9	14,3
	Pre-cycle 9 (n=7)	63,66	18,176	58,70	34,8	88,0	0,0	7	12,77	25,825	16,30	-20,7	58,7	0,0
	Pre-cycle 13 (n=6)	73,55	10,025	71,74	64,1	90,2	14,3	6	21,60	22,915	21,74	-14,1	57,6	14,3
	Pre-cycle 25 (n=6)	70,67	20,908	73,43	34,8	90,2	14,3	6	18,72	33,051	17,39	-16,3	68,5	14,3
	Pre-cycle 37 (n=3)	55,80	9,803	56,52	45,7	65,2	57,1	3	18,92	21,626	26,33	-5,4	35,9	57,1
	Pre-cycle 49 (n=2)	NC	NC	NC	65,2	82,6	71,4	2	NC	NC	NC	43,7	44,6	71,4
Raw Total Score	Baseline (n=7)	2,04	0,791	2,00	0,8	3,2	0,0							
	Pre-cycle 3 (n=7)	2,41	0,768	2,22	1,6	3,8	0,0	7	0,37	0,748	0,22	-0,7	1,4	0,0
	Pre-cycle 5 (n=6)	2,18	0,923	2,30	1,0	3,4	14,3	6	0,28	0,961	0,20	-0,8	1,8	14,3
	Pre-cycle 9 (n=7)	2,55	0,727	2,35	1,4	3,5	0,0	7	0,51	1,033	0,65	-0,8	2,3	0,0
	Pre-cycle 13 (n=6)	2,94	0,401	2,87	2,6	3,6	14,3	6	0,86	0,917	0,87	-0,6	2,3	14,3
	Pre-cycle 25 (n=6)	2,83	0,836	2,94	1,4	3,6	14,3	6	0,75	1,322	0,70	-0,7	2,7	14,3
	Pre-cycle 37 (n=3)	2,23	0,392	2,26	1,8	2,6	57,1	3	0,76	0,865	1,05	-0,2	1,4	57,1
	Pre-cycle 49 (n=2)	NC	NC	NC	2,6	3,3	71,4	2	NC	NC	NC	1,7	1,8	71,4

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.2 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - Gender = Female (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [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=7)	45,98	27,046	37,50	21,9	100,0	0,0							
	Pre-cycle 3 (n=7)	60,27	21,478	56,25	34,4	90,6	0,0	7	14,29	26,630	12,50	-25,0	43,8	0,0
	Pre-cycle 5 (n=6)	51,56	23,696	54,69	21,9	78,1	14,3	6	6,77	29,409	10,94	-28,1	43,8	14,3
	Pre-cycle 9 (n=7)	64,29	23,095	62,50	31,3	93,8	0,0	7	18,30	31,635	21,88	-21,9	71,9	0,0
	Pre-cycle 13 (n=6)	75,52	11,425	76,56	59,4	87,5	14,3	6	30,73	31,833	32,81	-25,0	65,6	14,3
	Pre-cycle 25 (n=6)	75,00	26,810	81,25	25,0	96,9	14,3	6	30,21	36,746	39,06	-28,1	71,9	14,3
	Pre-cycle 37 (n=3)	59,38	16,238	68,75	40,6	68,8	57,1	3	33,33	14,091	34,38	18,8	46,9	57,1
	Pre-cycle 49 (n=2)	NC	NC	NC	75,0	87,5	71,4	2	NC	NC	NC	53,1	53,1	71,4
Raw Physical functioning	Baseline (n=7)	1,84	1,082	1,50	0,9	4,0	0,0							
	Pre-cycle 3 (n=7)	2,41	0,859	2,25	1,4	3,6	0,0	7	0,57	1,065	0,50	-1,0	1,8	0,0
	Pre-cycle 5 (n=6)	2,06	0,948	2,19	0,9	3,1	14,3	6	0,27	1,176	0,44	-1,1	1,8	14,3
	Pre-cycle 9 (n=7)	2,57	0,924	2,50	1,3	3,8	0,0	7	0,73	1,265	0,88	-0,9	2,9	0,0
	Pre-cycle 13 (n=6)	3,02	0,457	3,06	2,4	3,5	14,3	6	1,23	1,273	1,31	-1,0	2,6	14,3
	Pre-cycle 25 (n=6)	3,00	1,072	3,25	1,0	3,9	14,3	6	1,21	1,470	1,56	-1,1	2,9	14,3
	Pre-cycle 37 (n=3)	2,38	0,650	2,75	1,6	2,8	57,1	3	1,33	0,564	1,38	0,8	1,9	57,1
	Pre-cycle 49 (n=2)	NC	NC	NC	3,0	3,5	71,4	2	NC	NC	NC	2,1	2,1	71,4

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.2 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - Gender = Female
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [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=7)	46,43	19,730	45,00	15,0	75,0	0,0							
	Pre-cycle 3 (n=7)	62,86	22,334	65,00	30,0	100,0	0,0	7	16,43	21,931	20,00	-15,0	50,0	0,0
	Pre-cycle 5 (n=6)	55,83	27,096	47,50	30,0	100,0	14,3	6	14,17	24,376	10,00	-10,0	50,0	14,3
	Pre-cycle 9 (n=7)	69,29	24,905	85,00	35,0	95,0	0,0	7	22,86	32,385	20,00	-30,0	75,0	0,0
	Pre-cycle 13 (n=6)	70,83	12,416	77,50	55,0	80,0	14,3	6	22,50	24,648	22,50	-10,0	60,0	14,3
	Pre-cycle 25 (n=6)	67,50	19,170	67,50	40,0	90,0	14,3	6	19,17	27,824	15,00	-10,0	70,0	14,3
	Pre-cycle 37 (n=3)	71,67	10,408	75,00	60,0	80,0	57,1	3	36,67	20,817	30,00	20,0	60,0	57,1
	Pre-cycle 49 (n=2)	NC	NC	NC	45,0	90,0	71,4	2	NC	NC	NC	30,0	40,0	71,4
Raw Emotional functioning	Baseline (n=7)	1,86	0,789	1,80	0,6	3,0	0,0							
	Pre-cycle 3 (n=7)	2,51	0,893	2,60	1,2	4,0	0,0	7	0,66	0,877	0,80	-0,6	2,0	0,0
	Pre-cycle 5 (n=6)	2,23	1,084	1,90	1,2	4,0	14,3	6	0,57	0,975	0,40	-0,4	2,0	14,3
	Pre-cycle 9 (n=7)	2,77	0,996	3,40	1,4	3,8	0,0	7	0,91	1,295	0,80	-1,2	3,0	0,0
	Pre-cycle 13 (n=6)	2,83	0,497	3,10	2,2	3,2	14,3	6	0,90	0,986	0,90	-0,4	2,4	14,3
	Pre-cycle 25 (n=6)	2,70	0,767	2,70	1,6	3,6	14,3	6	0,77	1,113	0,60	-0,4	2,8	14,3
	Pre-cycle 37 (n=3)	2,87	0,416	3,00	2,4	3,2	57,1	3	1,47	0,833	1,20	0,8	2,4	57,1
	Pre-cycle 49 (n=2)	NC	NC	NC	1,8	3,6	71,4	2	NC	NC	NC	1,2	1,6	71,4

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.2 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - Gender = Female
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [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=7)	53,57	27,343	60,00	10,0	80,0	0,0							
	Pre-cycle 3 (n=7)	59,29	21,492	55,00	40,0	100,0	0,0	7	5,71	22,440	5,00	-30,0	30,0	0,0
	Pre-cycle 5 (n=6)	55,00	27,749	67,50	15,0	80,0	14,3	6	5,83	18,280	2,50	-20,0	35,0	14,3
	Pre-cycle 9 (n=7)	57,86	28,263	45,00	25,0	95,0	0,0	7	4,29	32,842	10,00	-35,0	65,0	0,0
	Pre-cycle 13 (n=6)	73,33	19,664	80,00	50,0	100,0	14,3	6	16,67	28,225	10,00	-10,0	70,0	14,3
	Pre-cycle 25 (n=6)	68,33	24,014	72,50	35,0	95,0	14,3	6	11,67	43,780	2,50	-40,0	85,0	14,3
	Pre-cycle 37 (n=3)	43,33	7,638	45,00	35,0	50,0	57,1	3	3,33	29,297	15,00	-30,0	25,0	57,1
	Pre-cycle 49 (n=2)	NC	NC	NC	70,0	75,0	71,4	2	NC	NC	NC	40,0	60,0	71,4
Raw Social functioning	Baseline (n=7)	2,14	1,094	2,40	0,4	3,2	0,0							
	Pre-cycle 3 (n=7)	2,37	0,860	2,20	1,6	4,0	0,0	7	0,23	0,898	0,20	-1,2	1,2	0,0
	Pre-cycle 5 (n=6)	2,20	1,110	2,70	0,6	3,2	14,3	6	0,23	0,731	0,10	-0,8	1,4	14,3
	Pre-cycle 9 (n=7)	2,31	1,131	1,80	1,0	3,8	0,0	7	0,17	1,314	0,40	-1,4	2,6	0,0
	Pre-cycle 13 (n=6)	2,93	0,787	3,20	2,0	4,0	14,3	6	0,67	1,129	0,40	-0,4	2,8	14,3
	Pre-cycle 25 (n=6)	2,73	0,961	2,90	1,4	3,8	14,3	6	0,47	1,751	0,10	-1,6	3,4	14,3
	Pre-cycle 37 (n=3)	1,73	0,306	1,80	1,4	2,0	57,1	3	0,13	1,172	0,60	-1,2	1,0	57,1
	Pre-cycle 49 (n=2)	NC	NC	NC	2,8	3,0	71,4	2	NC	NC	NC	1,6	2,4	71,4

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.2 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - Gender = Female
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=7) [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=6)	64,17	23,541	65,00	35,0	90,0	14,3							
	Pre-cycle 3 (n=7)	58,57	22,120	55,00	30,0	90,0	0,0	6	-10,00	13,784	-7,50	-30,0	5,0	14,3
	Pre-cycle 5 (n=5)	64,00	19,812	60,00	45,0	95,0	28,6	4	-5,00	26,141	2,50	-40,0	15,0	42,9
	Pre-cycle 9 (n=7)	62,86	18,676	60,00	40,0	100,0	0,0	6	-0,83	18,005	0,00	-20,0	20,0	14,3
	Pre-cycle 13 (n=6)	73,33	16,330	70,00	55,0	95,0	14,3	5	9,00	12,942	5,00	-5,0	30,0	28,6
	Pre-cycle 25 (n=5)	67,00	16,047	75,00	45,0	80,0	28,6	5	0,00	31,024	-5,00	-40,0	45,0	28,6
	Pre-cycle 37 (n=3)	46,67	11,547	40,00	40,0	60,0	57,1	2	NC	NC	NC	-45,0	5,0	71,4
	Pre-cycle 49 (n=2)	NC	NC	NC	65,0	75,0	71,4	1	NC	NC	NC	30,0	30,0	85,7
Raw School functioning score	Baseline (n=6)	2,57	0,942	2,60	1,4	3,6	14,3							
	Pre-cycle 3 (n=7)	2,34	0,885	2,20	1,2	3,6	0,0	6	-0,40	0,551	-0,30	-1,2	0,2	14,3
	Pre-cycle 5 (n=5)	2,56	0,792	2,40	1,8	3,8	28,6	4	-0,20	1,046	0,10	-1,6	0,6	42,9
	Pre-cycle 9 (n=7)	2,51	0,747	2,40	1,6	4,0	0,0	6	-0,03	0,720	0,00	-0,8	0,8	14,3
	Pre-cycle 13 (n=6)	2,93	0,653	2,80	2,2	3,8	14,3	5	0,36	0,518	0,20	-0,2	1,2	28,6
	Pre-cycle 25 (n=5)	2,68	0,642	3,00	1,8	3,2	28,6	5	0,00	1,241	-0,20	-1,6	1,8	28,6
	Pre-cycle 37 (n=3)	1,87	0,462	1,60	1,6	2,4	57,1	2	NC	NC	NC	-1,8	0,2	71,4
	Pre-cycle 49 (n=2)	NC	NC	NC	2,6	3,0	71,4	1	NC	NC	NC	1,2	1,2	85,7

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.3 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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=10)	64,86	15,163	67,39	38,9	84,8	0,0							
	Pre-cycle 3 (n=10)	75,09	14,963	72,83	52,2	95,7	0,0	10	10,23	16,245	10,33	-17,4	36,1	0,0
	Pre-cycle 5 (n=9)	75,34	13,467	76,09	48,9	94,4	10,0	9	11,25	16,613	9,66	-13,0	45,9	10,0
	Pre-cycle 9 (n=10)	74,30	17,160	74,88	54,3	95,7	0,0	10	9,44	14,245	12,97	-20,7	27,2	0,0
	Pre-cycle 13 (n=10)	79,18	12,150	80,43	61,9	94,6	0,0	10	14,32	14,585	17,39	-14,1	32,6	0,0
	Pre-cycle 25 (n=8)	73,95	20,414	82,64	34,8	94,6	20,0	8	9,58	21,375	16,30	-16,3	41,7	20,0
	Pre-cycle 37 (n=5)	73,84	19,139	79,35	45,7	95,7	50,0	5	14,54	12,018	15,94	-5,4	26,3	50,0
	Pre-cycle 49 (n=3)	87,68	7,863	83,70	82,6	96,7	70,0	3	32,69	9,797	29,35	25,0	43,7	70,0
Raw Total Score	Baseline (n=10)	2,59	0,607	2,70	1,6	3,4	0,0							
	Pre-cycle 3 (n=10)	3,00	0,599	2,91	2,1	3,8	0,0	10	0,41	0,650	0,41	-0,7	1,4	0,0
	Pre-cycle 5 (n=9)	3,01	0,539	3,04	2,0	3,8	10,0	9	0,45	0,665	0,39	-0,5	1,8	10,0
	Pre-cycle 9 (n=10)	2,97	0,686	3,00	2,2	3,8	0,0	10	0,38	0,570	0,52	-0,8	1,1	0,0
	Pre-cycle 13 (n=10)	3,17	0,486	3,22	2,5	3,8	0,0	10	0,57	0,583	0,70	-0,6	1,3	0,0
	Pre-cycle 25 (n=8)	2,96	0,817	3,31	1,4	3,8	20,0	8	0,38	0,855	0,65	-0,7	1,7	20,0
	Pre-cycle 37 (n=5)	2,95	0,766	3,17	1,8	3,8	50,0	5	0,58	0,481	0,64	-0,2	1,1	50,0
	Pre-cycle 49 (n=3)	3,51	0,315	3,35	3,3	3,9	70,0	3	1,31	0,392	1,17	1,0	1,7	70,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.3 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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=10)	60,63	27,051	60,94	21,9	100,0	0,0							
	Pre-cycle 3 (n=10)	79,69	12,435	78,13	56,3	100,0	0,0	10	19,06	22,168	18,75	-25,0	43,8	0,0
	Pre-cycle 5 (n=9)	77,78	18,779	78,13	43,8	100,0	10,0	9	16,32	21,124	12,50	-28,1	43,8	10,0
	Pre-cycle 9 (n=10)	74,38	21,082	76,56	40,6	100,0	0,0	10	13,75	18,762	10,94	-12,5	43,8	0,0
	Pre-cycle 13 (n=10)	80,31	13,344	78,13	56,3	100,0	0,0	10	19,69	26,189	20,31	-25,0	56,3	0,0
	Pre-cycle 25 (n=8)	78,52	25,630	90,63	25,0	100,0	20,0	8	19,53	32,977	12,50	-28,1	65,6	20,0
	Pre-cycle 37 (n=5)	77,50	23,635	84,38	40,6	96,9	50,0	5	27,50	15,531	25,00	9,4	50,0	50,0
	Pre-cycle 49 (n=3)	94,79	6,505	96,88	87,5	100,0	70,0	3	42,71	29,536	53,13	9,4	65,6	70,0
Raw Physical functioning	Baseline (n=10)	2,43	1,082	2,44	0,9	4,0	0,0							
	Pre-cycle 3 (n=10)	3,19	0,497	3,13	2,3	4,0	0,0	10	0,76	0,887	0,75	-1,0	1,8	0,0
	Pre-cycle 5 (n=9)	3,11	0,751	3,13	1,8	4,0	10,0	9	0,65	0,845	0,50	-1,1	1,8	10,0
	Pre-cycle 9 (n=10)	2,98	0,843	3,06	1,6	4,0	0,0	10	0,55	0,750	0,44	-0,5	1,8	0,0
	Pre-cycle 13 (n=10)	3,21	0,534	3,13	2,3	4,0	0,0	10	0,79	1,048	0,81	-1,0	2,3	0,0
	Pre-cycle 25 (n=8)	3,14	1,025	3,63	1,0	4,0	20,0	8	0,78	1,319	0,50	-1,1	2,6	20,0
	Pre-cycle 37 (n=5)	3,10	0,945	3,38	1,6	3,9	50,0	5	1,10	0,621	1,00	0,4	2,0	50,0
	Pre-cycle 49 (n=3)	3,79	0,260	3,88	3,5	4,0	70,0	3	1,71	1,181	2,13	0,4	2,6	70,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.3 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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=10)	66,50	17,646	67,50	40,0	95,0	0,0							
	Pre-cycle 3 (n=10)	73,00	21,499	67,50	50,0	100,0	0,0	10	6,50	18,567	12,50	-35,0	25,0	0,0
	Pre-cycle 5 (n=9)	71,67	22,500	70,00	35,0	100,0	10,0	9	6,11	21,180	5,00	-25,0	50,0	10,0
	Pre-cycle 9 (n=10)	81,00	22,460	90,00	35,0	100,0	0,0	10	14,50	21,009	15,00	-30,0	50,0	0,0
	Pre-cycle 13 (n=10)	80,00	14,530	82,50	55,0	100,0	0,0	10	13,50	15,102	17,50	-10,0	30,0	0,0
	Pre-cycle 25 (n=8)	74,38	21,784	82,50	40,0	100,0	20,0	8	10,63	17,204	7,50	-10,0	40,0	20,0
	Pre-cycle 37 (n=5)	83,00	14,832	85,00	60,0	100,0	50,0	5	20,00	15,411	20,00	-5,0	35,0	50,0
	Pre-cycle 49 (n=3)	91,67	2,887	90,00	90,0	95,0	70,0	3	26,67	27,538	40,00	-5,0	45,0	70,0
Raw Emotional functioning	Baseline (n=10)	2,66	0,706	2,70	1,6	3,8	0,0							
	Pre-cycle 3 (n=10)	2,92	0,860	2,70	2,0	4,0	0,0	10	0,26	0,743	0,50	-1,4	1,0	0,0
	Pre-cycle 5 (n=9)	2,87	0,900	2,80	1,4	4,0	10,0	9	0,24	0,847	0,20	-1,0	2,0	10,0
	Pre-cycle 9 (n=10)	3,24	0,898	3,60	1,4	4,0	0,0	10	0,58	0,840	0,60	-1,2	2,0	0,0
	Pre-cycle 13 (n=10)	3,20	0,581	3,30	2,2	4,0	0,0	10	0,54	0,604	0,70	-0,4	1,2	0,0
	Pre-cycle 25 (n=8)	2,98	0,871	3,30	1,6	4,0	20,0	8	0,43	0,688	0,30	-0,4	1,6	20,0
	Pre-cycle 37 (n=5)	3,32	0,593	3,40	2,4	4,0	50,0	5	0,80	0,616	0,80	-0,2	1,4	50,0
	Pre-cycle 49 (n=3)	3,67	0,115	3,60	3,6	3,8	70,0	3	1,07	1,102	1,60	-0,2	1,8	70,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.3 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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=10)	66,00	17,448	65,00	35,0	95,0	0,0							
	Pre-cycle 3 (n=10)	74,00	21,318	70,00	45,0	100,0	0,0	10	8,00	20,440	15,00	-30,0	30,0	0,0
	Pre-cycle 5 (n=9)	73,89	7,817	75,00	65,0	85,0	10,0	9	9,44	15,701	5,00	-15,0	35,0	10,0
	Pre-cycle 9 (n=10)	67,50	21,246	72,50	35,0	90,0	0,0	10	1,50	21,609	0,00	-35,0	35,0	0,0
	Pre-cycle 13 (n=10)	79,00	19,264	82,50	50,0	100,0	0,0	10	13,00	17,670	12,50	-10,0	45,0	0,0
	Pre-cycle 25 (n=8)	63,75	19,955	62,50	35,0	90,0	20,0	8	-1,25	22,796	0,00	-40,0	35,0	20,0
	Pre-cycle 37 (n=5)	63,00	16,808	60,00	45,0	85,0	50,0	5	1,00	21,622	5,00	-30,0	25,0	50,0
	Pre-cycle 49 (n=3)	85,00	10,000	85,00	75,0	95,0	70,0	3	38,33	2,887	40,00	35,0	40,0	70,0
Raw Social functioning	Baseline (n=10)	2,64	0,698	2,60	1,4	3,8	0,0							
	Pre-cycle 3 (n=10)	2,96	0,853	2,80	1,8	4,0	0,0	10	0,32	0,818	0,60	-1,2	1,2	0,0
	Pre-cycle 5 (n=9)	2,96	0,313	3,00	2,6	3,4	10,0	9	0,38	0,628	0,20	-0,6	1,4	10,0
	Pre-cycle 9 (n=10)	2,70	0,850	2,90	1,4	3,6	0,0	10	0,06	0,864	0,00	-1,4	1,4	0,0
	Pre-cycle 13 (n=10)	3,16	0,771	3,30	2,0	4,0	0,0	10	0,52	0,707	0,50	-0,4	1,8	0,0
	Pre-cycle 25 (n=8)	2,55	0,798	2,50	1,4	3,6	20,0	8	-0,05	0,912	0,00	-1,6	1,4	20,0
	Pre-cycle 37 (n=5)	2,52	0,672	2,40	1,8	3,4	50,0	5	0,04	0,865	0,20	-1,2	1,0	50,0
	Pre-cycle 49 (n=3)	3,40	0,400	3,40	3,0	3,8	70,0	3	1,53	0,115	1,60	1,4	1,6	70,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.3 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=10) [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=9)	70,37	24,435	80,00	8,3	90,0	10,0							
	Pre-cycle 3 (n=9)	70,00	19,039	60,00	45,0	100,0	10,0	8	-10,00	17,113	-10,00	-30,0	20,0	20,0
	Pre-cycle 5 (n=7)	72,14	20,587	70,00	45,0	100,0	30,0	6	4,44	30,142	0,00	-40,0	41,7	40,0
	Pre-cycle 9 (n=9)	74,26	21,378	80,00	33,3	100,0	10,0	8	6,25	17,269	12,50	-20,0	25,0	20,0
	Pre-cycle 13 (n=9)	74,26	21,231	75,00	33,3	95,0	10,0	8	5,00	16,257	5,00	-25,0	25,0	20,0
	Pre-cycle 25 (n=5)	72,00	20,797	75,00	45,0	100,0	50,0	5	-10,00	21,506	-10,00	-40,0	20,0	50,0
	Pre-cycle 37 (n=4)	66,25	24,958	62,50	40,0	100,0	60,0	3	-10,00	32,787	-5,00	-45,0	20,0	70,0
	Pre-cycle 49 (n=3)	75,00	25,000	75,00	50,0	100,0	70,0	2	NC	NC	NC	-20,0	35,0	80,0
Raw School functioning score	Baseline (n=9)	2,81	0,977	3,20	0,3	3,6	10,0							
	Pre-cycle 3 (n=9)	2,80	0,762	2,40	1,8	4,0	10,0	8	-0,40	0,685	-0,40	-1,2	0,8	20,0
	Pre-cycle 5 (n=7)	2,89	0,823	2,80	1,8	4,0	30,0	6	0,18	1,206	0,00	-1,6	1,7	40,0
	Pre-cycle 9 (n=9)	2,97	0,855	3,20	1,3	4,0	10,0	8	0,25	0,691	0,50	-0,8	1,0	20,0
	Pre-cycle 13 (n=9)	2,97	0,849	3,00	1,3	3,8	10,0	8	0,20	0,650	0,20	-1,0	1,0	20,0
	Pre-cycle 25 (n=5)	2,88	0,832	3,00	1,8	4,0	50,0	5	-0,40	0,860	-0,40	-1,6	0,8	50,0
	Pre-cycle 37 (n=4)	2,65	0,998	2,50	1,6	4,0	60,0	3	-0,40	1,311	-0,20	-1,8	0,8	70,0
	Pre-cycle 49 (n=3)	3,00	1,000	3,00	2,0	4,0	70,0	2	NC	NC	NC	-0,8	1,4	80,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.4 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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=4)	58,06	17,317	52,17	44,6	83,3	0,0							
	Pre-cycle 3 (n=4)	61,14	26,778	52,72	39,1	100,0	0,0	4	3,08	10,293	0,54	-5,4	16,7	0,0
	Pre-cycle 5 (n=4)	58,84	29,700	58,15	25,0	94,0	0,0	4	0,78	17,662	1,55	-19,6	19,6	0,0
	Pre-cycle 9 (n=4)	65,01	23,730	67,39	34,8	90,5	0,0	4	6,95	14,237	6,29	-9,8	25,0	0,0
	Pre-cycle 13 (n=3)	69,98	18,151	67,39	53,3	89,3	25,0	3	7,42	9,326	5,95	-1,1	17,4	25,0
	Pre-cycle 25 (n=3)	60,51	5,986	60,87	54,3	66,3	25,0	3	-2,05	23,831	6,52	-29,0	16,3	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	63,0	76,1	50,0	2	NC	NC	NC	-20,3	21,7	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	57,6	63,0	50,0	2	NC	NC	NC	-25,7	8,7	50,0
	Pre-cycle 61 (n=1)	NC	NC	NC	59,8	59,8	75,0	1	NC	NC	NC	-23,6	-23,6	75,0
Raw Total Score	Baseline (n=4)	2,32	0,693	2,09	1,8	3,3	0,0							
	Pre-cycle 3 (n=4)	2,45	1,071	2,11	1,6	4,0	0,0	4	0,12	0,412	0,02	-0,2	0,7	0,0
	Pre-cycle 5 (n=4)	2,35	1,188	2,33	1,0	3,8	0,0	4	0,03	0,706	0,06	-0,8	0,8	0,0
	Pre-cycle 9 (n=4)	2,60	0,949	2,70	1,4	3,6	0,0	4	0,28	0,569	0,25	-0,4	1,0	0,0
	Pre-cycle 13 (n=3)	2,80	0,726	2,70	2,1	3,6	25,0	3	0,30	0,373	0,24	0,0	0,7	25,0
	Pre-cycle 25 (n=3)	2,42	0,239	2,43	2,2	2,7	25,0	3	-0,08	0,953	0,26	-1,2	0,7	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	2,5	3,0	50,0	2	NC	NC	NC	-0,8	0,9	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	2,3	2,5	50,0	2	NC	NC	NC	-1,0	0,3	50,0
	Pre-cycle 61 (n=1)	NC	NC	NC	2,4	2,4	75,0	1	NC	NC	NC	-0,9	-0,9	75,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.4 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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=4)	50,00	25,643	45,31	25,0	84,4	0,0							
	Pre-cycle 3 (n=4)	51,56	34,752	43,75	18,8	100,0	0,0	4	1,56	14,987	3,13	-15,6	15,6	0,0
	Pre-cycle 5 (n=4)	54,69	35,401	46,88	25,0	100,0	0,0	4	4,69	22,893	7,81	-25,0	28,1	0,0
	Pre-cycle 9 (n=4)	53,13	31,664	46,88	25,0	93,8	0,0	4	3,13	19,599	4,69	-21,9	25,0	0,0
	Pre-cycle 13 (n=3)	55,21	34,564	59,38	18,8	87,5	25,0	3	6,25	14,321	3,13	-6,3	21,9	25,0
	Pre-cycle 25 (n=3)	41,67	37,282	53,13	0,0	71,9	25,0	3	-7,29	36,219	-25,00	-31,3	34,4	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	34,4	59,4	50,0	2	NC	NC	NC	-25,0	9,4	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	15,6	59,4	50,0	2	NC	NC	NC	-25,0	-9,4	50,0
	Pre-cycle 61 (n=1)	NC	NC	NC	53,1	53,1	75,0	1	NC	NC	NC	-31,3	-31,3	75,0
Raw Physical functioning	Baseline (n=4)	2,00	1,026	1,81	1,0	3,4	0,0							
	Pre-cycle 3 (n=4)	2,06	1,390	1,75	0,8	4,0	0,0	4	0,06	0,599	0,13	-0,6	0,6	0,0
	Pre-cycle 5 (n=4)	2,19	1,416	1,88	1,0	4,0	0,0	4	0,19	0,916	0,31	-1,0	1,1	0,0
	Pre-cycle 9 (n=4)	2,13	1,267	1,88	1,0	3,8	0,0	4	0,13	0,784	0,19	-0,9	1,0	0,0
	Pre-cycle 13 (n=3)	2,21	1,383	2,38	0,8	3,5	25,0	3	0,25	0,573	0,13	-0,3	0,9	25,0
	Pre-cycle 25 (n=3)	1,67	1,491	2,13	0,0	2,9	25,0	3	-0,29	1,449	-1,00	-1,3	1,4	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	1,4	2,4	50,0	2	NC	NC	NC	-1,0	0,4	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	0,6	2,4	50,0	2	NC	NC	NC	-1,0	-0,4	50,0
	Pre-cycle 61 (n=1)	NC	NC	NC	2,1	2,1	75,0	1	NC	NC	NC	-1,3	-1,3	75,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.4 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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=4)	63,75	29,545	60,00	35,0	100,0	0,0							
	Pre-cycle 3 (n=4)	76,25	33,009	87,50	30,0	100,0	0,0	4	12,50	17,559	12,50	-5,0	30,0	0,0
	Pre-cycle 5 (n=4)	72,50	30,139	80,00	30,0	100,0	0,0	4	8,75	15,478	5,00	-5,0	30,0	0,0
	Pre-cycle 9 (n=4)	80,00	24,152	87,50	45,0	100,0	0,0	4	16,25	17,017	12,50	0,0	40,0	0,0
	Pre-cycle 13 (n=3)	90,00	10,000	90,00	80,0	100,0	25,0	3	16,67	17,559	15,00	0,0	35,0	25,0
	Pre-cycle 25 (n=3)	76,67	20,817	70,00	60,0	100,0	25,0	3	3,33	10,408	0,00	-5,0	15,0	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	70,0	100,0	50,0	2	NC	NC	NC	-5,0	0,0	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	85,0	100,0	50,0	2	NC	NC	NC	0,0	10,0	50,0
	Pre-cycle 61 (n=1)	NC	NC	NC	75,0	75,0	75,0	1	NC	NC	NC	0,0	0,0	75,0
Raw Emotional functioning	Baseline (n=4)	2,55	1,182	2,40	1,4	4,0	0,0							
	Pre-cycle 3 (n=4)	3,05	1,320	3,50	1,2	4,0	0,0	4	0,50	0,702	0,50	-0,2	1,2	0,0
	Pre-cycle 5 (n=4)	2,90	1,206	3,20	1,2	4,0	0,0	4	0,35	0,619	0,20	-0,2	1,2	0,0
	Pre-cycle 9 (n=4)	3,20	0,966	3,50	1,8	4,0	0,0	4	0,65	0,681	0,50	0,0	1,6	0,0
	Pre-cycle 13 (n=3)	3,60	0,400	3,60	3,2	4,0	25,0	3	0,67	0,702	0,60	0,0	1,4	25,0
	Pre-cycle 25 (n=3)	3,07	0,833	2,80	2,4	4,0	25,0	3	0,13	0,416	0,00	-0,2	0,6	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	2,8	4,0	50,0	2	NC	NC	NC	-0,2	0,0	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	3,4	4,0	50,0	2	NC	NC	NC	0,0	0,4	50,0
	Pre-cycle 61 (n=1)	NC	NC	NC	3,0	3,0	75,0	1	NC	NC	NC	0,0	0,0	75,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.4 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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=4)	67,50	28,431	67,50	35,0	100,0	0,0							
	Pre-cycle 3 (n=4)	65,00	26,458	60,00	40,0	100,0	0,0	4	-2,50	6,455	-2,50	-10,0	5,0	0,0
	Pre-cycle 5 (n=4)	60,00	37,639	62,50	15,0	100,0	0,0	4	-7,50	9,574	-5,00	-20,0	0,0	0,0
	Pre-cycle 9 (n=4)	72,50	34,278	82,50	25,0	100,0	0,0	4	5,00	12,247	7,50	-10,0	15,0	0,0
	Pre-cycle 13 (n=3)	80,00	20,000	80,00	60,0	100,0	25,0	3	1,67	2,887	0,00	0,0	5,0	25,0
	Pre-cycle 25 (n=3)	81,67	16,073	75,00	70,0	100,0	25,0	3	3,33	38,188	-5,00	-30,0	45,0	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	80,0	100,0	50,0	2	NC	NC	NC	-20,0	45,0	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	50,0	85,0	50,0	2	NC	NC	NC	-50,0	30,0	50,0
	Pre-cycle 61 (n=1)	NC	NC	NC	60,0	60,0	75,0	1	NC	NC	NC	-40,0	-40,0	75,0
Raw Social functioning	Baseline (n=4)	2,70	1,137	2,70	1,4	4,0	0,0							
	Pre-cycle 3 (n=4)	2,60	1,058	2,40	1,6	4,0	0,0	4	-0,10	0,258	-0,10	-0,4	0,2	0,0
	Pre-cycle 5 (n=4)	2,40	1,506	2,50	0,6	4,0	0,0	4	-0,30	0,383	-0,20	-0,8	0,0	0,0
	Pre-cycle 9 (n=4)	2,90	1,371	3,30	1,0	4,0	0,0	4	0,20	0,490	0,30	-0,4	0,6	0,0
	Pre-cycle 13 (n=3)	3,20	0,800	3,20	2,4	4,0	25,0	3	0,07	0,115	0,00	0,0	0,2	25,0
	Pre-cycle 25 (n=3)	3,27	0,643	3,00	2,8	4,0	25,0	3	0,13	1,528	-0,20	-1,2	1,8	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	3,2	4,0	50,0	2	NC	NC	NC	-0,8	1,8	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	2,0	3,4	50,0	2	NC	NC	NC	-2,0	1,2	50,0
	Pre-cycle 61 (n=1)	NC	NC	NC	2,4	2,4	75,0	1	NC	NC	NC	-1,6	-1,6	75,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.4 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=4) [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=4)	54,17	9,280	52,50	45,0	66,7	0,0							
	Pre-cycle 3 (n=4)	57,50	29,861	50,00	30,0	100,0	0,0	4	3,33	20,950	-2,50	-15,0	33,3	0,0
	Pre-cycle 5 (n=3)	57,78	26,736	60,00	30,0	83,3	25,0	3	2,22	23,590	15,00	-25,0	16,7	25,0
	Pre-cycle 9 (n=4)	59,17	12,802	65,00	40,0	66,7	0,0	4	5,00	12,910	5,00	-10,0	20,0	0,0
	Pre-cycle 13 (n=3)	61,67	11,547	55,00	55,0	75,0	25,0	3	6,11	5,358	8,33	0,0	10,0	25,0
	Pre-cycle 25 (n=3)	53,33	27,538	55,00	25,0	80,0	25,0	3	-2,22	34,974	10,00	-41,7	25,0	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	45,0	95,0	50,0	2	NC	NC	NC	-21,7	40,0	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	35,0	80,0	50,0	2	NC	NC	NC	-31,7	25,0	50,0
	Pre-cycle 61 (n=1)	NC	NC	NC	55,0	55,0	75,0	1	NC	NC	NC	-11,7	-11,7	75,0
Raw School functioning score	Baseline (n=4)	2,17	0,371	2,10	1,8	2,7	0,0							
	Pre-cycle 3 (n=4)	2,30	1,194	2,00	1,2	4,0	0,0	4	0,13	0,838	-0,10	-0,6	1,3	0,0
	Pre-cycle 5 (n=3)	2,31	1,069	2,40	1,2	3,3	25,0	3	0,09	0,944	0,60	-1,0	0,7	25,0
	Pre-cycle 9 (n=4)	2,37	0,512	2,60	1,6	2,7	0,0	4	0,20	0,516	0,20	-0,4	0,8	0,0
	Pre-cycle 13 (n=3)	2,47	0,462	2,20	2,2	3,0	25,0	3	0,24	0,214	0,33	0,0	0,4	25,0
	Pre-cycle 25 (n=3)	2,13	1,102	2,20	1,0	3,2	25,0	3	-0,09	1,399	0,40	-1,7	1,0	25,0
	Pre-cycle 37 (n=2)	NC	NC	NC	1,8	3,8	50,0	2	NC	NC	NC	-0,9	1,6	50,0
	Pre-cycle 49 (n=2)	NC	NC	NC	1,4	3,2	50,0	2	NC	NC	NC	-1,3	1,0	50,0
	Pre-cycle 61 (n=1)	NC	NC	NC	2,2	2,2	75,0	1	NC	NC	NC	-0,5	-0,5	75,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.5 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=2) [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=2)	NC	NC	NC	20,7	75,0	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	43,5	53,3	0,0	2	NC	NC	NC	-21,7	22,8	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	32,6	81,3	0,0	2	NC	NC	NC	6,3	12,0	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	51,1	79,3	0,0	2	NC	NC	NC	-23,9	58,7	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	66,3	78,3	0,0	2	NC	NC	NC	-8,7	57,6	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	66,3	89,1	0,0	2	NC	NC	NC	-8,7	68,5	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	56,5	69,6	0,0	2	NC	NC	NC	-5,4	35,9	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	60,9	65,2	0,0	2	NC	NC	NC	-14,1	44,6	0,0
Raw Total Score	Baseline (n=2)	NC	NC	NC	0,8	3,0	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	1,7	2,1	0,0	2	NC	NC	NC	-0,9	0,9	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	1,3	3,3	0,0	2	NC	NC	NC	0,3	0,5	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	2,0	3,2	0,0	2	NC	NC	NC	-1,0	2,3	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	2,7	3,1	0,0	2	NC	NC	NC	-0,3	2,3	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	2,7	3,6	0,0	2	NC	NC	NC	-0,3	2,7	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	2,3	2,8	0,0	2	NC	NC	NC	-0,2	1,4	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	2,4	2,6	0,0	2	NC	NC	NC	-0,6	1,8	0,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.5 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=2) [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=2)	NC	NC	NC	21,9	87,5	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	34,4	68,8	0,0	2	NC	NC	NC	-18,8	12,5	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	21,9	100,0	0,0	2	NC	NC	NC	0,0	12,5	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	65,6	93,8	0,0	2	NC	NC	NC	-21,9	71,9	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	78,1	87,5	0,0	2	NC	NC	NC	-9,4	65,6	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	81,3	93,8	0,0	2	NC	NC	NC	-6,3	71,9	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	68,8	81,3	0,0	2	NC	NC	NC	-6,3	46,9	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	75,0	75,0	0,0	2	NC	NC	NC	-12,5	53,1	0,0
Raw Physical functioning	Baseline (n=2)	NC	NC	NC	0,9	3,5	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	1,4	2,8	0,0	2	NC	NC	NC	-0,8	0,5	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	0,9	4,0	0,0	2	NC	NC	NC	0,0	0,5	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	2,6	3,8	0,0	2	NC	NC	NC	-0,9	2,9	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	3,1	3,5	0,0	2	NC	NC	NC	-0,4	2,6	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	3,3	3,8	0,0	2	NC	NC	NC	-0,3	2,9	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	2,8	3,3	0,0	2	NC	NC	NC	-0,3	1,9	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	3,0	3,0	0,0	2	NC	NC	NC	-0,5	2,1	0,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.5 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=2) [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=2)	NC	NC	NC	15,0	60,0	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	60,0	65,0	0,0	2	NC	NC	NC	0,0	50,0	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	40,0	75,0	0,0	2	NC	NC	NC	15,0	25,0	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	65,0	90,0	0,0	2	NC	NC	NC	5,0	75,0	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	70,0	75,0	0,0	2	NC	NC	NC	10,0	60,0	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	60,0	85,0	0,0	2	NC	NC	NC	0,0	70,0	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	55,0	75,0	0,0	2	NC	NC	NC	-5,0	60,0	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	45,0	55,0	0,0	2	NC	NC	NC	-5,0	30,0	0,0
Raw Emotional functioning	Baseline (n=2)	NC	NC	NC	0,6	2,4	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	2,4	2,6	0,0	2	NC	NC	NC	0,0	2,0	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	1,6	3,0	0,0	2	NC	NC	NC	0,6	1,0	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	2,6	3,6	0,0	2	NC	NC	NC	0,2	3,0	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	2,8	3,0	0,0	2	NC	NC	NC	0,4	2,4	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	2,4	3,4	0,0	2	NC	NC	NC	0,0	2,8	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	2,2	3,0	0,0	2	NC	NC	NC	-0,2	2,4	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	1,8	2,2	0,0	2	NC	NC	NC	-0,2	1,2	0,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.5 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7
- PN status at enrollment = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=2) [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=2)	NC	NC	NC	10,0	70,0	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	30,0	40,0	0,0	2	NC	NC	NC	-40,0	30,0	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	25,0	70,0	0,0	2	NC	NC	NC	0,0	15,0	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	30,0	75,0	0,0	2	NC	NC	NC	-40,0	65,0	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	50,0	80,0	0,0	2	NC	NC	NC	-20,0	70,0	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	55,0	95,0	0,0	2	NC	NC	NC	-15,0	85,0	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	35,0	60,0	0,0	2	NC	NC	NC	-10,0	25,0	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	65,0	70,0	0,0	2	NC	NC	NC	-5,0	60,0	0,0
Raw Social functioning	Baseline (n=2)	NC	NC	NC	0,4	2,8	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	1,2	1,6	0,0	2	NC	NC	NC	-1,6	1,2	0,0
	Pre-cycle 5 (n=2)	NC	NC	NC	1,0	2,8	0,0	2	NC	NC	NC	0,0	0,6	0,0
	Pre-cycle 9 (n=2)	NC	NC	NC	1,2	3,0	0,0	2	NC	NC	NC	-1,6	2,6	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	2,0	3,2	0,0	2	NC	NC	NC	-0,8	2,8	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	2,2	3,8	0,0	2	NC	NC	NC	-0,6	3,4	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	1,4	2,4	0,0	2	NC	NC	NC	-0,4	1,0	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	2,6	2,8	0,0	2	NC	NC	NC	-0,2	2,4	0,0

[a] Parents/legal guardians of children 3-7 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.

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Table 2.12.3.2.1.5 PedsQL parent-report scores over time and change from baseline over time - Ages 3-7 - PN status at enrollment = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=2) [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=2)	NC	NC	NC	35,0	75,0	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	40,0	45,0	0,0	2	NC	NC	NC	-30,0	5,0	0,0
	Pre-cycle 5 (n=1)	NC	NC	NC	50,0	50,0	50,0	1	NC	NC	NC	15,0	15,0	50,0
	Pre-cycle 9 (n=2)	NC	NC	NC	35,0	50,0	0,0	2	NC	NC	NC	-40,0	15,0	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	60,0	65,0	0,0	2	NC	NC	NC	-15,0	30,0	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	60,0	80,0	0,0	2	NC	NC	NC	-15,0	45,0	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	40,0	75,0	0,0	2	NC	NC	NC	0,0	5,0	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	40,0	65,0	0,0	2	NC	NC	NC	-35,0	30,0	0,0
Raw School functioning score	Baseline (n=2)	NC	NC	NC	1,4	3,0	0,0							
	Pre-cycle 3 (n=2)	NC	NC	NC	1,6	1,8	0,0	2	NC	NC	NC	-1,2	0,2	0,0
	Pre-cycle 5 (n=1)	NC	NC	NC	2,0	2,0	50,0	1	NC	NC	NC	0,6	0,6	50,0
	Pre-cycle 9 (n=2)	NC	NC	NC	1,4	2,0	0,0	2	NC	NC	NC	-1,6	0,6	0,0
	Pre-cycle 13 (n=2)	NC	NC	NC	2,4	2,6	0,0	2	NC	NC	NC	-0,6	1,2	0,0
	Pre-cycle 25 (n=2)	NC	NC	NC	2,4	3,2	0,0	2	NC	NC	NC	-0,6	1,8	0,0
	Pre-cycle 37 (n=2)	NC	NC	NC	1,6	3,0	0,0	2	NC	NC	NC	0,0	0,2	0,0
	Pre-cycle 49 (n=2)	NC	NC	NC	1,6	2,6	0,0	2	NC	NC	NC	-1,4	1,2	0,0

[a] Parents/legal guardians of children 3-7 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.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	7	77.8	40.0, 97.2
	Pre-cycle 9 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=9)	Categories of change [d]			
		Improvement	7	77.8	40.0, 97.2
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	1	11.1	0.3, 48.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 9 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	7	77.8	40.0, 97.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Overall (N=9)	Categories of change [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	3	33.3	7.5, 70.1
		No improvement or deterioration	2	22.2	2.8, 60.0

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 9 (N=9)	Categories of change [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	4	44.4	13.7, 78.8

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Overall (N=9)	Categories of change [d]			
		Improvement	7	77.8	40.0, 97.2
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	1	11.1	0.3, 48.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 9 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	5	55.6	21.2, 86.3

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	3	42.9	9.9, 81.6
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	1	20.0	0.5, 71.6
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Overall (N=9)	Categories of change [d]			
		Improvement	6	66.7	29.9, 92.5
		Deterioration	4	44.4	13.7, 78.8
		No improvement or deterioration	0	0	0, 33.6

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	3	37.5	8.5, 75.5
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 13 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	4	50.0	15.7, 84.3

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	3	60.0	14.7, 94.7
		No improvement or deterioration	0	0	0, 52.2
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	3	60.0	14.7, 94.7
		No improvement or deterioration	0	0	0, 52.2
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Overall (N=9)	Categories of change [d]			
		Improvement	6	66.7	29.9, 92.5
		Deterioration	6	66.7	29.9, 92.5
		No improvement or deterioration	0	0	0, 33.6

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 9 (N=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	5	83.3	35.9, 99.6
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	1	16.7	0.4, 64.1

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	0	0	0, 45.9
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (N=7)	Categories of change [d]			
		Improvement	5	71.4	29.0, 96.3
		Deterioration	3	42.9	9.9, 81.6
		No improvement or deterioration	0	0	0, 41.0

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 9 (N=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	5	83.3	35.9, 99.6
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	0	0	0, 45.9

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (N=7)	Categories of change [d]			
		Improvement	5	71.4	29.0, 96.3
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	0	0	0, 41.0

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 9 (N=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (N=7)	Categories of change [d]			
		Improvement	5	71.4	29.0, 96.3
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	1	14.3	0.4, 57.9

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 9 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (N=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	3	42.9	9.9, 81.6
		No improvement or deterioration	0	0	0, 41.0

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=6)	Categories of change [d]			
		Improvement	0	0	0, 45.9
		Deterioration	3	50.0	11.8, 88.2
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 9 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 13 (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	4	80.0	28.4, 99.5

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	3	50.0	11.8, 88.2
		No improvement or deterioration	2	33.3	4.3, 77.7

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	4	40.0	12.2, 73.8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	4	40.0	12.2, 73.8

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	2	25.0	3.2, 65.1
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	4	80.0	28.4, 99.5
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	1	20.0	0.5, 71.6
	Pre-cycle 49 (N=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
	Overall (N=10)	Categories of change [d]			
		Improvement	8	80.0	44.4, 97.5
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	1	10.0	0.3, 44.5

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	4	40.0	12.2, 73.8
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	4	40.0	12.2, 73.8

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	4	80.0	28.4, 99.5
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	1	20.0	0.5, 71.6
	Pre-cycle 49 (N=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Overall (N=10)	Categories of change [d]			
		Improvement	7	70.0	34.8, 93.3
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	2	20.0	2.5, 55.6

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	3	30.0	6.7, 65.2
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	3	30.0	6.7, 65.2
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	4	40.0	12.2, 73.8

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	4	50.0	15.7, 84.3
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	4	80.0	28.4, 99.5
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	1	20.0	0.5, 71.6
	Pre-cycle 49 (N=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6
	Overall (N=10)	Categories of change [d]			
		Improvement	8	80.0	44.4, 97.5
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	0	0	0, 30.8

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	3	30.0	6.7, 65.2
	Pre-cycle 5 (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	5	50.0	18.7, 81.3

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	3	37.5	8.5, 75.5
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 37 (N=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 49 (N=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8
	Overall (N=10)	Categories of change [d]			
		Improvement	7	70.0	34.8, 93.3
		Deterioration	4	40.0	12.2, 73.8
		No improvement or deterioration	0	0	0, 30.8

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	4	50.0	15.7, 84.3
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	2	25.0	3.2, 65.1
	Pre-cycle 13 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	5	62.5	24.5, 91.5

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	2	40.0	5.3, 85.3
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 37 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	5	55.6	21.2, 86.3
		No improvement or deterioration	1	11.1	0.3, 48.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 13 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	2	50.0	6.8, 93.2
		No improvement or deterioration	0	0	0, 60.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	1	25.0	0.6, 80.6
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	2	66.7	9.4, 99.2
		No improvement or deterioration	0	0	0, 70.8
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Overall (N=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	3	75.0	19.4, 99.4
		No improvement or deterioration	0	0	0, 60.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (N=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Overall (N=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	4	100	39.8, 100
	Pre-cycle 5 (N=4)	Categories of change [d]			
		Improvement	0	0	0, 60.2
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 13 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Overall (N=4)	Categories of change [d]			
		Improvement	2	50.0	6.8, 93.2
		Deterioration	2	50.0	6.8, 93.2
		No improvement or deterioration	0	0	0, 60.2

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	1	25.0	0.6, 80.6
		No improvement or deterioration	2	50.0	6.8, 93.2
	Pre-cycle 5 (N=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	0	0	0, 70.8
	Pre-cycle 9 (N=4)	Categories of change [d]			
		Improvement	1	25.0	0.6, 80.6
		Deterioration	0	0	0, 60.2
		No improvement or deterioration	3	75.0	19.4, 99.4
	Pre-cycle 13 (N=3)	Categories of change [d]			
		Improvement	0	0	0, 70.8
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	3	100	29.2, 100

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	1	33.3	0.8, 90.6
		No improvement or deterioration	1	33.3	0.8, 90.6
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Overall (N=4)	Categories of change [d]			
		Improvement	3	75.0	19.4, 99.4
		Deterioration	3	75.0	19.4, 99.4
		No improvement or deterioration	1	25.0	0.6, 80.6

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 5 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 9 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 13 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req22b5.sas Executed: 2023-06-01T10:35

Table 5.1.2.2.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req22b5.sas Executed: 2023-06-01T10:35

Table 5.1.2.2.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 5 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 9 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 13 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req22b5.sas Executed: 2023-06-01T10:35

Table 5.1.2.2.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req22b5.sas Executed: 2023-06-01T10:35

Table 5.1.2.2.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 5 (N=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 9 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 13 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req22b5.sas Executed: 2023-06-01T10:35

Table 5.1.2.2.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

Program: P:\AZ\Selumetinib\PhaseII\PMR Payer\Prog\Output\req22b5.sas Executed: 2023-06-01T10:35

Table 5.1.2.2.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 5 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 9 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 13 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Overall (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 5 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 9 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 13 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.2.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 2-7 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Pre-cycle 37 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC
	Overall (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	1	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 2 to 7 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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2.1.5.3 Subgruppenanalysen zum PedsQL – Elternberichtet (8-18 Jahre)

Table 2.12.3.2.2.1 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - Gender = Male
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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)	59,99	20,226	55,43	31,9	98,9	0,0							
	Pre-cycle 3 (n=20)	68,30	12,886	66,85	42,4	91,3	4,8	20	9,72	11,233	12,86	-12,0	25,8	4,8
	Pre-cycle 5 (n=20)	70,10	15,161	72,13	45,7	94,6	4,8	20	11,51	12,887	11,38	-15,6	45,7	4,8
	Pre-cycle 9 (n=20)	69,12	15,556	70,65	40,2	94,6	4,8	20	10,53	16,832	12,98	-20,7	37,5	4,8
	Pre-cycle 13 (n=19)	71,68	17,993	68,48	39,1	98,9	9,5	19	12,35	15,676	8,70	-10,9	43,2	9,5
	Pre-cycle 25 (n=14)	80,18	14,817	80,43	55,4	100,0	33,3	14	17,76	17,583	19,93	-12,0	53,3	33,3
	Pre-cycle 37 (n=11)	81,79	14,499	84,72	56,5	98,9	47,6	11	19,86	17,718	22,83	-2,2	59,7	47,6
	Pre-cycle 49 (n=12)	80,95	17,154	85,33	44,6	98,9	42,9	12	20,20	20,353	11,75	-1,1	62,8	42,9
	Pre-cycle 61 (n=3)	81,52	4,738	79,35	78,3	87,0	85,7	3	27,76	16,966	23,91	13,0	46,3	85,7
Raw Total Score	Baseline (n=21)	2,40	0,809	2,22	1,3	4,0	0,0							
	Pre-cycle 3 (n=20)	2,73	0,515	2,67	1,7	3,7	4,8	20	0,39	0,449	0,51	-0,5	1,0	4,8
	Pre-cycle 5 (n=20)	2,80	0,606	2,89	1,8	3,8	4,8	20	0,46	0,515	0,46	-0,6	1,8	4,8
	Pre-cycle 9 (n=20)	2,76	0,622	2,83	1,6	3,8	4,8	20	0,42	0,673	0,52	-0,8	1,5	4,8
	Pre-cycle 13 (n=19)	2,87	0,720	2,74	1,6	4,0	9,5	19	0,49	0,627	0,35	-0,4	1,7	9,5
	Pre-cycle 25 (n=14)	3,21	0,593	3,22	2,2	4,0	33,3	14	0,71	0,703	0,80	-0,5	2,1	33,3
	Pre-cycle 37 (n=11)	3,27	0,580	3,39	2,3	4,0	47,6	11	0,79	0,709	0,91	-0,1	2,4	47,6
	Pre-cycle 49 (n=12)	3,24	0,686	3,41	1,8	4,0	42,9	12	0,81	0,814	0,47	0,0	2,5	42,9
	Pre-cycle 61 (n=3)	3,26	0,190	3,17	3,1	3,5	85,7	3	1,11	0,679	0,96	0,5	1,9	85,7

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.1 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - Gender = Male
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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)	61,61	28,058	68,75	9,4	100,0	0,0							
	Pre-cycle 3 (n=20)	69,53	22,463	73,44	18,8	100,0	4,8	20	9,84	15,251	7,81	-31,3	31,3	4,8
	Pre-cycle 5 (n=20)	68,59	20,290	70,31	21,9	93,8	4,8	20	8,91	19,771	10,94	-18,8	75,0	4,8
	Pre-cycle 9 (n=20)	69,22	25,373	71,88	12,5	100,0	4,8	20	9,53	26,017	15,63	-71,9	37,5	4,8
	Pre-cycle 13 (n=19)	72,53	22,476	78,13	18,8	100,0	9,5	19	11,35	17,867	9,38	-12,5	46,9	9,5
	Pre-cycle 25 (n=14)	83,93	15,449	87,50	53,1	100,0	33,3	14	17,63	20,715	17,19	-21,9	71,9	33,3
	Pre-cycle 37 (n=11)	80,97	18,722	87,50	50,0	100,0	47,6	11	15,91	19,185	15,63	-18,8	56,3	47,6
	Pre-cycle 49 (n=12)	84,64	19,695	93,75	37,5	100,0	42,9	12	20,83	25,643	14,06	-12,5	68,8	42,9
	Pre-cycle 61 (n=3)	82,29	15,729	84,38	65,6	96,9	85,7	3	21,88	25,579	15,63	0,0	50,0	85,7
Raw Physical functioning	Baseline (n=21)	2,46	1,122	2,75	0,4	4,0	0,0							
	Pre-cycle 3 (n=20)	2,78	0,899	2,94	0,8	4,0	4,8	20	0,39	0,610	0,31	-1,3	1,3	4,8
	Pre-cycle 5 (n=20)	2,74	0,812	2,81	0,9	3,8	4,8	20	0,36	0,791	0,44	-0,8	3,0	4,8
	Pre-cycle 9 (n=20)	2,77	1,015	2,88	0,5	4,0	4,8	20	0,38	1,041	0,63	-2,9	1,5	4,8
	Pre-cycle 13 (n=19)	2,90	0,899	3,13	0,8	4,0	9,5	19	0,45	0,715	0,38	-0,5	1,9	9,5
	Pre-cycle 25 (n=14)	3,36	0,618	3,50	2,1	4,0	33,3	14	0,71	0,829	0,69	-0,9	2,9	33,3
	Pre-cycle 37 (n=11)	3,24	0,749	3,50	2,0	4,0	47,6	11	0,64	0,767	0,63	-0,8	2,3	47,6
	Pre-cycle 49 (n=12)	3,39	0,788	3,75	1,5	4,0	42,9	12	0,83	1,026	0,56	-0,5	2,8	42,9
	Pre-cycle 61 (n=3)	3,29	0,629	3,38	2,6	3,9	85,7	3	0,88	1,023	0,63	0,0	2,0	85,7

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.1 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - Gender = Male
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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)	65,48	21,903	65,00	25,0	100,0	0,0							
	Pre-cycle 3 (n=20)	76,25	14,498	75,00	55,0	100,0	4,8	20	12,25	19,633	10,00	-20,0	50,0	4,8
	Pre-cycle 5 (n=20)	76,75	17,568	72,50	45,0	100,0	4,8	20	12,75	18,316	15,00	-35,0	40,0	4,8
	Pre-cycle 9 (n=20)	76,25	20,318	80,00	25,0	100,0	4,8	20	12,25	24,734	15,00	-40,0	50,0	4,8
	Pre-cycle 13 (n=19)	81,05	17,447	85,00	40,0	100,0	9,5	19	16,84	21,552	15,00	-25,0	55,0	9,5
	Pre-cycle 25 (n=14)	86,79	15,764	90,00	55,0	100,0	33,3	14	22,50	25,552	25,00	-20,0	55,0	33,3
	Pre-cycle 37 (n=11)	87,27	12,721	90,00	65,0	100,0	47,6	11	25,45	25,442	30,00	-10,0	60,0	47,6
	Pre-cycle 49 (n=12)	87,50	16,307	95,00	55,0	100,0	42,9	12	25,42	20,830	27,50	-10,0	65,0	42,9
	Pre-cycle 61 (n=3)	85,00	15,000	85,00	70,0	100,0	85,7	3	33,33	15,275	30,00	20,0	50,0	85,7
Raw Emotional functioning	Baseline (n=21)	2,62	0,876	2,60	1,0	4,0	0,0							
	Pre-cycle 3 (n=20)	3,05	0,580	3,00	2,2	4,0	4,8	20	0,49	0,785	0,40	-0,8	2,0	4,8
	Pre-cycle 5 (n=20)	3,07	0,703	2,90	1,8	4,0	4,8	20	0,51	0,733	0,60	-1,4	1,6	4,8
	Pre-cycle 9 (n=20)	3,05	0,813	3,20	1,0	4,0	4,8	20	0,49	0,989	0,60	-1,6	2,0	4,8
	Pre-cycle 13 (n=19)	3,24	0,698	3,40	1,6	4,0	9,5	19	0,67	0,862	0,60	-1,0	2,2	9,5
	Pre-cycle 25 (n=14)	3,47	0,631	3,60	2,2	4,0	33,3	14	0,90	1,022	1,00	-0,8	2,2	33,3
	Pre-cycle 37 (n=11)	3,49	0,509	3,60	2,6	4,0	47,6	11	1,02	1,018	1,20	-0,4	2,4	47,6
	Pre-cycle 49 (n=12)	3,50	0,652	3,80	2,2	4,0	42,9	12	1,02	0,833	1,10	-0,4	2,6	42,9
	Pre-cycle 61 (n=3)	3,40	0,600	3,40	2,8	4,0	85,7	3	1,33	0,611	1,20	0,8	2,0	85,7

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.1 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - Gender = Male (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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)	52,86	24,778	50,00	15,0	100,0	0,0							
	Pre-cycle 3 (n=20)	63,50	18,645	57,50	35,0	95,0	4,8	20	12,00	12,074	15,00	-10,0	35,0	4,8
	Pre-cycle 5 (n=20)	68,75	23,276	75,00	15,0	100,0	4,8	20	17,25	24,574	17,50	-25,0	80,0	4,8
	Pre-cycle 9 (n=20)	64,50	24,165	70,00	20,0	100,0	4,8	20	13,00	19,358	15,00	-20,0	50,0	4,8
	Pre-cycle 13 (n=19)	63,42	26,980	55,00	20,0	100,0	9,5	19	11,32	21,137	5,00	-20,0	55,0	9,5
	Pre-cycle 25 (n=14)	73,21	21,627	77,50	35,0	100,0	33,3	14	15,71	22,690	10,00	-10,0	60,0	33,3
	Pre-cycle 37 (n=11)	75,91	22,893	70,00	40,0	100,0	47,6	11	16,82	24,111	20,00	-15,0	70,0	47,6
	Pre-cycle 49 (n=12)	74,17	26,700	80,00	30,0	100,0	42,9	12	16,67	28,710	15,00	-30,0	70,0	42,9
	Pre-cycle 61 (n=3)	80,00	18,028	85,00	60,0	95,0	85,7	3	35,00	30,000	35,00	5,0	65,0	85,7
Raw Social functioning	Baseline (n=21)	2,11	0,991	2,00	0,6	4,0	0,0							
	Pre-cycle 3 (n=20)	2,54	0,746	2,30	1,4	3,8	4,8	20	0,48	0,483	0,60	-0,4	1,4	4,8
	Pre-cycle 5 (n=20)	2,75	0,931	3,00	0,6	4,0	4,8	20	0,69	0,983	0,70	-1,0	3,2	4,8
	Pre-cycle 9 (n=20)	2,58	0,967	2,80	0,8	4,0	4,8	20	0,52	0,774	0,60	-0,8	2,0	4,8
	Pre-cycle 13 (n=19)	2,54	1,079	2,20	0,8	4,0	9,5	19	0,45	0,845	0,20	-0,8	2,2	9,5
	Pre-cycle 25 (n=14)	2,93	0,865	3,10	1,4	4,0	33,3	14	0,63	0,908	0,40	-0,4	2,4	33,3
	Pre-cycle 37 (n=11)	3,04	0,916	2,80	1,6	4,0	47,6	11	0,67	0,964	0,80	-0,6	2,8	47,6
	Pre-cycle 49 (n=12)	2,97	1,068	3,20	1,2	4,0	42,9	12	0,67	1,148	0,60	-1,2	2,8	42,9
	Pre-cycle 61 (n=3)	3,20	0,721	3,40	2,4	3,8	85,7	3	1,40	1,200	1,40	0,2	2,6	85,7

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.1 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - Gender = Male
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		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)	61,18	18,836	65,00	20,0	95,0	19,0							
	Pre-cycle 3 (n=19)	63,16	17,337	60,00	25,0	95,0	9,5	15	3,67	19,591	0,00	-30,0	40,0	28,6
	Pre-cycle 5 (n=14)	67,14	17,289	65,00	40,0	100,0	33,3	10	6,50	17,646	5,00	-15,0	35,0	52,4
	Pre-cycle 9 (n=16)	65,00	16,733	60,00	40,0	95,0	23,8	13	4,62	19,839	10,00	-45,0	30,0	38,1
	Pre-cycle 13 (n=16)	67,50	23,452	75,00	20,0	100,0	23,8	14	5,36	15,250	2,50	-15,0	35,0	33,3
	Pre-cycle 25 (n=11)	76,82	20,034	75,00	40,0	100,0	47,6	9	15,00	16,583	5,00	0,0	50,0	57,1
	Pre-cycle 37 (n=8)	82,50	17,728	82,50	60,0	100,0	61,9	6	16,67	9,832	20,00	5,0	25,0	71,4
	Pre-cycle 49 (n=9)	74,44	21,858	80,00	45,0	100,0	57,1	6	10,83	7,360	12,50	0,0	20,0	71,4
	Pre-cycle 61 (n=3)	78,33	7,638	80,00	70,0	85,0	85,7	2	NC	NC	NC	10,0	25,0	90,5
Raw School functioning score	Baseline (n=17)	2,45	0,753	2,60	0,8	3,8	19,0							
	Pre-cycle 3 (n=19)	2,53	0,693	2,40	1,0	3,8	9,5	15	0,15	0,784	0,00	-1,2	1,6	28,6
	Pre-cycle 5 (n=14)	2,69	0,692	2,60	1,6	4,0	33,3	10	0,26	0,706	0,20	-0,6	1,4	52,4
	Pre-cycle 9 (n=16)	2,60	0,669	2,40	1,6	3,8	23,8	13	0,18	0,794	0,40	-1,8	1,2	38,1
	Pre-cycle 13 (n=16)	2,70	0,938	3,00	0,8	4,0	23,8	14	0,21	0,610	0,10	-0,6	1,4	33,3
	Pre-cycle 25 (n=11)	3,07	0,801	3,00	1,6	4,0	47,6	9	0,60	0,663	0,20	0,0	2,0	57,1
	Pre-cycle 37 (n=8)	3,30	0,709	3,30	2,4	4,0	61,9	6	0,67	0,393	0,80	0,2	1,0	71,4
	Pre-cycle 49 (n=9)	2,98	0,874	3,20	1,8	4,0	57,1	6	0,43	0,294	0,50	0,0	0,8	71,4
	Pre-cycle 61 (n=3)	3,13	0,306	3,20	2,8	3,4	85,7	2	NC	NC	NC	0,4	1,0	90,5

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.2 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - Gender = Female
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=13) [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=13)	61,79	18,823	61,11	27,2	88,0	0,0							
	Pre-cycle 3 (n=11)	69,87	15,497	70,83	47,8	97,2	15,4	11	8,31	17,147	4,35	-17,4	43,7	15,4
	Pre-cycle 5 (n=12)	66,81	16,279	66,85	30,6	88,9	7,7	12	5,67	12,296	2,60	-11,4	28,3	7,7
	Pre-cycle 9 (n=12)	69,89	20,738	75,10	39,1	98,9	7,7	12	8,75	8,681	9,36	-4,3	23,9	7,7
	Pre-cycle 13 (n=11)	71,99	14,361	75,00	52,8	94,6	15,4	11	12,21	15,727	8,94	-8,3	34,8	15,4
	Pre-cycle 25 (n=9)	72,26	17,178	73,91	38,0	91,7	30,8	9	12,00	17,654	17,39	-22,8	33,7	30,8
	Pre-cycle 37 (n=9)	69,90	13,493	70,65	39,1	82,6	30,8	9	9,63	11,247	8,70	-5,4	23,1	30,8
	Pre-cycle 49 (n=6)	71,56	24,464	78,26	31,5	96,7	53,8	6	9,92	16,482	6,52	-6,8	33,7	53,8
Raw Total Score	Baseline (n=13)	2,47	0,753	2,44	1,1	3,5	0,0							
	Pre-cycle 3 (n=11)	2,79	0,620	2,83	1,9	3,9	15,4	11	0,33	0,686	0,17	-0,7	1,7	15,4
	Pre-cycle 5 (n=12)	2,67	0,651	2,67	1,2	3,6	7,7	12	0,23	0,492	0,10	-0,5	1,1	7,7
	Pre-cycle 9 (n=12)	2,80	0,830	3,00	1,6	4,0	7,7	12	0,35	0,347	0,37	-0,2	1,0	7,7
	Pre-cycle 13 (n=11)	2,88	0,574	3,00	2,1	3,8	15,4	11	0,49	0,629	0,36	-0,3	1,4	15,4
	Pre-cycle 25 (n=9)	2,89	0,687	2,96	1,5	3,7	30,8	9	0,48	0,706	0,70	-0,9	1,3	30,8
	Pre-cycle 37 (n=9)	2,80	0,540	2,83	1,6	3,3	30,8	9	0,39	0,450	0,35	-0,2	0,9	30,8
	Pre-cycle 49 (n=6)	2,86	0,979	3,13	1,3	3,9	53,8	6	0,40	0,659	0,26	-0,3	1,3	53,8

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.2 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - Gender = Female
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=13) [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=13)	62,98	19,634	59,38	25,0	87,5	0,0							
	Pre-cycle 3 (n=11)	67,61	18,449	68,75	40,6	96,9	15,4	11	6,53	16,797	6,25	-12,5	43,8	15,4
	Pre-cycle 5 (n=12)	60,68	20,490	57,81	31,3	90,6	7,7	12	-0,26	11,264	0,00	-25,0	18,8	7,7
	Pre-cycle 9 (n=12)	70,94	22,702	79,69	28,1	100,0	7,7	12	10,01	14,657	7,81	-6,3	43,8	7,7
	Pre-cycle 13 (n=11)	71,02	21,564	65,63	40,6	100,0	15,4	11	12,22	11,814	15,63	-9,4	25,0	15,4
	Pre-cycle 25 (n=9)	80,90	17,777	87,50	50,0	100,0	30,8	9	21,53	13,114	28,13	0,0	37,5	30,8
	Pre-cycle 37 (n=9)	76,39	12,413	75,00	53,1	93,8	30,8	9	17,01	11,808	15,63	-3,1	34,4	30,8
	Pre-cycle 49 (n=6)	73,44	29,630	82,81	28,1	100,0	53,8	6	12,50	25,156	4,69	-21,9	43,8	53,8
Raw Physical functioning	Baseline (n=13)	2,52	0,785	2,38	1,0	3,5	0,0							
	Pre-cycle 3 (n=11)	2,70	0,738	2,75	1,6	3,9	15,4	11	0,26	0,672	0,25	-0,5	1,8	15,4
	Pre-cycle 5 (n=12)	2,43	0,820	2,31	1,3	3,6	7,7	12	-0,01	0,451	0,00	-1,0	0,8	7,7
	Pre-cycle 9 (n=12)	2,84	0,908	3,19	1,1	4,0	7,7	12	0,40	0,586	0,31	-0,3	1,8	7,7
	Pre-cycle 13 (n=11)	2,84	0,863	2,63	1,6	4,0	15,4	11	0,49	0,473	0,63	-0,4	1,0	15,4
	Pre-cycle 25 (n=9)	3,24	0,711	3,50	2,0	4,0	30,8	9	0,86	0,525	1,13	0,0	1,5	30,8
	Pre-cycle 37 (n=9)	3,06	0,497	3,00	2,1	3,8	30,8	9	0,68	0,472	0,63	-0,1	1,4	30,8
	Pre-cycle 49 (n=6)	2,94	1,185	3,31	1,1	4,0	53,8	6	0,50	1,006	0,19	-0,9	1,8	53,8

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.2 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - Gender = Female
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=13) [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=13)	67,31	19,644	75,00	30,0	90,0	0,0							
	Pre-cycle 3 (n=12)	78,75	17,726	82,50	50,0	100,0	7,7	12	10,83	17,034	10,00	-15,0	50,0	7,7
	Pre-cycle 5 (n=12)	78,75	18,602	85,00	35,0	100,0	7,7	12	10,83	18,930	7,50	-20,0	35,0	7,7
	Pre-cycle 9 (n=12)	77,50	18,647	75,00	45,0	100,0	7,7	12	9,58	16,714	7,50	-15,0	40,0	7,7
	Pre-cycle 13 (n=11)	85,91	15,300	90,00	65,0	100,0	15,4	11	19,09	25,673	15,00	-20,0	70,0	15,4
	Pre-cycle 25 (n=9)	78,33	22,913	80,00	45,0	100,0	30,8	9	9,44	24,805	10,00	-25,0	50,0	30,8
	Pre-cycle 37 (n=9)	75,00	18,540	70,00	45,0	100,0	30,8	9	6,11	14,743	5,00	-15,0	35,0	30,8
	Pre-cycle 49 (n=6)	72,50	23,399	65,00	40,0	100,0	53,8	6	5,83	18,280	5,00	-15,0	35,0	53,8
Raw Emotional functioning	Baseline (n=13)	2,69	0,786	3,00	1,2	3,6	0,0							
	Pre-cycle 3 (n=12)	3,15	0,709	3,30	2,0	4,0	7,7	12	0,43	0,681	0,40	-0,6	2,0	7,7
	Pre-cycle 5 (n=12)	3,15	0,744	3,40	1,4	4,0	7,7	12	0,43	0,757	0,30	-0,8	1,4	7,7
	Pre-cycle 9 (n=12)	3,10	0,746	3,00	1,8	4,0	7,7	12	0,38	0,669	0,30	-0,6	1,6	7,7
	Pre-cycle 13 (n=11)	3,44	0,612	3,60	2,6	4,0	15,4	11	0,76	1,027	0,60	-0,8	2,8	15,4
	Pre-cycle 25 (n=9)	3,13	0,917	3,20	1,8	4,0	30,8	9	0,38	0,992	0,40	-1,0	2,0	30,8
	Pre-cycle 37 (n=9)	3,00	0,742	2,80	1,8	4,0	30,8	9	0,24	0,590	0,20	-0,6	1,4	30,8
	Pre-cycle 49 (n=6)	2,90	0,936	2,60	1,6	4,0	53,8	6	0,23	0,731	0,20	-0,6	1,4	53,8

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.2 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - Gender = Female
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=13) [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=13)	59,42	25,211	60,00	25,0	100,0	0,0							
	Pre-cycle 3 (n=11)	69,55	23,607	70,00	15,0	100,0	15,4	11	7,05	21,703	10,00	-30,0	35,0	15,4
	Pre-cycle 5 (n=12)	69,17	20,431	70,00	25,0	100,0	7,7	12	9,79	18,416	0,00	-10,0	45,0	7,7
	Pre-cycle 9 (n=12)	67,50	25,717	75,00	25,0	100,0	7,7	12	8,13	18,063	3,75	-15,0	55,0	7,7
	Pre-cycle 13 (n=11)	70,00	22,472	60,00	40,0	100,0	15,4	11	11,59	25,891	2,50	-30,0	65,0	15,4
	Pre-cycle 25 (n=9)	62,22	28,407	70,00	25,0	100,0	30,8	9	5,28	24,124	10,00	-45,0	35,0	30,8
	Pre-cycle 37 (n=9)	61,94	23,644	75,00	10,0	80,0	30,8	9	5,00	22,256	0,00	-25,0	40,0	30,8
	Pre-cycle 49 (n=6)	75,00	36,056	92,50	10,0	100,0	53,8	6	14,17	31,689	7,50	-25,0	65,0	53,8
Raw Social functioning	Baseline (n=13)	2,38	1,008	2,40	1,0	4,0	0,0							
	Pre-cycle 3 (n=11)	2,78	0,944	2,80	0,6	4,0	15,4	11	0,28	0,868	0,40	-1,2	1,4	15,4
	Pre-cycle 5 (n=12)	2,77	0,817	2,80	1,0	4,0	7,7	12	0,39	0,737	0,00	-0,4	1,8	7,7
	Pre-cycle 9 (n=12)	2,70	1,029	3,00	1,0	4,0	7,7	12	0,33	0,723	0,15	-0,6	2,2	7,7
	Pre-cycle 13 (n=11)	2,80	0,899	2,40	1,6	4,0	15,4	11	0,46	1,036	0,10	-1,2	2,6	15,4
	Pre-cycle 25 (n=9)	2,49	1,136	2,80	1,0	4,0	30,8	9	0,21	0,965	0,40	-1,8	1,4	30,8
	Pre-cycle 37 (n=9)	2,48	0,946	3,00	0,4	3,2	30,8	9	0,20	0,890	0,00	-1,0	1,6	30,8
	Pre-cycle 49 (n=6)	3,00	1,442	3,70	0,4	4,0	53,8	6	0,57	1,268	0,30	-1,0	2,6	53,8

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.2 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - Gender = Female
(Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=13) [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)	56,25	27,313	62,50	15,0	95,0	7,7							
	Pre-cycle 3 (n=6)	60,00	19,494	50,00	45,0	85,0	53,8	5	12,00	35,812	15,00	-40,0	60,0	61,5
	Pre-cycle 5 (n=8)	61,88	16,022	60,00	45,0	90,0	38,5	7	3,57	19,518	10,00	-30,0	25,0	46,2
	Pre-cycle 9 (n=11)	61,36	27,394	55,00	15,0	100,0	15,4	10	8,50	13,550	10,00	-20,0	25,0	23,1
	Pre-cycle 13 (n=10)	62,50	18,745	62,50	35,0	90,0	23,1	10	7,50	29,368	2,50	-45,0	45,0	23,1
	Pre-cycle 25 (n=8)	58,75	22,160	55,00	20,0	85,0	38,5	7	0,71	32,330	5,00	-40,0	60,0	46,2
	Pre-cycle 37 (n=8)	59,38	22,903	60,00	20,0	90,0	38,5	7	-0,71	19,457	5,00	-30,0	20,0	46,2
	Pre-cycle 49 (n=6)	64,17	24,580	70,00	20,0	85,0	53,8	5	2,00	13,964	5,00	-15,0	15,0	61,5
Raw School functioning score	Baseline (n=12)	2,25	1,093	2,50	0,6	3,8	7,7							
	Pre-cycle 3 (n=6)	2,40	0,780	2,00	1,8	3,4	53,8	5	0,48	1,432	0,60	-1,6	2,4	61,5
	Pre-cycle 5 (n=8)	2,48	0,641	2,40	1,8	3,6	38,5	7	0,14	0,781	0,40	-1,2	1,0	46,2
	Pre-cycle 9 (n=11)	2,45	1,096	2,20	0,6	4,0	15,4	10	0,34	0,542	0,40	-0,8	1,0	23,1
	Pre-cycle 13 (n=10)	2,50	0,750	2,50	1,4	3,6	23,1	10	0,30	1,175	0,10	-1,8	1,8	23,1
	Pre-cycle 25 (n=8)	2,35	0,886	2,20	0,8	3,4	38,5	7	0,03	1,293	0,20	-1,6	2,4	46,2
	Pre-cycle 37 (n=8)	2,38	0,916	2,40	0,8	3,6	38,5	7	-0,03	0,778	0,20	-1,2	0,8	46,2
	Pre-cycle 49 (n=6)	2,57	0,983	2,80	0,8	3,4	53,8	5	0,08	0,559	0,20	-0,6	0,6	61,5

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.3 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [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=11)	56,39	21,692	53,26	27,2	98,9	0,0							
	Pre-cycle 3 (n=11)	68,79	10,201	69,57	55,4	87,0	0,0	11	12,40	16,226	16,30	-12,0	43,7	0,0
	Pre-cycle 5 (n=11)	67,13	13,784	64,13	45,7	89,1	0,0	11	10,74	14,643	11,96	-15,6	28,3	0,0
	Pre-cycle 9 (n=11)	66,30	15,764	70,65	39,1	84,8	0,0	11	9,91	19,969	11,96	-20,7	37,5	0,0
	Pre-cycle 13 (n=10)	67,57	16,348	60,33	52,2	98,9	9,1	10	13,15	17,369	10,87	-10,9	43,2	9,1
	Pre-cycle 25 (n=6)	75,86	14,997	77,48	55,6	100,0	45,5	6	20,30	17,020	22,98	0,0	43,2	45,5
	Pre-cycle 37 (n=6)	80,92	15,109	81,25	56,5	96,7	45,5	6	25,36	21,356	26,93	-2,2	59,7	45,5
	Pre-cycle 49 (n=6)	74,96	21,578	72,71	44,6	98,9	45,5	6	19,40	22,360	14,43	-1,1	62,8	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	78,3	79,3	81,8	2	NC	NC	NC	23,9	46,3	81,8
Raw Total Score	Baseline (n=11)	2,26	0,868	2,13	1,1	4,0	0,0							
	Pre-cycle 3 (n=11)	2,75	0,408	2,78	2,2	3,5	0,0	11	0,50	0,649	0,65	-0,5	1,7	0,0
	Pre-cycle 5 (n=11)	2,69	0,551	2,57	1,8	3,6	0,0	11	0,43	0,586	0,48	-0,6	1,1	0,0
	Pre-cycle 9 (n=11)	2,65	0,631	2,83	1,6	3,4	0,0	11	0,40	0,799	0,48	-0,8	1,5	0,0
	Pre-cycle 13 (n=10)	2,70	0,654	2,41	2,1	4,0	9,1	10	0,53	0,695	0,43	-0,4	1,7	9,1
	Pre-cycle 25 (n=6)	3,03	0,600	3,10	2,2	4,0	45,5	6	0,81	0,681	0,92	0,0	1,7	45,5
	Pre-cycle 37 (n=6)	3,24	0,604	3,25	2,3	3,9	45,5	6	1,01	0,854	1,08	-0,1	2,4	45,5
	Pre-cycle 49 (n=6)	3,00	0,863	2,91	1,8	4,0	45,5	6	0,78	0,894	0,58	0,0	2,5	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	3,1	3,2	81,8	2	NC	NC	NC	1,0	1,9	81,8

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.3 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [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=11)	63,64	22,890	68,75	25,0	100,0	0,0							
	Pre-cycle 3 (n=11)	76,99	10,940	78,13	62,5	100,0	0,0	11	13,35	16,600	12,50	-6,3	43,8	0,0
	Pre-cycle 5 (n=11)	66,48	16,482	68,75	43,8	93,8	0,0	11	2,84	13,365	0,00	-18,8	21,9	0,0
	Pre-cycle 9 (n=11)	72,73	18,910	75,00	28,1	100,0	0,0	11	9,09	17,703	12,50	-15,6	34,4	0,0
	Pre-cycle 13 (n=10)	69,38	18,564	67,19	40,6	100,0	9,1	10	7,81	17,384	4,69	-12,5	37,5	9,1
	Pre-cycle 25 (n=6)	82,81	17,650	84,38	53,1	100,0	45,5	6	19,27	11,762	18,75	0,0	34,4	45,5
	Pre-cycle 37 (n=6)	82,81	19,541	90,63	50,0	100,0	45,5	6	19,27	20,099	17,19	0,0	56,3	45,5
	Pre-cycle 49 (n=6)	83,33	24,260	90,63	37,5	100,0	45,5	6	19,79	22,332	12,50	0,0	59,4	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	65,6	84,4	81,8	2	NC	NC	NC	0,0	50,0	81,8
Raw Physical functioning	Baseline (n=11)	2,55	0,916	2,75	1,0	4,0	0,0							
	Pre-cycle 3 (n=11)	3,08	0,438	3,13	2,5	4,0	0,0	11	0,53	0,664	0,50	-0,3	1,8	0,0
	Pre-cycle 5 (n=11)	2,66	0,659	2,75	1,8	3,8	0,0	11	0,11	0,535	0,00	-0,8	0,9	0,0
	Pre-cycle 9 (n=11)	2,91	0,756	3,00	1,1	4,0	0,0	11	0,36	0,708	0,50	-0,6	1,4	0,0
	Pre-cycle 13 (n=10)	2,78	0,743	2,69	1,6	4,0	9,1	10	0,31	0,695	0,19	-0,5	1,5	9,1
	Pre-cycle 25 (n=6)	3,31	0,706	3,38	2,1	4,0	45,5	6	0,77	0,470	0,75	0,0	1,4	45,5
	Pre-cycle 37 (n=6)	3,31	0,782	3,63	2,0	4,0	45,5	6	0,77	0,804	0,69	0,0	2,3	45,5
	Pre-cycle 49 (n=6)	3,33	0,970	3,63	1,5	4,0	45,5	6	0,79	0,893	0,50	0,0	2,4	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	2,6	3,4	81,8	2	NC	NC	NC	0,0	2,0	81,8

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.3 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [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=11)	58,64	26,466	60,00	25,0	100,0	0,0							
	Pre-cycle 3 (n=11)	75,45	12,739	75,00	55,0	100,0	0,0	11	16,82	26,199	20,00	-20,0	50,0	0,0
	Pre-cycle 5 (n=11)	75,45	17,671	70,00	55,0	100,0	0,0	11	16,82	21,127	20,00	-35,0	40,0	0,0
	Pre-cycle 9 (n=11)	76,36	17,334	75,00	35,0	100,0	0,0	11	17,73	28,754	20,00	-40,0	50,0	0,0
	Pre-cycle 13 (n=10)	79,50	17,709	80,00	45,0	100,0	9,1	10	23,00	26,055	12,50	-10,0	70,0	9,1
	Pre-cycle 25 (n=6)	81,67	15,055	82,50	55,0	100,0	45,5	6	30,00	32,094	45,00	-20,0	55,0	45,5
	Pre-cycle 37 (n=6)	82,50	12,942	85,00	65,0	95,0	45,5	6	30,83	31,530	42,50	-10,0	60,0	45,5
	Pre-cycle 49 (n=6)	77,50	17,536	80,00	55,0	100,0	45,5	6	25,83	26,347	25,00	-10,0	65,0	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	70,0	85,0	81,8	2	NC	NC	NC	30,0	50,0	81,8
Raw Emotional functioning	Baseline (n=11)	2,35	1,059	2,40	1,0	4,0	0,0							
	Pre-cycle 3 (n=11)	3,02	0,510	3,00	2,2	4,0	0,0	11	0,67	1,048	0,80	-0,8	2,0	0,0
	Pre-cycle 5 (n=11)	3,02	0,707	2,80	2,2	4,0	0,0	11	0,67	0,845	0,80	-1,4	1,6	0,0
	Pre-cycle 9 (n=11)	3,05	0,693	3,00	1,4	4,0	0,0	11	0,71	1,150	0,80	-1,6	2,0	0,0
	Pre-cycle 13 (n=10)	3,18	0,708	3,20	1,8	4,0	9,1	10	0,92	1,042	0,50	-0,4	2,8	9,1
	Pre-cycle 25 (n=6)	3,27	0,602	3,30	2,2	4,0	45,5	6	1,20	1,284	1,80	-0,8	2,2	45,5
	Pre-cycle 37 (n=6)	3,30	0,518	3,40	2,6	3,8	45,5	6	1,23	1,261	1,70	-0,4	2,4	45,5
	Pre-cycle 49 (n=6)	3,10	0,701	3,20	2,2	4,0	45,5	6	1,03	1,054	1,00	-0,4	2,6	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	2,8	3,4	81,8	2	NC	NC	NC	1,2	2,0	81,8

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.3 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [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=11)	45,91	23,751	40,00	20,0	100,0	0,0							
	Pre-cycle 3 (n=11)	60,00	17,176	55,00	35,0	90,0	0,0	11	14,09	12,613	15,00	-10,0	35,0	0,0
	Pre-cycle 5 (n=11)	63,64	19,886	65,00	25,0	95,0	0,0	11	17,73	21,836	20,00	-15,0	45,0	0,0
	Pre-cycle 9 (n=11)	52,73	24,327	50,00	20,0	90,0	0,0	11	6,82	21,711	5,00	-20,0	50,0	0,0
	Pre-cycle 13 (n=10)	55,50	24,883	50,00	30,0	100,0	9,1	10	12,00	20,710	10,00	-20,0	45,0	9,1
	Pre-cycle 25 (n=6)	65,00	26,077	62,50	35,0	100,0	45,5	6	17,50	25,836	10,00	-10,0	60,0	45,5
	Pre-cycle 37 (n=6)	75,00	25,884	80,00	40,0	100,0	45,5	6	27,50	26,410	22,50	-10,0	70,0	45,5
	Pre-cycle 49 (n=6)	65,83	31,371	62,50	30,0	100,0	45,5	6	18,33	33,267	20,00	-30,0	70,0	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	85,0	95,0	81,8	2	NC	NC	NC	35,0	65,0	81,8
Raw Social functioning	Baseline (n=11)	1,84	0,950	1,60	0,8	4,0	0,0							
	Pre-cycle 3 (n=11)	2,40	0,687	2,20	1,4	3,6	0,0	11	0,56	0,505	0,60	-0,4	1,4	0,0
	Pre-cycle 5 (n=11)	2,55	0,795	2,60	1,0	3,8	0,0	11	0,71	0,873	0,80	-0,6	1,8	0,0
	Pre-cycle 9 (n=11)	2,11	0,973	2,00	0,8	3,6	0,0	11	0,27	0,868	0,20	-0,8	2,0	0,0
	Pre-cycle 13 (n=10)	2,22	0,995	2,00	1,2	4,0	9,1	10	0,48	0,828	0,40	-0,8	1,8	9,1
	Pre-cycle 25 (n=6)	2,60	1,043	2,50	1,4	4,0	45,5	6	0,70	1,033	0,40	-0,4	2,4	45,5
	Pre-cycle 37 (n=6)	3,00	1,035	3,20	1,6	4,0	45,5	6	1,10	1,056	0,90	-0,4	2,8	45,5
	Pre-cycle 49 (n=6)	2,63	1,255	2,50	1,2	4,0	45,5	6	0,73	1,331	0,80	-1,2	2,8	45,5
	Pre-cycle 61 (n=2)	NC	NC	NC	3,4	3,8	81,8	2	NC	NC	NC	1,4	2,6	81,8

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.3 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [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=8)	56,25	27,091	55,00	20,0	95,0	27,3							
	Pre-cycle 3 (n=10)	56,50	17,488	55,00	25,0	85,0	9,1	7	-1,43	21,931	5,00	-30,0	25,0	36,4
	Pre-cycle 5 (n=9)	60,00	16,771	60,00	40,0	90,0	18,2	6	4,17	17,151	5,00	-15,0	25,0	45,5
	Pre-cycle 9 (n=9)	56,11	17,460	50,00	40,0	90,0	18,2	7	0,71	25,889	0,00	-45,0	30,0	36,4
	Pre-cycle 13 (n=8)	63,13	25,903	62,50	20,0	100,0	27,3	6	5,00	8,944	2,50	-5,0	20,0	45,5
	Pre-cycle 25 (n=3)	73,33	23,629	65,00	55,0	100,0	72,7	2	NC	NC	NC	5,0	10,0	81,8
	Pre-cycle 37 (n=3)	78,33	18,930	70,00	65,0	100,0	72,7	1	NC	NC	NC	5,0	5,0	90,9
	Pre-cycle 49 (n=5)	69,00	26,315	55,00	45,0	100,0	54,5	2	NC	NC	NC	0,0	5,0	81,8
	Pre-cycle 61 (n=2)	NC	NC	NC	70,0	80,0	81,8	1	NC	NC	NC	25,0	25,0	90,9
Raw School functioning score	Baseline (n=8)	2,25	1,084	2,20	0,8	3,8	27,3							
	Pre-cycle 3 (n=10)	2,26	0,700	2,20	1,0	3,4	9,1	7	-0,06	0,877	0,20	-1,2	1,0	36,4
	Pre-cycle 5 (n=9)	2,40	0,671	2,40	1,6	3,6	18,2	6	0,17	0,686	0,20	-0,6	1,0	45,5
	Pre-cycle 9 (n=9)	2,24	0,698	2,00	1,6	3,6	18,2	7	0,03	1,036	0,00	-1,8	1,2	36,4
	Pre-cycle 13 (n=8)	2,53	1,036	2,50	0,8	4,0	27,3	6	0,20	0,358	0,10	-0,2	0,8	45,5
	Pre-cycle 25 (n=3)	2,93	0,945	2,60	2,2	4,0	72,7	2	NC	NC	NC	0,2	0,4	81,8
	Pre-cycle 37 (n=3)	3,13	0,757	2,80	2,6	4,0	72,7	1	NC	NC	NC	0,2	0,2	90,9
	Pre-cycle 49 (n=5)	2,76	1,053	2,20	1,8	4,0	54,5	2	NC	NC	NC	0,0	0,2	81,8
	Pre-cycle 61 (n=2)	NC	NC	NC	2,8	3,2	81,8	1	NC	NC	NC	1,0	1,0	90,9

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.4 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [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=11)	67,98	16,821	73,91	43,5	93,5	0,0							
	Pre-cycle 3 (n=10)	72,68	12,300	73,28	51,1	91,3	9,1	10	4,85	11,942	5,43	-17,4	20,7	9,1
	Pre-cycle 5 (n=10)	75,71	15,380	83,12	52,2	94,6	9,1	10	7,88	7,672	8,03	-5,4	21,7	9,1
	Pre-cycle 9 (n=10)	76,91	11,475	75,54	61,1	94,6	9,1	10	9,09	13,100	10,87	-12,0	26,1	9,1
	Pre-cycle 13 (n=9)	80,80	14,814	83,70	51,1	97,8	18,2	9	10,39	17,477	4,35	-9,8	40,2	18,2
	Pre-cycle 25 (n=9)	82,41	15,271	83,70	55,4	100,0	18,2	9	12,00	22,988	7,61	-22,8	53,3	18,2
	Pre-cycle 37 (n=7)	82,63	11,854	80,56	66,3	98,9	36,4	7	10,11	13,442	16,30	-5,4	22,8	36,4
	Pre-cycle 49 (n=7)	86,76	8,070	85,87	75,0	98,6	36,4	7	18,28	20,404	10,87	-3,3	50,8	36,4
	Pre-cycle 61 (n=1)	NC	NC	NC	87,0	87,0	90,9	1	NC	NC	NC	13,0	13,0	90,9
Raw Total Score	Baseline (n=11)	2,72	0,673	2,96	1,7	3,7	0,0							
	Pre-cycle 3 (n=10)	2,91	0,492	2,93	2,0	3,7	9,1	10	0,19	0,478	0,22	-0,7	0,8	9,1
	Pre-cycle 5 (n=10)	3,03	0,615	3,32	2,1	3,8	9,1	10	0,32	0,307	0,32	-0,2	0,9	9,1
	Pre-cycle 9 (n=10)	3,08	0,459	3,02	2,4	3,8	9,1	10	0,36	0,524	0,43	-0,5	1,0	9,1
	Pre-cycle 13 (n=9)	3,23	0,593	3,35	2,0	3,9	18,2	9	0,42	0,699	0,17	-0,4	1,6	18,2
	Pre-cycle 25 (n=9)	3,30	0,611	3,35	2,2	4,0	18,2	9	0,48	0,920	0,30	-0,9	2,1	18,2
	Pre-cycle 37 (n=7)	3,31	0,474	3,22	2,7	4,0	36,4	7	0,40	0,538	0,65	-0,2	0,9	36,4
	Pre-cycle 49 (n=7)	3,47	0,323	3,43	3,0	3,9	36,4	7	0,73	0,816	0,43	-0,1	2,0	36,4
	Pre-cycle 61 (n=1)	NC	NC	NC	3,5	3,5	90,9	1	NC	NC	NC	0,5	0,5	90,9

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.4 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [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=11)	69,60	23,885	81,25	28,1	96,9	0,0							
	Pre-cycle 3 (n=10)	70,94	16,275	73,44	37,5	87,5	9,1	10	3,13	16,601	4,69	-31,3	25,0	9,1
	Pre-cycle 5 (n=10)	72,81	18,165	81,25	40,6	90,6	9,1	10	5,00	10,745	7,81	-12,5	18,8	9,1
	Pre-cycle 9 (n=10)	75,31	23,820	82,81	18,8	100,0	9,1	10	7,50	32,682	17,19	-71,9	37,5	9,1
	Pre-cycle 13 (n=9)	87,50	11,267	81,25	75,0	100,0	18,2	9	15,63	16,756	15,63	-3,1	46,9	18,2
	Pre-cycle 25 (n=9)	88,54	10,364	87,50	71,9	100,0	18,2	9	16,67	25,531	9,38	-21,9	71,9	18,2
	Pre-cycle 37 (n=7)	83,04	13,604	81,25	62,5	100,0	36,4	7	9,38	16,634	12,50	-18,8	34,4	36,4
	Pre-cycle 49 (n=7)	89,29	8,240	93,75	78,1	96,9	36,4	7	16,96	29,584	3,13	-12,5	68,8	36,4
	Pre-cycle 61 (n=1)	NC	NC	NC	96,9	96,9	90,9	1	NC	NC	NC	15,6	15,6	90,9
Raw Physical functioning	Baseline (n=11)	2,78	0,955	3,25	1,1	3,9	0,0							
	Pre-cycle 3 (n=10)	2,84	0,651	2,94	1,5	3,5	9,1	10	0,13	0,664	0,19	-1,3	1,0	9,1
	Pre-cycle 5 (n=10)	2,91	0,727	3,25	1,6	3,6	9,1	10	0,20	0,430	0,31	-0,5	0,8	9,1
	Pre-cycle 9 (n=10)	3,01	0,953	3,31	0,8	4,0	9,1	10	0,30	1,307	0,69	-2,9	1,5	9,1
	Pre-cycle 13 (n=9)	3,50	0,451	3,25	3,0	4,0	18,2	9	0,63	0,670	0,63	-0,1	1,9	18,2
	Pre-cycle 25 (n=9)	3,54	0,415	3,50	2,9	4,0	18,2	9	0,67	1,021	0,38	-0,9	2,9	18,2
	Pre-cycle 37 (n=7)	3,32	0,544	3,25	2,5	4,0	36,4	7	0,38	0,665	0,50	-0,8	1,4	36,4
	Pre-cycle 49 (n=7)	3,57	0,330	3,75	3,1	3,9	36,4	7	0,68	1,183	0,13	-0,5	2,8	36,4
	Pre-cycle 61 (n=1)	NC	NC	NC	3,9	3,9	90,9	1	NC	NC	NC	0,6	0,6	90,9

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.4 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [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=11)	70,91	15,136	65,00	50,0	100,0	0,0							
	Pre-cycle 3 (n=10)	80,50	16,741	85,00	55,0	100,0	9,1	10	8,50	15,284	5,00	-15,0	35,0	9,1
	Pre-cycle 5 (n=10)	80,50	18,477	85,00	45,0	100,0	9,1	10	8,50	19,010	10,00	-20,0	35,0	9,1
	Pre-cycle 9 (n=10)	76,50	23,811	85,00	25,0	100,0	9,1	10	4,50	20,474	2,50	-40,0	30,0	9,1
	Pre-cycle 13 (n=9)	87,78	19,058	95,00	40,0	100,0	18,2	9	14,44	24,167	15,00	-25,0	45,0	18,2
	Pre-cycle 25 (n=9)	80,56	21,570	90,00	50,0	100,0	18,2	9	7,22	25,509	15,00	-25,0	40,0	18,2
	Pre-cycle 37 (n=7)	85,00	16,073	90,00	65,0	100,0	36,4	7	12,14	19,760	15,00	-15,0	40,0	36,4
	Pre-cycle 49 (n=7)	90,00	17,078	100,00	65,0	100,0	36,4	7	20,00	19,791	20,00	-10,0	40,0	36,4
	Pre-cycle 61 (n=1)	NC	NC	NC	100,0	100,0	90,9	1	NC	NC	NC	20,0	20,0	90,9
Raw Emotional functioning	Baseline (n=11)	2,84	0,605	2,60	2,0	4,0	0,0							
	Pre-cycle 3 (n=10)	3,22	0,670	3,40	2,2	4,0	9,1	10	0,34	0,611	0,20	-0,6	1,4	9,1
	Pre-cycle 5 (n=10)	3,22	0,739	3,40	1,8	4,0	9,1	10	0,34	0,760	0,40	-0,8	1,4	9,1
	Pre-cycle 9 (n=10)	3,06	0,952	3,40	1,0	4,0	9,1	10	0,18	0,819	0,10	-1,6	1,2	9,1
	Pre-cycle 13 (n=9)	3,51	0,762	3,80	1,6	4,0	18,2	9	0,58	0,967	0,60	-1,0	1,8	18,2
	Pre-cycle 25 (n=9)	3,22	0,863	3,60	2,0	4,0	18,2	9	0,29	1,020	0,60	-1,0	1,6	18,2
	Pre-cycle 37 (n=7)	3,40	0,643	3,60	2,6	4,0	36,4	7	0,49	0,790	0,60	-0,6	1,6	36,4
	Pre-cycle 49 (n=7)	3,60	0,683	4,00	2,6	4,0	36,4	7	0,80	0,792	0,80	-0,4	1,6	36,4
	Pre-cycle 61 (n=1)	NC	NC	NC	4,0	4,0	90,9	1	NC	NC	NC	0,8	0,8	90,9

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.4 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [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=11)	65,91	19,341	65,00	40,0	100,0	0,0							
	Pre-cycle 3 (n=10)	72,00	19,607	77,50	40,0	95,0	9,1	10	5,50	15,357	10,00	-30,0	25,0	9,1
	Pre-cycle 5 (n=10)	73,50	25,172	77,50	15,0	100,0	9,1	10	7,00	16,021	2,50	-25,0	30,0	9,1
	Pre-cycle 9 (n=10)	80,50	13,427	82,50	55,0	100,0	9,1	10	14,00	14,298	17,50	-15,0	30,0	9,1
	Pre-cycle 13 (n=9)	74,44	22,700	75,00	45,0	100,0	18,2	9	5,00	22,913	0,00	-30,0	35,0	18,2
	Pre-cycle 25 (n=9)	78,33	21,065	85,00	45,0	100,0	18,2	9	8,89	27,016	5,00	-45,0	40,0	18,2
	Pre-cycle 37 (n=7)	77,86	17,525	75,00	55,0	100,0	36,4	7	5,00	12,583	5,00	-15,0	25,0	36,4
	Pre-cycle 49 (n=7)	87,14	19,970	95,00	45,0	100,0	36,4	7	19,29	24,054	15,00	-10,0	60,0	36,4
	Pre-cycle 61 (n=1)	NC	NC	NC	60,0	60,0	90,9	1	NC	NC	NC	5,0	5,0	90,9
Raw Social functioning	Baseline (n=11)	2,64	0,774	2,60	1,6	4,0	0,0							
	Pre-cycle 3 (n=10)	2,88	0,784	3,10	1,6	3,8	9,1	10	0,22	0,614	0,40	-1,2	1,0	9,1
	Pre-cycle 5 (n=10)	2,94	1,007	3,10	0,6	4,0	9,1	10	0,28	0,641	0,10	-1,0	1,2	9,1
	Pre-cycle 9 (n=10)	3,22	0,537	3,30	2,2	4,0	9,1	10	0,56	0,572	0,70	-0,6	1,2	9,1
	Pre-cycle 13 (n=9)	2,98	0,908	3,00	1,8	4,0	18,2	9	0,20	0,917	0,00	-1,2	1,4	18,2
	Pre-cycle 25 (n=9)	3,13	0,843	3,40	1,8	4,0	18,2	9	0,36	1,081	0,20	-1,8	1,6	18,2
	Pre-cycle 37 (n=7)	3,11	0,701	3,00	2,2	4,0	36,4	7	0,20	0,503	0,20	-0,6	1,0	36,4
	Pre-cycle 49 (n=7)	3,49	0,799	3,80	1,8	4,0	36,4	7	0,77	0,962	0,60	-0,4	2,4	36,4
	Pre-cycle 61 (n=1)	NC	NC	NC	2,4	2,4	90,9	1	NC	NC	NC	0,2	0,2	90,9

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.4 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=11) [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=11)	64,55	19,552	70,00	35,0	95,0	0,0							
	Pre-cycle 3 (n=8)	67,50	16,690	70,00	45,0	95,0	27,3	8	2,50	20,529	2,50	-40,0	25,0	27,3
	Pre-cycle 5 (n=6)	81,67	12,910	82,50	65,0	100,0	45,5	6	16,67	14,376	17,50	-5,0	35,0	45,5
	Pre-cycle 9 (n=8)	77,50	14,880	82,50	50,0	95,0	27,3	8	12,50	10,000	10,00	-5,0	30,0	27,3
	Pre-cycle 13 (n=9)	69,44	23,511	75,00	25,0	100,0	18,2	9	3,33	26,810	0,00	-45,0	40,0	18,2
	Pre-cycle 25 (n=8)	76,88	22,351	77,50	40,0	100,0	27,3	8	7,50	27,903	5,00	-40,0	50,0	27,3
	Pre-cycle 37 (n=6)	85,00	17,889	92,50	60,0	100,0	45,5	6	10,00	21,909	20,00	-30,0	25,0	45,5
	Pre-cycle 49 (n=6)	75,83	15,943	77,50	55,0	95,0	45,5	6	10,00	12,649	15,00	-15,0	20,0	45,5
	Pre-cycle 61 (n=1)	NC	NC	NC	85,0	85,0	90,9	1	NC	NC	NC	10,0	10,0	90,9
Raw School functioning score	Baseline (n=11)	2,58	0,782	2,80	1,4	3,8	0,0							
	Pre-cycle 3 (n=8)	2,70	0,668	2,80	1,8	3,8	27,3	8	0,10	0,821	0,10	-1,6	1,0	27,3
	Pre-cycle 5 (n=6)	3,27	0,516	3,30	2,6	4,0	45,5	6	0,67	0,575	0,70	-0,2	1,4	45,5
	Pre-cycle 9 (n=8)	3,10	0,595	3,30	2,0	3,8	27,3	8	0,50	0,400	0,40	-0,2	1,2	27,3
	Pre-cycle 13 (n=9)	2,78	0,940	3,00	1,0	4,0	18,2	9	0,13	1,072	0,00	-1,8	1,6	18,2
	Pre-cycle 25 (n=8)	3,08	0,894	3,10	1,6	4,0	27,3	8	0,30	1,116	0,20	-1,6	2,0	27,3
	Pre-cycle 37 (n=6)	3,40	0,716	3,70	2,4	4,0	45,5	6	0,40	0,876	0,80	-1,2	1,0	45,5
	Pre-cycle 49 (n=6)	3,03	0,638	3,10	2,2	3,8	45,5	6	0,40	0,506	0,60	-0,6	0,8	45,5
	Pre-cycle 61 (n=1)	NC	NC	NC	3,4	3,4	90,9	1	NC	NC	NC	0,4	0,4	90,9

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.5 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=12) [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=12)	57,91	19,173	58,70	33,7	88,0	0,0							
	Pre-cycle 3 (n=10)	65,11	17,906	62,59	42,4	97,2	16,7	10	10,08	11,183	10,39	-8,9	29,3	16,7
	Pre-cycle 5 (n=11)	64,38	16,161	63,04	30,6	87,0	8,3	11	9,21	15,356	9,78	-11,4	45,7	8,3
	Pre-cycle 9 (n=11)	65,69	22,002	58,70	39,1	98,9	8,3	11	10,51	8,324	10,03	-2,4	23,9	8,3
	Pre-cycle 13 (n=11)	68,27	16,385	75,00	39,1	91,7	8,3	11	13,10	13,003	18,48	-8,3	28,3	8,3
	Pre-cycle 25 (n=8)	72,01	17,311	71,74	38,0	91,3	33,3	8	15,85	10,479	17,39	1,9	33,7	33,3
	Pre-cycle 37 (n=7)	66,40	14,026	66,30	39,1	82,6	41,7	7	11,75	8,368	8,70	3,0	23,1	41,7
	Pre-cycle 49 (n=5)	68,73	26,655	70,83	31,5	96,7	58,3	5	11,51	16,910	9,96	-6,8	33,7	58,3
Raw Total Score	Baseline (n=12)	2,32	0,767	2,35	1,3	3,5	0,0							
	Pre-cycle 3 (n=10)	2,60	0,716	2,50	1,7	3,9	16,7	10	0,40	0,447	0,42	-0,4	1,2	16,7
	Pre-cycle 5 (n=11)	2,58	0,646	2,52	1,2	3,5	8,3	11	0,37	0,614	0,39	-0,5	1,8	8,3
	Pre-cycle 9 (n=11)	2,63	0,880	2,35	1,6	4,0	8,3	11	0,42	0,333	0,40	-0,1	1,0	8,3
	Pre-cycle 13 (n=11)	2,73	0,655	3,00	1,6	3,7	8,3	11	0,52	0,520	0,74	-0,3	1,1	8,3
	Pre-cycle 25 (n=8)	2,88	0,692	2,87	1,5	3,7	33,3	8	0,63	0,419	0,70	0,1	1,3	33,3
	Pre-cycle 37 (n=7)	2,66	0,561	2,65	1,6	3,3	41,7	7	0,47	0,335	0,35	0,1	0,9	41,7
	Pre-cycle 49 (n=5)	2,75	1,066	2,83	1,3	3,9	58,3	5	0,46	0,676	0,40	-0,3	1,3	58,3

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.5 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=12) [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=12)	53,91	26,952	53,13	9,4	100,0	0,0							
	Pre-cycle 3 (n=10)	57,81	28,764	53,13	18,8	100,0	16,7	10	9,06	13,048	9,38	-12,5	28,1	16,7
	Pre-cycle 5 (n=11)	58,24	24,696	56,25	21,9	93,8	8,3	11	8,52	25,391	6,25	-25,0	75,0	8,3
	Pre-cycle 9 (n=11)	62,05	28,606	56,25	12,5	100,0	8,3	11	12,34	15,328	9,38	-6,3	43,8	8,3
	Pre-cycle 13 (n=11)	61,65	24,964	62,50	18,8	96,9	8,3	11	11,93	13,751	9,38	-9,4	37,5	8,3
	Pre-cycle 25 (n=8)	76,17	19,332	82,81	50,0	96,9	33,3	8	21,88	12,045	25,00	0,0	37,5	33,3
	Pre-cycle 37 (n=7)	71,43	14,255	75,00	53,1	93,8	41,7	7	20,98	9,835	25,00	3,1	34,4	41,7
	Pre-cycle 49 (n=5)	66,25	32,431	56,25	28,1	100,0	58,3	5	17,50	26,937	18,75	-21,9	43,8	58,3
Raw Physical functioning	Baseline (n=12)	2,16	1,078	2,13	0,4	4,0	0,0							
	Pre-cycle 3 (n=10)	2,31	1,151	2,13	0,8	4,0	16,7	10	0,36	0,522	0,38	-0,5	1,1	16,7
	Pre-cycle 5 (n=11)	2,33	0,988	2,25	0,9	3,8	8,3	11	0,34	1,016	0,25	-1,0	3,0	8,3
	Pre-cycle 9 (n=11)	2,48	1,144	2,25	0,5	4,0	8,3	11	0,49	0,613	0,38	-0,3	1,8	8,3
	Pre-cycle 13 (n=11)	2,47	0,999	2,50	0,8	3,9	8,3	11	0,48	0,550	0,38	-0,4	1,5	8,3
	Pre-cycle 25 (n=8)	3,05	0,773	3,31	2,0	3,9	33,3	8	0,88	0,482	1,00	0,0	1,5	33,3
	Pre-cycle 37 (n=7)	2,86	0,570	3,00	2,1	3,8	41,7	7	0,84	0,393	1,00	0,1	1,4	41,7
	Pre-cycle 49 (n=5)	2,65	1,297	2,25	1,1	4,0	58,3	5	0,70	1,077	0,75	-0,9	1,8	58,3

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.5 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=12) [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=12)	68,75	19,084	70,00	40,0	95,0	0,0							
	Pre-cycle 3 (n=11)	75,91	17,863	75,00	50,0	100,0	8,3	11	9,55	10,596	10,00	-5,0	30,0	8,3
	Pre-cycle 5 (n=11)	76,82	18,340	75,00	35,0	100,0	8,3	11	10,45	14,909	5,00	-15,0	35,0	8,3
	Pre-cycle 9 (n=11)	77,27	18,890	80,00	45,0	100,0	8,3	11	10,91	13,382	10,00	-15,0	30,0	8,3
	Pre-cycle 13 (n=11)	81,82	13,833	80,00	65,0	100,0	8,3	11	15,45	19,424	15,00	-20,0	45,0	8,3
	Pre-cycle 25 (n=8)	88,13	19,628	100,00	45,0	100,0	33,3	8	19,38	17,204	12,50	0,0	50,0	33,3
	Pre-cycle 37 (n=7)	77,86	20,587	75,00	45,0	100,0	41,7	7	9,29	13,048	5,00	-5,0	35,0	41,7
	Pre-cycle 49 (n=5)	78,00	25,642	85,00	40,0	100,0	58,3	5	9,00	18,507	10,00	-15,0	35,0	58,3
Raw Emotional functioning	Baseline (n=12)	2,75	0,763	2,80	1,6	3,8	0,0							
	Pre-cycle 3 (n=11)	3,04	0,715	3,00	2,0	4,0	8,3	11	0,38	0,424	0,40	-0,2	1,2	8,3
	Pre-cycle 5 (n=11)	3,07	0,734	3,00	1,4	4,0	8,3	11	0,42	0,596	0,20	-0,6	1,4	8,3
	Pre-cycle 9 (n=11)	3,09	0,756	3,20	1,8	4,0	8,3	11	0,44	0,535	0,40	-0,6	1,2	8,3
	Pre-cycle 13 (n=11)	3,27	0,553	3,20	2,6	4,0	8,3	11	0,62	0,777	0,60	-0,8	1,8	8,3
	Pre-cycle 25 (n=8)	3,53	0,785	4,00	1,8	4,0	33,3	8	0,78	0,688	0,50	0,0	2,0	33,3
	Pre-cycle 37 (n=7)	3,11	0,823	3,00	1,8	4,0	41,7	7	0,37	0,522	0,20	-0,2	1,4	41,7
	Pre-cycle 49 (n=5)	3,12	1,026	3,40	1,6	4,0	58,3	5	0,36	0,740	0,40	-0,6	1,4	58,3

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.5 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18 - PN status at enrollment = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=12) [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=12)	54,38	28,045	45,00	15,0	100,0	0,0							
	Pre-cycle 3 (n=10)	65,50	24,204	70,00	15,0	100,0	16,7	10	10,75	19,862	10,00	-22,5	35,0	16,7
	Pre-cycle 5 (n=11)	70,00	21,679	75,00	25,0	100,0	8,3	11	17,95	27,812	12,50	-10,0	80,0	8,3
	Pre-cycle 9 (n=11)	65,00	26,173	55,00	35,0	100,0	8,3	11	12,95	20,026	5,00	-5,0	55,0	8,3
	Pre-cycle 13 (n=11)	68,18	26,389	65,00	20,0	100,0	8,3	11	16,14	24,631	5,00	-10,0	65,0	8,3
	Pre-cycle 25 (n=8)	61,25	26,424	70,00	25,0	100,0	33,3	8	10,31	18,824	10,00	-10,0	40,0	33,3
	Pre-cycle 37 (n=7)	56,79	24,779	65,00	10,0	80,0	41,7	7	4,29	25,278	0,00	-25,0	40,0	41,7
	Pre-cycle 49 (n=5)	67,00	35,986	80,00	10,0	100,0	58,3	5	8,00	34,205	-5,00	-25,0	65,0	58,3
Raw Social functioning	Baseline (n=12)	2,18	1,122	1,80	0,6	4,0	0,0							
	Pre-cycle 3 (n=10)	2,62	0,968	2,80	0,6	4,0	16,7	10	0,43	0,794	0,40	-0,9	1,4	16,7
	Pre-cycle 5 (n=11)	2,80	0,867	3,00	1,0	4,0	8,3	11	0,72	1,112	0,50	-0,4	3,2	8,3
	Pre-cycle 9 (n=11)	2,60	1,047	2,20	1,4	4,0	8,3	11	0,52	0,801	0,20	-0,2	2,2	8,3
	Pre-cycle 13 (n=11)	2,73	1,056	2,60	0,8	4,0	8,3	11	0,65	0,985	0,20	-0,4	2,6	8,3
	Pre-cycle 25 (n=8)	2,45	1,057	2,80	1,0	4,0	33,3	8	0,41	0,753	0,40	-0,4	1,6	33,3
	Pre-cycle 37 (n=7)	2,27	0,991	2,60	0,4	3,2	41,7	7	0,17	1,011	0,00	-1,0	1,6	41,7
	Pre-cycle 49 (n=5)	2,68	1,439	3,20	0,4	4,0	58,3	5	0,32	1,368	-0,20	-1,0	2,6	58,3

[a] Parents/legal guardians of children 8 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.

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Table 2.12.3.2.2.5 PedsQL parent-report scores over time and change from baseline over time - Ages 8-18
- PN status at enrollment = Unknown (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

		Selumetinib 25 mg/m² BID (N=12) [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=10)	55,50	22,540	65,00	15,0	80,0	16,7							
	Pre-cycle 3 (n=7)	65,00	18,484	60,00	45,0	95,0	41,7	5	21,00	28,810	15,00	-10,0	60,0	58,3
	Pre-cycle 5 (n=7)	57,86	9,063	55,00	45,0	70,0	41,7	5	-7,00	16,432	-10,00	-30,0	15,0	58,3
	Pre-cycle 9 (n=10)	59,00	24,810	57,50	15,0	100,0	16,7	8	5,00	13,093	5,00	-20,0	20,0	33,3
	Pre-cycle 13 (n=9)	63,89	16,729	70,00	35,0	80,0	25,0	9	10,00	23,585	5,00	-25,0	45,0	25,0
	Pre-cycle 25 (n=8)	60,00	21,213	65,00	20,0	85,0	33,3	6	10,83	27,462	7,50	-25,0	60,0	50,0
	Pre-cycle 37 (n=7)	55,71	21,297	55,00	20,0	80,0	41,7	6	5,00	15,811	7,50	-25,0	20,0	50,0
	Pre-cycle 49 (n=4)	63,75	30,653	75,00	20,0	85,0	66,7	3	3,33	12,583	5,00	-10,0	15,0	75,0
Raw School functioning score	Baseline (n=10)	2,22	0,902	2,60	0,6	3,2	16,7							
	Pre-cycle 3 (n=7)	2,60	0,739	2,40	1,8	3,8	41,7	5	0,84	1,152	0,60	-0,4	2,4	58,3
	Pre-cycle 5 (n=7)	2,31	0,363	2,20	1,8	2,8	41,7	5	-0,28	0,657	-0,40	-1,2	0,6	58,3
	Pre-cycle 9 (n=10)	2,36	0,992	2,30	0,6	4,0	16,7	8	0,20	0,524	0,20	-0,8	0,8	33,3
	Pre-cycle 13 (n=9)	2,56	0,669	2,80	1,4	3,2	25,0	9	0,40	0,943	0,20	-1,0	1,8	25,0
	Pre-cycle 25 (n=8)	2,40	0,849	2,60	0,8	3,4	33,3	6	0,43	1,098	0,30	-1,0	2,4	50,0
	Pre-cycle 37 (n=7)	2,23	0,852	2,20	0,8	3,2	41,7	6	0,20	0,632	0,30	-1,0	0,8	50,0
	Pre-cycle 49 (n=4)	2,55	1,226	3,00	0,8	3,4	66,7	3	0,13	0,503	0,20	-0,4	0,6	75,0

[a] Parents/legal guardians of children 8 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.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=20)	Categories of change [d]			
		Improvement	9	45.0	23.1, 68.5
		Deterioration	0	0	0, 16.8
		No improvement or deterioration	11	55.0	31.5, 76.9
	Pre-cycle 5 (N=20)	Categories of change [d]			
		Improvement	6	30.0	11.9, 54.3
		Deterioration	1	5.0	0.1, 24.9
		No improvement or deterioration	13	65.0	40.8, 84.6
	Pre-cycle 9 (N=20)	Categories of change [d]			
		Improvement	9	45.0	23.1, 68.5
		Deterioration	2	10.0	1.2, 31.7
		No improvement or deterioration	9	45.0	23.1, 68.5
	Pre-cycle 13 (N=19)	Categories of change [d]			
		Improvement	8	42.1	20.3, 66.5
		Deterioration	0	0	0, 17.6
		No improvement or deterioration	11	57.9	33.5, 79.7

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	8	57.1	28.9, 82.3
		Deterioration	0	0	0, 23.2
		No improvement or deterioration	6	42.9	17.7, 71.1
	Pre-cycle 37 (N=11)	Categories of change [d]			
		Improvement	7	63.6	30.8, 89.1
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	4	36.4	10.9, 69.2
	Pre-cycle 49 (N=12)	Categories of change [d]			
		Improvement	5	41.7	15.2, 72.3
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	7	58.3	27.7, 84.8
	Pre-cycle 61 (N=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=20)	Categories of change [d]			
		Improvement	16	80.0	56.3, 94.3
		Deterioration	2	10.0	1.2, 31.7
		No improvement or deterioration	3	15.0	3.2, 37.9

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=20)	Categories of change [d]			
		Improvement	7	35.0	15.4, 59.2
		Deterioration	1	5.0	0.1, 24.9
		No improvement or deterioration	12	60.0	36.1, 80.9
	Pre-cycle 5 (N=20)	Categories of change [d]			
		Improvement	6	30.0	11.9, 54.3
		Deterioration	1	5.0	0.1, 24.9
		No improvement or deterioration	13	65.0	40.8, 84.6
	Pre-cycle 9 (N=20)	Categories of change [d]			
		Improvement	11	55.0	31.5, 76.9
		Deterioration	3	15.0	3.2, 37.9
		No improvement or deterioration	6	30.0	11.9, 54.3
	Pre-cycle 13 (N=19)	Categories of change [d]			
		Improvement	8	42.1	20.3, 66.5
		Deterioration	0	0	0, 17.6
		No improvement or deterioration	11	57.9	33.5, 79.7

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	9	64.3	35.1, 87.2
		Deterioration	1	7.1	0.2, 33.9
		No improvement or deterioration	4	28.6	8.4, 58.1
	Pre-cycle 37 (N=11)	Categories of change [d]			
		Improvement	7	63.6	30.8, 89.1
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	3	27.3	6.0, 61.0
	Pre-cycle 49 (N=12)	Categories of change [d]			
		Improvement	6	50.0	21.1, 78.9
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	6	50.0	21.1, 78.9
	Pre-cycle 61 (N=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Overall (N=20)	Categories of change [d]			
		Improvement	16	80.0	56.3, 94.3
		Deterioration	4	20.0	5.7, 43.7
		No improvement or deterioration	1	5.0	0.1, 24.9

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=20)	Categories of change [d]			
		Improvement	10	50.0	27.2, 72.8
		Deterioration	3	15.0	3.2, 37.9
		No improvement or deterioration	7	35.0	15.4, 59.2
	Pre-cycle 5 (N=20)	Categories of change [d]			
		Improvement	12	60.0	36.1, 80.9
		Deterioration	2	10.0	1.2, 31.7
		No improvement or deterioration	6	30.0	11.9, 54.3
	Pre-cycle 9 (N=20)	Categories of change [d]			
		Improvement	11	55.0	31.5, 76.9
		Deterioration	3	15.0	3.2, 37.9
		No improvement or deterioration	6	30.0	11.9, 54.3
	Pre-cycle 13 (N=19)	Categories of change [d]			
		Improvement	10	52.6	28.9, 75.6
		Deterioration	1	5.3	0.1, 26.0
		No improvement or deterioration	8	42.1	20.3, 66.5

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	9	64.3	35.1, 87.2
		Deterioration	1	7.1	0.2, 33.9
		No improvement or deterioration	4	28.6	8.4, 58.1
	Pre-cycle 37 (N=11)	Categories of change [d]			
		Improvement	7	63.6	30.8, 89.1
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	4	36.4	10.9, 69.2
	Pre-cycle 49 (N=12)	Categories of change [d]			
		Improvement	9	75.0	42.8, 94.5
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	3	25.0	5.5, 57.2
	Pre-cycle 61 (N=3)	Categories of change [d]			
		Improvement	3	100	29.2, 100
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	0	0	0, 70.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Overall (N=20)	Categories of change [d]			
		Improvement	17	85.0	62.1, 96.8
		Deterioration	4	20.0	5.7, 43.7
		No improvement or deterioration	2	10.0	1.2, 31.7

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=20)	Categories of change [d]			
		Improvement	11	55.0	31.5, 76.9
		Deterioration	0	0	0, 16.8
		No improvement or deterioration	9	45.0	23.1, 68.5
	Pre-cycle 5 (N=20)	Categories of change [d]			
		Improvement	13	65.0	40.8, 84.6
		Deterioration	3	15.0	3.2, 37.9
		No improvement or deterioration	4	20.0	5.7, 43.7
	Pre-cycle 9 (N=20)	Categories of change [d]			
		Improvement	11	55.0	31.5, 76.9
		Deterioration	2	10.0	1.2, 31.7
		No improvement or deterioration	7	35.0	15.4, 59.2
	Pre-cycle 13 (N=19)	Categories of change [d]			
		Improvement	7	36.8	16.3, 61.6
		Deterioration	2	10.5	1.3, 33.1
		No improvement or deterioration	10	52.6	28.9, 75.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=14)	Categories of change [d]			
		Improvement	7	50.0	23.0, 77.0
		Deterioration	0	0	0, 23.2
		No improvement or deterioration	7	50.0	23.0, 77.0
	Pre-cycle 37 (N=11)	Categories of change [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	4	36.4	10.9, 69.2
	Pre-cycle 49 (N=12)	Categories of change [d]			
		Improvement	7	58.3	27.7, 84.8
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	4	33.3	9.9, 65.1
	Pre-cycle 61 (N=3)	Categories of change [d]			
		Improvement	2	66.7	9.4, 99.2
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	1	33.3	0.8, 90.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Overall (N=20)	Categories of change [d]			
		Improvement	15	75.0	50.9, 91.3
		Deterioration	8	40.0	19.1, 63.9
		No improvement or deterioration	1	5.0	0.1, 24.9

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=15)	Categories of change [d]			
		Improvement	4	26.7	7.8, 55.1
		Deterioration	3	20.0	4.3, 48.1
		No improvement or deterioration	8	53.3	26.6, 78.7
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 9 (N=13)	Categories of change [d]			
		Improvement	4	30.8	9.1, 61.4
		Deterioration	2	15.4	1.9, 45.4
		No improvement or deterioration	7	53.8	25.1, 80.8
	Pre-cycle 13 (N=14)	Categories of change [d]			
		Improvement	4	28.6	8.4, 58.1
		Deterioration	2	14.3	1.8, 42.8
		No improvement or deterioration	8	57.1	28.9, 82.3

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 61 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.1 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Male (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Overall (N=16)	Categories of change [d]			
		Improvement	11	68.8	41.3, 89.0
		Deterioration	6	37.5	15.2, 64.6
		No improvement or deterioration	0	0	0, 20.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	3	25.0	5.5, 57.2
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	9	75.0	42.8, 94.5
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	2	16.7	2.1, 48.4
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	10	83.3	51.6, 97.9
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	6	54.5	23.4, 83.3

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	3	33.3	7.5, 70.1
	Pre-cycle 37 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Overall (N=12)	Categories of change [d]			
		Improvement	7	58.3	27.7, 84.8
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	4	33.3	9.9, 65.1

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	9	81.8	48.2, 97.7
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	1	8.3	0.2, 38.5
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	10	83.3	51.6, 97.9
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	3	25.0	5.5, 57.2
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	9	75.0	42.8, 94.5
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	5	45.5	16.7, 76.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	6	66.7	29.9, 92.5
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	3	33.3	7.5, 70.1
	Pre-cycle 37 (N=9)	Categories of change [d]			
		Improvement	6	66.7	29.9, 92.5
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	3	33.3	7.5, 70.1
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Overall (N=12)	Categories of change [d]			
		Improvement	9	75.0	42.8, 94.5
		Deterioration	2	16.7	2.1, 48.4
		No improvement or deterioration	2	16.7	2.1, 48.4

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	7	58.3	27.7, 84.8
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	5	41.7	15.2, 72.3
		Deterioration	2	16.7	2.1, 48.4
		No improvement or deterioration	5	41.7	15.2, 72.3
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	5	41.7	15.2, 72.3
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	6	50.0	21.1, 78.9
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	7	63.6	30.8, 89.1
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	2	18.2	2.3, 51.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	3	33.3	7.5, 70.1
	Pre-cycle 37 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	5	55.6	21.2, 86.3
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Overall (N=12)	Categories of change [d]			
		Improvement	9	75.0	42.8, 94.5
		Deterioration	5	41.7	15.2, 72.3
		No improvement or deterioration	1	8.3	0.2, 38.5

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	4	36.4	10.9, 69.2
	Pre-cycle 5 (N=12)	Categories of change [d]			
		Improvement	4	33.3	9.9, 65.1
		Deterioration	0	0	0, 26.5
		No improvement or deterioration	8	66.7	34.9, 90.1
	Pre-cycle 9 (N=12)	Categories of change [d]			
		Improvement	3	25.0	5.5, 57.2
		Deterioration	1	8.3	0.2, 38.5
		No improvement or deterioration	8	66.7	34.9, 90.1
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	6	54.5	23.4, 83.3

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	2	22.2	2.8, 60.0
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	6	66.7	29.9, 92.5
	Pre-cycle 37 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Overall (N=12)	Categories of change [d]			
		Improvement	7	58.3	27.7, 84.8
		Deterioration	3	25.0	5.5, 57.2
		No improvement or deterioration	4	33.3	9.9, 65.1

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	1	20.0	0.5, 71.6
	Pre-cycle 5 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	4	40.0	12.2, 73.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.2 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - Gender = Female (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=7)	Categories of change [d]			
		Improvement	1	14.3	0.4, 57.9
		Deterioration	3	42.9	9.9, 81.6
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Overall (N=11)	Categories of change [d]			
		Improvement	8	72.7	39.0, 94.0
		Deterioration	3	27.3	6.0, 61.0
		No improvement or deterioration	0	0	0, 28.5

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	4	36.4	10.9, 69.2
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	6	60.0	26.2, 87.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 61 (N=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=11)	Categories of change [d]			
		Improvement	8	72.7	39.0, 94.0
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	2	18.2	2.3, 51.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	3	27.3	6.0, 61.0
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	6	54.5	23.4, 83.3
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	6	60.0	26.2, 87.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	5	83.3	35.9, 99.6
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 61 (N=2)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Overall (N=11)	Categories of change [d]			
		Improvement	8	72.7	39.0, 94.0
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	2	18.2	2.3, 51.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	7	63.6	30.8, 89.1
		Deterioration	3	27.3	6.0, 61.0
		No improvement or deterioration	1	9.1	0.2, 41.3
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	9	81.8	48.2, 97.7
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	1	9.1	0.2, 41.3
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	8	72.7	39.0, 94.0
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	1	9.1	0.2, 41.3
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	5	50.0	18.7, 81.3

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 61 (N=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Overall (N=11)	Categories of change [d]			
		Improvement	10	90.9	58.7, 99.8
		Deterioration	3	27.3	6.0, 61.0
		No improvement or deterioration	0	0	0, 28.5

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	7	63.6	30.8, 89.1
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	4	36.4	10.9, 69.2
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	8	72.7	39.0, 94.0
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	1	9.1	0.2, 41.3
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 13 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	5	50.0	18.7, 81.3

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	5	83.3	35.9, 99.6
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 61 (N=2)	Categories of change [d]			
		Improvement	2	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Overall (N=11)	Categories of change [d]			
		Improvement	9	81.8	48.2, 97.7
		Deterioration	5	45.5	16.7, 76.6
		No improvement or deterioration	0	0	0, 28.5

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	3	42.9	9.9, 81.6
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	2	33.3	4.3, 77.7
		No improvement or deterioration	2	33.3	4.3, 77.7
	Pre-cycle 9 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 13 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	5	83.3	35.9, 99.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 37 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC
	Pre-cycle 49 (N=2)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	2	NC	NC
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.3 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Overall (N=8)	Categories of change [d]			
		Improvement	5	62.5	24.5, 91.5
		Deterioration	4	50.0	15.7, 84.3
		No improvement or deterioration	0	0	0, 36.9

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	7	70.0	34.8, 93.3
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	6	66.7	29.9, 92.5

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 49 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Overall (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	3	30.0	6.7, 65.2

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	7	70.0	34.8, 93.3
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	2	20.0	2.5, 55.6
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	8	80.0	44.4, 97.5
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	2	20.0	2.5, 55.6
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	0	0	0, 33.6
		No improvement or deterioration	4	44.4	13.7, 78.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	3	42.9	9.9, 81.6
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 49 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Overall (N=10)	Categories of change [d]			
		Improvement	8	80.0	44.4, 97.5
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	0	0	0, 30.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	2	20.0	2.5, 55.6
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	6	60.0	26.2, 87.8
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	3	33.3	7.5, 70.1

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	5	55.6	21.2, 86.3
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	2	22.2	2.8, 60.0
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 49 (N=7)	Categories of change [d]			
		Improvement	5	71.4	29.0, 96.3
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	2	28.6	3.7, 71.0
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	1	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	0	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Overall (N=10)	Categories of change [d]			
		Improvement	7	70.0	34.8, 93.3
		Deterioration	3	30.0	6.7, 65.2
		No improvement or deterioration	2	20.0	2.5, 55.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 5 (N=10)	Categories of change [d]			
		Improvement	4	40.0	12.2, 73.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	5	50.0	18.7, 81.3
	Pre-cycle 9 (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	3	30.0	6.7, 65.2
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	4	44.4	13.7, 78.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	1	11.1	0.3, 48.2
		No improvement or deterioration	4	44.4	13.7, 78.8
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	1	14.3	0.4, 57.9
		No improvement or deterioration	4	57.1	18.4, 90.1
	Pre-cycle 49 (N=7)	Categories of change [d]			
		Improvement	4	57.1	18.4, 90.1
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Overall (N=10)	Categories of change [d]			
		Improvement	6	60.0	26.2, 87.8
		Deterioration	3	30.0	6.7, 65.2
		No improvement or deterioration	2	20.0	2.5, 55.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	5	62.5	24.5, 91.5
	Pre-cycle 5 (N=6)	Categories of change [d]			
		Improvement	3	50.0	11.8, 88.2
		Deterioration	0	0	0, 45.9
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	5	62.5	24.5, 91.5
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	3	33.3	7.5, 70.1
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	4	44.4	13.7, 78.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set) Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	3	37.5	8.5, 75.5
		Deterioration	2	25.0	3.2, 65.1
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 49 (N=6)	Categories of change [d]			
		Improvement	4	66.7	22.3, 95.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	1	16.7	0.4, 64.1
	Pre-cycle 61 (N=1)	Categories of change [d]			
		Improvement	0	NC	NC
		Deterioration	0	NC	NC
		No improvement or deterioration	1	NC	NC

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.4 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Non-progressive (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Overall (N=10)	Categories of change [d]			
		Improvement	7	70.0	34.8, 93.3
		Deterioration	3	30.0	6.7, 65.2
		No improvement or deterioration	0	0	0, 30.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.
NC = not calculated.

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Table 5.1.2.3.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	3	30.0	6.7, 65.2
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	7	70.0	34.8, 93.3
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	2	18.2	2.3, 51.8
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	9	81.8	48.2, 97.7
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	3	27.3	6.0, 61.0
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	8	72.7	39.0, 94.0
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	6	54.5	23.4, 83.3
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	5	45.5	16.7, 76.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Total Score	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	5	62.5	24.5, 91.5
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	3	37.5	8.5, 75.5
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	3	60.0	14.7, 94.7
	Overall (N=11)	Categories of change [d]			
		Improvement	9	81.8	48.2, 97.7
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	2	18.2	2.3, 51.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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
		Deterioration	0	0	0, 30.8
		No improvement or deterioration	7	70.0	34.8, 93.3
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	2	18.2	2.3, 51.8
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	8	72.7	39.0, 94.0
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	6	54.5	23.4, 83.3

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Physical Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	6	75.0	34.9, 96.8
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	2	25.0	3.2, 65.1
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	6	85.7	42.1, 99.6
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	1	14.3	0.4, 57.9
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	1	20.0	0.5, 71.6
	Overall (N=11)	Categories of change [d]			
		Improvement	9	81.8	48.2, 97.7
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	1	9.1	0.2, 41.3

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 3 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	1	9.1	0.2, 41.3
		No improvement or deterioration	5	45.5	16.7, 76.6
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	7	63.6	30.8, 89.1
		Deterioration	2	18.2	2.3, 51.8
		No improvement or deterioration	2	18.2	2.3, 51.8

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Emotional Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	4	50.0	15.7, 84.3
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	4	50.0	15.7, 84.3
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	0	0	0, 41.0
		No improvement or deterioration	5	71.4	29.0, 96.3
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	2	40.0	5.3, 85.3
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	2	40.0	5.3, 85.3
	Overall (N=11)	Categories of change [d]			
		Improvement	9	81.8	48.2, 97.7
		Deterioration	3	27.3	6.0, 61.0
		No improvement or deterioration	1	9.1	0.2, 41.3

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 3 (N=10)	Categories of change [d]			
		Improvement	5	50.0	18.7, 81.3
		Deterioration	1	10.0	0.3, 44.5
		No improvement or deterioration	4	40.0	12.2, 73.8
	Pre-cycle 5 (N=11)	Categories of change [d]			
		Improvement	5	45.5	16.7, 76.6
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	6	54.5	23.4, 83.3
	Pre-cycle 9 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	7	63.6	30.8, 89.1
	Pre-cycle 13 (N=11)	Categories of change [d]			
		Improvement	4	36.4	10.9, 69.2
		Deterioration	0	0	0, 28.5
		No improvement or deterioration	7	63.6	30.8, 89.1

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
Social Functioning	Pre-cycle 25 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	0	0	0, 36.9
		No improvement or deterioration	6	75.0	34.9, 96.8
	Pre-cycle 37 (N=7)	Categories of change [d]			
		Improvement	2	28.6	3.7, 71.0
		Deterioration	2	28.6	3.7, 71.0
		No improvement or deterioration	3	42.9	9.9, 81.6
	Pre-cycle 49 (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	3	60.0	14.7, 94.7
	Overall (N=11)	Categories of change [d]			
		Improvement	7	63.6	30.8, 89.1
		Deterioration	3	27.3	6.0, 61.0
		No improvement or deterioration	3	27.3	6.0, 61.0

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 3 (N=5)	Categories of change [d]			
		Improvement	3	60.0	14.7, 94.7
		Deterioration	0	0	0, 52.2
		No improvement or deterioration	2	40.0	5.3, 85.3
	Pre-cycle 5 (N=5)	Categories of change [d]			
		Improvement	1	20.0	0.5, 71.6
		Deterioration	1	20.0	0.5, 71.6
		No improvement or deterioration	3	60.0	14.7, 94.7
	Pre-cycle 9 (N=8)	Categories of change [d]			
		Improvement	2	25.0	3.2, 65.1
		Deterioration	1	12.5	0.3, 52.7
		No improvement or deterioration	5	62.5	24.5, 91.5
	Pre-cycle 13 (N=9)	Categories of change [d]			
		Improvement	4	44.4	13.7, 78.8
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	3	33.3	7.5, 70.1

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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Table 5.1.2.3.5 PedsQL parent-report score categories of change over time - percentage of patients with Improvement and Deterioration based on clinically meaningful threshold - Ages 8-18 - PN status = Unknown (Full analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

Parameter	Time point	Response category	n	% [b]	95% CI [c]
School Functioning	Pre-cycle 25 (N=6)	Categories of change [d]			
		Improvement	1	16.7	0.4, 64.1
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	4	66.7	22.3, 95.7
	Pre-cycle 37 (N=6)	Categories of change [d]			
		Improvement	2	33.3	4.3, 77.7
		Deterioration	1	16.7	0.4, 64.1
		No improvement or deterioration	3	50.0	11.8, 88.2
	Pre-cycle 49 (N=3)	Categories of change [d]			
		Improvement	1	33.3	0.8, 90.6
		Deterioration	0	0	0, 70.8
		No improvement or deterioration	2	66.7	9.4, 99.2
	Overall (N=9)	Categories of change [d]			
		Improvement	7	77.8	40.0, 97.2
		Deterioration	2	22.2	2.8, 60.0
		No improvement or deterioration	0	0	0, 33.6

[a] Parents or legal guardians of children from 8 to 18 years of age at enrolment completed the parent proxy 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 are based on a clinically meaningful threshold (CMT) of 15.

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3 Endpunktkategorie Sicherheit

3.1 Endpunkt Unerwünschte Ereignisse

3.1.1 Operationalisierung Adverse Events of Special Interest (AESI)

Tabelle 15: Operationalisierung von Adverse Events of Special Interest (AESI) in der Studie SPRINT

Medical concept	AE of special interest	Approach to delineating PTs
Skin and mucous membrane events	Acneiform rash	HLT Acnes HLT Pustular conditions
	Non-acneiform rash	HLT Rashes, eruptions and exanthems NEC HLT Pruritis NEC
	Nail disorder events	HLT Nail and nail bed conditions PT Paronychia
	Oral mucositis	HLT Oral soft tissue disorders NEC HLT Stomatitis and ulceration
Bone marrow effects	Leukopenic events	SMQ Hematopoietic leucopenia
	Thrombocytopenic events	SMQ Hematopoietic thrombocytopenias
	Erythropenic events:	SMQ Hematopoietic erythropenia
Retinal events	RPED/central serous retinopathy events Retinal vein occlusion events Other retinal disorders	SMQ Retinal disorders
Cardiac events	Ejection fraction decreased Other cardiac events	SMQ Cardiac failure
Muscular events	Muscle events CPK increased	SMQ Rhabdomyolysis/myopathy
Physeal dysplasia	Physeal dysplasia	HLT Epiphyseal disorders

AE Adverse event; CPK Creatine phosphokinase; HLT High Level Term; NEC Not elsewhere classified; PT Preferred Term; RPED Retinal pigment epithelial detachment; SMQ Standardised MedDRA Query.

3.1.2 Gesamtraten Adverse Events of Special Interest (AESI)

Tabelle 16: Ergebnisse für den Endpunkt „Gesamtraten unerwünschter Ereignisse von besonderem Interesse“

Studie	**Selumetinib 25 mg/m² BID**
SPRINT **Phase II, Stratum I** **Datenschnitt: 31. März 2021**	***Safety*-Population** **N = 50**
Gesamtraten AESI	**Anzahl Patientinnen und Patienten n (%)**
Jegliches AESI	49 (98,0)
Nicht-schweres AESI (CTCAE ≤ 2)	49 (98,0)
Schweres AESI (CTCAE ≥ 3)	14 (28,0)
Schwerwiegendes AESI	4 (8,0)
AESI – Herzinsuffizienz	
Gesamtrate	21/50 (42,0)
Nicht-schwer (CTCAE Grad < 3)	21/50 (42,0)
Schwer (CTCAE Grad ≥ 3)	0/50 (0,0)
SUE	1/50 (2,0)
AESI – Erythropenie-Effekte	
Gesamtrate	27/50 (54,0)
Nicht-schwer (CTCAE Grad < 3)	26/50 (52,0)
Schwer (CTCAE Grad ≥ 3)	2/50 (4,0)
SUE	2/50 (4,0)
AESI – Leukopenie-Effekte	
Gesamtrate	29/50 (58,0)
Nicht-schwer (CTCAE Grad < 3)	29/50 (58,0)
Schwer (CTCAE Grad ≥ 3)	2/50 (4,0)
SUE	0 (0,0)
AESI – Muskelbezogene Effekte	
Gesamtrate	44/50 (88,0)
Nicht-schwer (CTCAE Grad < 3)	44/50 (88,0)
Schwer (CTCAE Grad ≥ 3)	5/50 (10,0)
SUE	2/50 (4,0)
AESI – Nagelstörungen	
Gesamtrate	28/50 (56,0)
Nicht-schwer (CTCAE Grad < 3)	28/50 (56,0)
Schwer (CTCAE Grad ≥ 3)	4/50 (8,0)
SUE	0 (0,0)
AESI – Auswirkungen der oralen Mukositis	
Gesamtrate	28/50 (56,0)
Nicht-schwer (CTCAE Grad < 3)	28/50 (56,0)
Schwer (CTCAE Grad ≥ 3)	0/50 (0,0)
SUE	0/50 (0,0)
AESI – Körperliche Displasie	
Gesamtrate	0/50 (0,0)
Nicht-schwer (CTCAE Grad < 3)	0/50 (0,0)
Schwer (CTCAE Grad ≥ 3)	0/50 (0,0)
SUE	0/50 (0,0)
AESI – Ausschlag, akneiform	
Gesamtrate	28/50 (56,0)
Nicht-schwer (CTCAE Grad < 3)	28/50 (56,0)
Schwer (CTCAE Grad ≥ 3)	3/50 (6,0)
SUE	0/50 (0,0)
AESI – Ausschlag, nicht-akneiform	
Gesamtrate	38/50 (76,0)
Nicht-schwer (CTCAE Grad < 3)	38/50 (76,0)
Schwer (CTCAE Grad ≥ 3)	1/50 (2,0)
SUE	0/50 (0,0)
AESI – Netzhauteffekte	
Gesamtrate	10/50 (20,0)

Studie	**Selumetinib 25 mg/m² BID**
SPRINT **Phase II, Stratum I** **Datenschnitt: 31. März 2021**	***Safety*-Population** **N = 50**
Gesamtraten AESI	**Anzahl Patientinnen und Patienten n (%)**
Nicht-schwer (CTCAE Grad < 3)	10/50 (20,0)
Schwer (CTCAE Grad ≥ 3)	0/50 (0,0)
SUE	0/50 (0,0)
AESI – Thrombozytopenie-Effekte	
Gesamtrate	6/50 (12,0)
Nicht-schwer (CTCAE Grad < 3)	6/50 (12,0)
Schwer (CTCAE Grad ≥ 3)	0/50 (0,0)
SUE	0/50 (0,0)

AESI: Unerwünschte Ereignisse von besonderem Interesse (engl. Adverse Events of Special Interest); BID: Zweimal täglich; CTCAE: Common Terminology Criteria for Adverse Events; PT: Preferred Term; SOC: System Organ Class; SUE: Schwerwiegendes unerwünschtes Ereignis; UE: Unerwünschte Ereignisse

Quelle: AstraZeneca. Clinical Study Report Addendum – SPRINT (D1532C00057): A Phase I/II Study of the Mitogen Activated Protein Kinase Kinase (MEK) 1 Inhibitor Selumetinib (AZD6244; HYD Sulfate) in Children with Neurofibromatosis Type 1 (NF1) and Inoperable Plexiform Neurofibromas (PN) (SPRINT Phase II Stratum 1) Long Term Efficacy and Safety Update. Stand: 05.04.2022.

3.1.3 Subgruppenanalysen zu den unerwünschten Ereignissen

3.1.3.1 Subgruppenanalysen zu den unerwünschten Ereignissen (Übersicht)

Table 3.1.1.1 Adverse Events in any category - patient level - Gender = Male (Safety analysis set)

Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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)	14 (46,7)
Any non-severe AE (CTCAE <=2)	30 (100)
Any severe AE (CTCAE >=3)	23 (76,7)
Any AE leading to death	0
Any AE leading to permanent discontinuation of study drug	5 (16,7)
Any AE leading to dose reduction	11 (36,7)
Any AE leading to interruption of study drug	27 (90,0)
Any AESI	30 (100)
Any serious AESI (including events with outcome of death)	4 (13,3)
Any non-severe AESI (CTCAE <=2)	30 (100)
Any severe AESI (CTCAE >=3)	11 (36,7)
Any AE excluding disease-related AEs [b]	30 (100)
Any serious adverse event (SAE including outcome of death) excluding disease-related SAEs [b]	11 (36,7)
Any severe AE (CTCAE >=3) excluding disease-related AEs [b]	22 (73,3)

[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).

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Table 3.1.1.2 Adverse Events in any category - patient level - Gender = Female (Safety analysis set)

Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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)	1 (5,0)
Any non-severe AE (CTCAE <=2)	19 (95,0)
Any severe AE (CTCAE >=3)	11 (55,0)
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	16 (80,0)
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)	3 (15,0)
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).

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Table 3.1.1.3 Adverse Events in any category - patient level - PN status at enrollment = Progressive (Safety analysis set)

Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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)	4 (19,0)
Any non-severe AE (CTCAE <=2)	21 (100)
Any severe AE (CTCAE >=3)	14 (66,7)
Any AE leading to death	0
Any AE leading to permanent discontinuation of study drug	1 (4,8)
Any AE leading to dose reduction	9 (42,9)
Any AE leading to interruption of study drug	19 (90,5)
Any AESI	21 (100)
Any serious AESI (including events with outcome of death)	2 (9,5)
Any non-severe AESI (CTCAE <=2)	21 (100)
Any severe AESI (CTCAE >=3)	7 (33,3)
Any AE excluding disease-related AEs [b]	21 (100)
Any serious adverse event (SAE including outcome of death) excluding disease-related SAEs [b]	4 (19,0)
Any severe AE (CTCAE >=3) excluding disease-related AEs [b]	14 (66,7)

[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).

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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, data cut-off: 31 March 2021 (DC02)

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)	6 (40,0)
Any non-severe AE (CTCAE <=2)	14 (93,3)
Any severe AE (CTCAE >=3)	11 (73,3)
Any AE leading to death	0
Any AE leading to permanent discontinuation of study drug	2 (13,3)
Any AE leading to dose reduction	3 (20,0)
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)	4 (26,7)
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).

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Table 3.1.1.5 Adverse Events in any category - patient level - PN status at enrollment = Unknown (Safety analysis set)

Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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)	5 (35,7)
Any non-severe AE (CTCAE <=2)	14 (100)
Any severe AE (CTCAE >=3)	9 (64,3)
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	12 (85,7)
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)	3 (21,4)
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).

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3.1.3.2 Subgruppenanalysen zu den unerwünschten Ereignissen nach SOC und PT

Table 3.1.2.1 Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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)
Bronchiolitis	1 (3,3)
Bronchitis	1 (3,3)
Bronchitis viral	1 (3,3)
COVID-19	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	4 (13,3)
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	3 (10,0)
Injection site infection	1 (3,3)
Medical device site infection	1 (3,3)
Metapneumovirus infection	1 (3,3)
Mucosal infection	2 (6,7)
Nail infection	2 (6,7)
Osteomyelitis	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Otitis externa	2 (6,7)
Otitis media	11 (36,7)
Paronychia	19 (63,3)
Perineal abscess	1 (3,3)
Pharyngitis	5 (16,7)
Pharyngitis streptococcal	6 (20,0)
Pilonidal cyst	1 (3,3)
Pneumonia	1 (3,3)
Rash pustular	4 (13,3)
Sinusitis	5 (16,7)
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	10 (33,3)
Urinary tract infection	2 (6,7)
Viral diarrhoea	2 (6,7)
Viral upper respiratory tract infection	1 (3,3)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	7 (23,3)
Dysplastic naevus	1 (3,3)
Glioma	1 (3,3)
Neurofibrosarcoma	1 (3,3)
Skin papilloma	2 (6,7)
Tumour pain	2 (6,7)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	21 (70,0)
Anaemia	20 (66,7)
Lymph node pain	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Lymphadenopathy	2 (6,7)
IMMUNE SYSTEM DISORDERS	5 (16,7)
Contrast media allergy	1 (3,3)
Drug hypersensitivity	1 (3,3)
Hypersensitivity	5 (16,7)
METABOLISM AND NUTRITION DISORDERS	29 (96,7)
Decreased appetite	5 (16,7)
Dehydration	5 (16,7)
Hypercalcaemia	2 (6,7)
Hyperglycaemia	9 (30,0)
Hyperkalaemia	7 (23,3)
Hypermagnesaemia	5 (16,7)
Hypernatraemia	8 (26,7)
Hyperuricaemia	1 (3,3)
Hypoalbuminaemia	17 (56,7)
Hypocalcaemia	9 (30,0)
Hypoglycaemia	10 (33,3)
Hypokalaemia	9 (30,0)
Hypomagnesaemia	2 (6,7)
Hyponatraemia	11 (36,7)
Hypophosphataemia	8 (26,7)
Lactose intolerance	1 (3,3)
PSYCHIATRIC DISORDERS	14 (46,7)
Agitation	1 (3,3)
Anxiety	3 (10,0)
Attention deficit hyperactivity disorder	1 (3,3)
Depression	3 (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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Insomnia	7 (23,3)
Irritability	4 (13,3)
Personality change	1 (3,3)
Restlessness	1 (3,3)
Suicidal ideation	2 (6,7)
Tic	1 (3,3)
NERVOUS SYSTEM DISORDERS	23 (76,7)
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)
Encephalomalacia	1 (3,3)
Headache	19 (63,3)
Neuralgia	1 (3,3)
Paraesthesia	1 (3,3)
Phantom limb syndrome	1 (3,3)
Presyncope	3 (10,0)
Syncope	1 (3,3)
EYE DISORDERS	13 (43,3)
Blepharitis	2 (6,7)
Chorioretinal scar	1 (3,3)
Corneal cyst	1 (3,3)
Dry eye	2 (6,7)
Eye discharge	1 (3,3)
Eye pain	1 (3,3)
Eyelid skin dryness	1 (3,3)
Keratitis	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Lacrimation increased	4 (13,3)
Ocular hypertension	1 (3,3)
Periorbital oedema	1 (3,3)
Photophobia	2 (6,7)
Retinal tear	1 (3,3)
Vision blurred	4 (13,3)
Visual field defect	1 (3,3)
EAR AND LABYRINTH DISORDERS	10 (33,3)
Ear pain	5 (16,7)
External ear inflammation	2 (6,7)
Hypoacusis	1 (3,3)
Middle ear effusion	1 (3,3)
Motion sickness	1 (3,3)
Tinnitus	2 (6,7)
CARDIAC DISORDERS	10 (33,3)
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	14 (46,7)
Aortic stenosis	1 (3,3)
Flushing	2 (6,7)
Haematoma	1 (3,3)
Hypertension	8 (26,7)
Hypotension	1 (3,3)
Phlebitis	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	24 (80,0)
Asthma	1 (3,3)
Atelectasis	2 (6,7)
Cough	13 (43,3)
Dysphonia	1 (3,3)
Dyspnoea	2 (6,7)
Epistaxis	11 (36,7)
Hypoxia	3 (10,0)
Increased bronchial secretion	2 (6,7)
Increased upper airway secretion	1 (3,3)
Nasal congestion	11 (36,7)
Oropharyngeal pain	15 (50,0)
Rhinitis allergic	12 (40,0)
Rhinorrhoea	4 (13,3)
Sleep apnoea syndrome	1 (3,3)
Sneezing	3 (10,0)
Tracheal inflammation	1 (3,3)
Upper-airway cough syndrome	2 (6,7)
Wheezing	1 (3,3)
GASTROINTESTINAL DISORDERS	30 (100)
Abdominal distension	3 (10,0)
Abdominal pain	15 (50,0)
Abdominal pain upper	12 (40,0)
Anal incontinence	2 (6,7)
Constipation	15 (50,0)
Dental caries	1 (3,3)
Diarrhoea	26 (86,7)
Dry mouth	1 (3,3)
Dyspepsia	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
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	22 (73,3)
Oral pain	3 (10,0)
Post-tussive vomiting	1 (3,3)
Proctalgia	1 (3,3)
Stomatitis	14 (46,7)
Toothache	1 (3,3)
Vomiting	27 (90,0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	30 (100)
Alopecia	4 (13,3)
Blister	1 (3,3)
Dermatitis acneiform	15 (50,0)
Dermatitis allergic	2 (6,7)
Dermatitis atopic	2 (6,7)
Dermatitis diaper	1 (3,3)
Dry skin	20 (66,7)
Eczema	9 (30,0)
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	13 (43,3)
Rash	3 (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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Rash erythematous	1 (3,3)
Rash maculo-papular	16 (53,3)
Rash pruritic	1 (3,3)
Seborrhoeic dermatitis	2 (6,7)
Skin fissures	2 (6,7)
Skin hyperpigmentation	1 (3,3)
Skin hypopigmentation	1 (3,3)
Skin irritation	1 (3,3)
Skin lesion	1 (3,3)
Skin ulcer	3 (10,0)
Urticaria	2 (6,7)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	23 (76,7)
Arthralgia	4 (13,3)
Arthritis	1 (3,3)
Back pain	8 (26,7)
Flank pain	1 (3,3)
Growth retardation	1 (3,3)
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)
Neck pain	5 (16,7)
Osteoporosis	1 (3,3)
Pain in extremity	9 (30,0)
Scoliosis	2 (6,7)
Sever's disease	1 (3,3)
Synovial cyst	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.
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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
RENAL AND URINARY DISORDERS	16 (53,3)
Acute kidney injury	1 (3,3)
Haematuria	5 (16,7)
Haemoglobinuria	2 (6,7)
Proteinuria	10 (33,3)
Urinary incontinence	5 (16,7)
Urinary tract pain	1 (3,3)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	29 (96,7)
Axillary pain	1 (3,3)
Chills	2 (6,7)
Face oedema	1 (3,3)
Fatigue	17 (56,7)
Hypothermia	1 (3,3)
Illness	1 (3,3)
Influenza like illness	13 (43,3)
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 rash	1 (3,3)
Non-cardiac chest pain	1 (3,3)
Oedema peripheral	7 (23,3)
Pain	6 (20,0)
Pyrexia	22 (73,3)
Vessel puncture site bruise	1 (3,3)
Xerosis	1 (3,3)
INVESTIGATIONS	30 (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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Activated partial thromboplastin time prolonged	1 (3,3)
Alanine aminotransferase increased	11 (36,7)
Amylase increased	6 (20,0)
Aspartate aminotransferase increased	12 (40,0)
Blood alkaline phosphatase increased	5 (16,7)
Blood bilirubin increased	1 (3,3)
Blood creatine phosphokinase increased	24 (80,0)
Blood creatinine increased	10 (33,3)
Breath sounds abnormal	1 (3,3)
Ejection fraction decreased	8 (26,7)
Electrocardiogram QT prolonged	1 (3,3)
Haemoglobin increased	9 (30,0)
Haptoglobin decreased	1 (3,3)
Lipase increased	10 (33,3)
Lymphocyte count decreased	10 (33,3)
Lymphocyte count increased	8 (26,7)
Neutrophil count decreased	13 (43,3)
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	7 (23,3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	21 (70,0)
Arthropod bite	2 (6,7)
Conjunctival abrasion	1 (3,3)
Contusion	3 (10,0)
Fall	11 (36,7)
Fracture	9 (30,0)
Joint dislocation	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.
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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Limb injury	2 (6,7)
Post procedural haemorrhage	1 (3,3)
Procedural hypotension	1 (3,3)
Procedural pain	1 (3,3)
Skin abrasion	2 (6,7)
Skin laceration	2 (6,7)
Stoma site irritation	1 (3,3)
Sunburn	1 (3,3)
Tracheal haemorrhage	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.
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Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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	17 (85,0)
Body tinea	3 (15,0)
Cellulitis	1 (5,0)
Conjunctivitis	4 (20,0)
Eye infection	1 (5,0)
Folliculitis	1 (5,0)
Gastroenteritis	1 (5,0)
Gastroenteritis viral	2 (10,0)
Gingivitis	1 (5,0)
Hordeolum	2 (10,0)
Influenza	1 (5,0)
Otitis media	4 (20,0)
Paronychia	9 (45,0)
Pharyngitis	4 (20,0)
Pharyngitis streptococcal	1 (5,0)
Pneumonia	4 (20,0)
Respiratory syncytial virus infection	1 (5,0)
Sinusitis	2 (10,0)
Skin infection	3 (15,0)
Tracheitis	1 (5,0)
Upper respiratory tract infection	3 (15,0)
Urinary tract infection	3 (15,0)
Vaginal infection	1 (5,0)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	8 (40,0)
Anaemia	7 (35,0)
Lymph node pain	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.
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Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

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	3 (15,0)
Hyperglycaemia	6 (30,0)
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	6 (30,0)
Hypomagnesaemia	3 (15,0)
Hypophosphataemia	1 (5,0)
PSYCHIATRIC DISORDERS	11 (55,0)
Anxiety	4 (20,0)
Attention deficit hyperactivity disorder	1 (5,0)
Autoscopy	1 (5,0)
Depression	1 (5,0)
Hallucination, auditory	1 (5,0)
Insomnia	5 (25,0)
Irritability	1 (5,0)
Personality change	1 (5,0)
Suicidal ideation	1 (5,0)
NERVOUS SYSTEM DISORDERS	13 (65,0)
Aphasia	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.
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Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Dizziness	8 (40,0)
Dysaesthesia	1 (5,0)
Dyspraxia	1 (5,0)
Headache	9 (45,0)
Lethargy	1 (5,0)
Paraesthesia	3 (15,0)
Presyncope	1 (5,0)
Seizure	1 (5,0)
Syncope	2 (10,0)
EYE DISORDERS	9 (45,0)
Amblyopia strabismic	1 (5,0)
Cataract	1 (5,0)
Dry eye	1 (5,0)
Eye oedema	1 (5,0)
Eye pain	4 (20,0)
Eye pruritus	1 (5,0)
Lacrimation increased	4 (20,0)
Vision blurred	3 (15,0)
Vitreous disorder	1 (5,0)
EAR AND LABYRINTH DISORDERS	5 (25,0)
Ear pain	2 (10,0)
External ear inflammation	1 (5,0)
Hypoacusis	1 (5,0)
Tinnitus	1 (5,0)
Vertigo	1 (5,0)
CARDIAC DISORDERS	3 (15,0)
Sinus tachycardia	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.
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Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
VASCULAR DISORDERS	3 (15,0)
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	10 (50,0)
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	11 (55,0)
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	10 (50,0)
Abdominal pain upper	9 (45,0)
Anal haemorrhage	1 (5,0)
Cheilitis	2 (10,0)
Constipation	6 (30,0)
Dental caries	4 (20,0)
Diarrhoea	11 (55,0)
Dry mouth	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.
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Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Dysphagia	1 (5,0)
Faeces discoloured	1 (5,0)
Flatulence	1 (5,0)
Gastrooesophageal reflux disease	2 (10,0)
Haemorrhoids	1 (5,0)
Impaired gastric emptying	1 (5,0)
Nausea	14 (70,0)
Oesophageal stenosis	1 (5,0)
Oesophagitis	1 (5,0)
Oral pain	2 (10,0)
Proctalgia	1 (5,0)
Stomatitis	12 (60,0)
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	13 (65,0)
Dermatitis atopic	1 (5,0)
Dry skin	14 (70,0)
Ecchymosis	1 (5,0)
Eczema	5 (25,0)
Erythema	1 (5,0)
Hair colour changes	7 (35,0)
Pain of skin	1 (5,0)
Photosensitivity reaction	1 (5,0)
Pityriasis alba	1 (5,0)
Pruritus	13 (65,0)
Rash maculo-papular	9 (45,0)

[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 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Skin exfoliation	2 (10,0)
Skin hypopigmentation	2 (10,0)
Urticaria	1 (5,0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	16 (80,0)
Arthralgia	7 (35,0)
Axillary mass	1 (5,0)
Back pain	3 (15,0)
Bone pain	2 (10,0)
Limb asymmetry	1 (5,0)
Muscle spasms	1 (5,0)
Muscle twitching	1 (5,0)
Neck pain	4 (20,0)
Pain in extremity	9 (45,0)
Tendonitis	1 (5,0)
RENAL AND URINARY DISORDERS	15 (75,0)
Dysuria	1 (5,0)
Haematuria	10 (50,0)
Haemoglobinuria	1 (5,0)
Nephrolithiasis	1 (5,0)
Pollakiuria	2 (10,0)
Proteinuria	4 (20,0)
Urinary incontinence	4 (20,0)
Urinary retention	1 (5,0)
Urinary tract pain	2 (10,0)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	7 (35,0)
Adnexa uteri cyst	1 (5,0)
Dysmenorrhoea	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.
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Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Heavy menstrual bleeding	1 (5,0)
Menstruation irregular	2 (10,0)
Oligomenorrhoea	1 (5,0)
Ovarian cyst	2 (10,0)
Vulvovaginal dryness	1 (5,0)
Vulvovaginal inflammation	1 (5,0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	15 (75,0)
Face oedema	1 (5,0)
Facial pain	2 (10,0)
Fatigue	11 (55,0)
Gait disturbance	1 (5,0)
Influenza like illness	3 (15,0)
Localised oedema	7 (35,0)
Non-cardiac chest pain	2 (10,0)
Oedema peripheral	2 (10,0)
Pain	5 (25,0)
Peripheral swelling	1 (5,0)
Pyrexia	9 (45,0)
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	15 (75,0)
Blood creatinine increased	7 (35,0)
Ejection fraction decreased	5 (25,0)
Haemoglobin increased	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.
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Table 3.1.2.2 Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Lipase increased	6 (30,0)
Lymphocyte count decreased	5 (25,0)
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)
Weight decreased	1 (5,0)
Weight increased	2 (10,0)
White blood cell count decreased	4 (20,0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	8 (40,0)
Arthropod bite	1 (5,0)
Arthropod sting	1 (5,0)
Conjunctival abrasion	1 (5,0)
Contusion	1 (5,0)
Fall	3 (15,0)
Fracture	2 (10,0)
Head injury	1 (5,0)
Joint injury	1 (5,0)
Poisoning	1 (5,0)
Skin abrasion	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).

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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, data cut-off: 31 March 2021 (DC02)

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)
COVID-19	1 (4,8)
Cellulitis	1 (4,8)
Clostridium difficile colitis	1 (4,8)
Conjunctivitis	4 (19,0)
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)
Mucosal infection	1 (4,8)
Nail infection	1 (4,8)
Otitis externa	2 (9,5)
Otitis media	10 (47,6)
Paronychia	14 (66,7)
Pharyngitis	4 (19,0)
Pharyngitis streptococcal	6 (28,6)
Pneumonia	1 (4,8)
Rash pustular	2 (9,5)
Sinusitis	5 (23,8)

[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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Skin infection	5 (23,8)
Staphylococcal skin infection	1 (4,8)
Tinea infection	1 (4,8)
Upper respiratory tract infection	8 (38,1)
Urinary tract infection	2 (9,5)
Viral diarrhoea	2 (9,5)
Viral upper respiratory tract infection	1 (4,8)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	5 (23,8)
Glioma	1 (4,8)
Skin papilloma	2 (9,5)
Tumour pain	2 (9,5)
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)
Drug hypersensitivity	1 (4,8)
Hypersensitivity	5 (23,8)
METABOLISM AND NUTRITION DISORDERS	21 (100)
Decreased appetite	7 (33,3)
Dehydration	2 (9,5)
Hyperglycaemia	5 (23,8)
Hyperkalaemia	6 (28,6)
Hypermagnesaemia	4 (19,0)
Hypernatraemia	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.
MedDRA version 21.0. CTCAE = Common Terminology Criteria for Adverse Events (version 4.0).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Hypoalbuminaemia	13 (61,9)
Hypocalcaemia	6 (28,6)
Hypoglycaemia	7 (33,3)
Hypokalaemia	6 (28,6)
Hypomagnesaemia	3 (14,3)
Hyponatraemia	3 (14,3)
Hypophosphataemia	4 (19,0)
PSYCHIATRIC DISORDERS	12 (57,1)
Agitation	1 (4,8)
Anxiety	2 (9,5)
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)
Restlessness	1 (4,8)
Suicidal ideation	1 (4,8)
Tic	1 (4,8)
NERVOUS SYSTEM DISORDERS	16 (76,2)
Disturbance in attention	2 (9,5)
Dizziness	7 (33,3)
Dysaesthesia	1 (4,8)
Headache	13 (61,9)
Paraesthesia	2 (9,5)
Presyncope	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.
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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
EYE DISORDERS	13 (61,9)
Amblyopia strabismic	1 (4,8)
Corneal cyst	1 (4,8)
Dry eye	3 (14,3)
Eye discharge	1 (4,8)
Eye pain	2 (9,5)
Keratitis	1 (4,8)
Lacrimation increased	6 (28,6)
Ocular hypertension	1 (4,8)
Periorbital oedema	1 (4,8)
Photophobia	2 (9,5)
Retinal tear	1 (4,8)
Vision blurred	3 (14,3)
Visual field defect	1 (4,8)
EAR AND LABYRINTH DISORDERS	7 (33,3)
Ear pain	4 (19,0)
External ear inflammation	1 (4,8)
Hypoacusis	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)

[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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	18 (85,7)
Asthma	1 (4,8)
Atelectasis	1 (4,8)
Cough	14 (66,7)
Dyspnoea	1 (4,8)
Epistaxis	8 (38,1)
Hiccups	1 (4,8)
Nasal congestion	12 (57,1)
Oropharyngeal pain	12 (57,1)
Rhinitis allergic	8 (38,1)
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	13 (61,9)
Abdominal pain upper	11 (52,4)
Anal incontinence	2 (9,5)
Constipation	12 (57,1)
Dental caries	2 (9,5)
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)

[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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Oral pain	3 (14,3)
Post-tussive vomiting	1 (4,8)
Proctalgia	1 (4,8)
Stomatitis	12 (57,1)
Toothache	1 (4,8)
Vomiting	19 (90,5)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	21 (100)
Alopecia	8 (38,1)
Blister	1 (4,8)
Dermatitis	1 (4,8)
Dermatitis acneiform	7 (33,3)
Dermatitis allergic	2 (9,5)
Dermatitis atopic	2 (9,5)
Dry skin	15 (71,4)
Eczema	11 (52,4)
Erythema	2 (9,5)
Hair colour changes	6 (28,6)
Miliaria	1 (4,8)
Pain of skin	3 (14,3)
Pruritus	14 (66,7)
Rash	2 (9,5)
Rash maculo-papular	11 (52,4)
Seborrhoeic dermatitis	2 (9,5)
Skin fissures	2 (9,5)
Skin hypopigmentation	1 (4,8)
Skin ulcer	1 (4,8)
Urticaria	2 (9,5)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	17 (81,0)

[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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Arthralgia	4 (19,0)
Arthritis	1 (4,8)
Back pain	4 (19,0)
Bone pain	1 (4,8)
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	4 (19,0)
Pain in extremity	8 (38,1)
Scoliosis	2 (9,5)
Synovial cyst	1 (4,8)
Tendonitis	1 (4,8)
RENAL AND URINARY DISORDERS	16 (76,2)
Dysuria	1 (4,8)
Haematuria	4 (19,0)
Haemoglobinuria	1 (4,8)
Pollakiuria	2 (9,5)
Proteinuria	7 (33,3)
Urinary incontinence	6 (28,6)
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)

[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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Fatigue	13 (61,9)
Gait disturbance	1 (4,8)
Illness	1 (4,8)
Influenza like illness	11 (52,4)
Localised oedema	4 (19,0)
Malaise	3 (14,3)
Non-cardiac chest pain	1 (4,8)
Oedema peripheral	2 (9,5)
Pain	1 (4,8)
Pyrexia	14 (66,7)
Xerosis	1 (4,8)
INVESTIGATIONS	21 (100)
Activated partial thromboplastin time prolonged	1 (4,8)
Alanine aminotransferase increased	7 (33,3)
Amylase increased	4 (19,0)
Aspartate aminotransferase increased	9 (42,9)
Blood alkaline phosphatase increased	4 (19,0)
Blood bilirubin increased	1 (4,8)
Blood creatine phosphokinase increased	18 (85,7)
Blood creatinine increased	7 (33,3)
Breath sounds abnormal	1 (4,8)
Ejection fraction decreased	4 (19,0)
Haemoglobin increased	10 (47,6)
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	12 (57,1)
Platelet count decreased	3 (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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Weight decreased	1 (4,8)
Weight increased	3 (14,3)
White blood cell count decreased	4 (19,0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	15 (71,4)
Arthropod bite	1 (4,8)
Conjunctival abrasion	2 (9,5)
Contusion	1 (4,8)
Fall	8 (38,1)
Fracture	5 (23,8)
Head injury	1 (4,8)
Limb injury	2 (9,5)
Poisoning	1 (4,8)
Skin abrasion	2 (9,5)
Skin laceration	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.
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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, data cut-off: 31 March 2021 (DC02)

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	12 (80,0)
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	3 (20,0)
Fungal skin infection	1 (6,7)
Furuncle	1 (6,7)
Gastroenteritis	1 (6,7)
Gastroenteritis viral	1 (6,7)
Influenza	2 (13,3)
Metapneumovirus infection	1 (6,7)
Mucosal infection	1 (6,7)
Nail infection	1 (6,7)
Otitis media	1 (6,7)
Paronychia	8 (53,3)
Perineal abscess	1 (6,7)
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)

[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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	8 (53,3)
Anaemia	8 (53,3)
METABOLISM AND NUTRITION DISORDERS	14 (93,3)
Decreased appetite	1 (6,7)
Dehydration	3 (20,0)
Hypercalcaemia	1 (6,7)
Hyperglycaemia	4 (26,7)
Hyperkalaemia	4 (26,7)
Hypermagnesaemia	2 (13,3)
Hypernatraemia	4 (26,7)
Hyperuricaemia	1 (6,7)
Hypoalbuminaemia	5 (33,3)
Hypocalcaemia	5 (33,3)
Hypoglycaemia	6 (40,0)
Hypokalaemia	4 (26,7)
Hypomagnesaemia	1 (6,7)
Hyponatraemia	5 (33,3)
Hypophosphataemia	3 (20,0)
Lactose intolerance	1 (6,7)
PSYCHIATRIC DISORDERS	6 (40,0)
Anxiety	4 (26,7)
Depression	2 (13,3)
Insomnia	4 (26,7)
Irritability	2 (13,3)
Suicidal ideation	1 (6,7)
NERVOUS SYSTEM DISORDERS	11 (73,3)
Cognitive disorder	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.
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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Depressed level of consciousness	1 (6,7)
Dizziness	6 (40,0)
Drooling	1 (6,7)
Dyspraxia	1 (6,7)
Headache	9 (60,0)
Phantom limb syndrome	1 (6,7)
Presyncope	1 (6,7)
Syncope	1 (6,7)
EYE DISORDERS	3 (20,0)
Blepharitis	2 (13,3)
Chorioretinal scar	1 (6,7)
Vision blurred	2 (13,3)
Vitreous disorder	1 (6,7)
EAR AND LABYRINTH DISORDERS	6 (40,0)
Ear pain	2 (13,3)
External ear inflammation	2 (13,3)
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	10 (66,7)

[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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Aortic stenosis	1 (6,7)
Flushing	2 (13,3)
Haematoma	1 (6,7)
Hypertension	6 (40,0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	10 (66,7)
Atelectasis	2 (13,3)
Cough	3 (20,0)
Epistaxis	5 (33,3)
Hypoxia	1 (6,7)
Increased bronchial secretion	1 (6,7)
Increased upper airway secretion	1 (6,7)
Nasal congestion	2 (13,3)
Oropharyngeal pain	6 (40,0)
Rhinitis allergic	4 (26,7)
Rhinorrhoea	1 (6,7)
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)
Cheilitis	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)

[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 3.1.2.4 Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Gastrooesophageal reflux disease	1 (6,7)
Haemorrhoids	1 (6,7)
Mouth haemorrhage	1 (6,7)
Mouth ulceration	1 (6,7)
Nausea	11 (73,3)
Oral pain	2 (13,3)
Stomatitis	6 (40,0)
Tongue discolouration	1 (6,7)
Vomiting	12 (80,0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	14 (93,3)
Alopecia	2 (13,3)
Dermatitis acneiform	10 (66,7)
Dermatitis atopic	1 (6,7)
Dermatitis diaper	1 (6,7)
Dry skin	10 (66,7)
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	8 (53,3)
Rash pruritic	1 (6,7)
Skin hypopigmentation	1 (6,7)
Skin ulcer	1 (6,7)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	12 (80,0)
Arthralgia	6 (40,0)
Back pain	3 (20,0)
Bone pain	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.
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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Flank pain	1 (6,7)
Growth retardation	1 (6,7)
Joint lock	1 (6,7)
Limb asymmetry	1 (6,7)
Muscle spasms	1 (6,7)
Myalgia	1 (6,7)
Neck pain	3 (20,0)
Osteoporosis	1 (6,7)
Pain in extremity	5 (33,3)
RENAL AND URINARY DISORDERS	6 (40,0)
Acute kidney injury	1 (6,7)
Haematuria	4 (26,7)
Haemoglobinuria	1 (6,7)
Proteinuria	4 (26,7)
Urinary incontinence	1 (6,7)
Urinary tract pain	1 (6,7)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	3 (20,0)
Adnexa uteri cyst	1 (6,7)
Heavy menstrual bleeding	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	2 (13,3)
Fatigue	9 (60,0)

[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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Hypothermia	1 (6,7)
Influenza like illness	4 (26,7)
Injection site reaction	1 (6,7)
Localised oedema	3 (20,0)
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	4 (26,7)
Pain	6 (40,0)
Pyrexia	8 (53,3)
Vessel puncture site bruise	1 (6,7)
INVESTIGATIONS	14 (93,3)
Alanine aminotransferase increased	6 (40,0)
Amylase increased	5 (33,3)
Aspartate aminotransferase increased	7 (46,7)
Blood alkaline phosphatase increased	4 (26,7)
Blood creatine phosphokinase increased	12 (80,0)
Blood creatinine increased	4 (26,7)
Ejection fraction decreased	3 (20,0)
Haemoglobin increased	2 (13,3)
Lipase increased	4 (26,7)
Lymphocyte count decreased	7 (46,7)
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)

[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 3.1.2.4 Adverse events by system organ class and preferred term
- PN status at enrollment = Non-progressive (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Weight decreased	1 (6,7)
Weight increased	2 (13,3)
White blood cell count decreased	5 (33,3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	6 (40,0)
Arthropod bite	1 (6,7)
Contusion	2 (13,3)
Fall	3 (20,0)
Fracture	4 (26,7)
Skin abrasion	1 (6,7)
Stoma site irritation	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).

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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, data cut-off: 31 March 2021 (DC02)

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)
Body tinea	1 (7,1)
Bronchiolitis	1 (7,1)
Cellulitis	2 (14,3)
Conjunctivitis	1 (7,1)
Conjunctivitis viral	1 (7,1)
Eye infection	1 (7,1)
Gastroenteritis	1 (7,1)
Gastroenteritis viral	1 (7,1)
Gingivitis	1 (7,1)
Hordeolum	1 (7,1)
Influenza	1 (7,1)
Medical device site infection	1 (7,1)
Osteomyelitis	1 (7,1)
Otitis media	4 (28,6)
Paronychia	6 (42,9)
Pharyngitis	4 (28,6)
Pharyngitis streptococcal	1 (7,1)
Pilonidal cyst	1 (7,1)
Pneumonia	4 (28,6)
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	3 (21,4)
Urinary tract infection	1 (7,1)
Vaginal infection	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	2 (14,3)
Dysplastic naevus	1 (7,1)
Neurofibrosarcoma	1 (7,1)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	8 (57,1)
Anaemia	8 (57,1)
Lymph node pain	1 (7,1)
IMMUNE SYSTEM DISORDERS	1 (7,1)
Hypersensitivity	1 (7,1)
METABOLISM AND NUTRITION DISORDERS	13 (92,9)
Decreased appetite	5 (35,7)
Dehydration	3 (21,4)
Hypercalcaemia	1 (7,1)
Hyperglycaemia	6 (42,9)
Hyperkalaemia	2 (14,3)
Hypernatraemia	2 (14,3)
Hypoalbuminaemia	8 (57,1)
Hypocalcaemia	4 (28,6)
Hypoglycaemia	3 (21,4)
Hypokalaemia	5 (35,7)
Hypomagnesaemia	1 (7,1)
Hyponatraemia	3 (21,4)
Hypophosphataemia	2 (14,3)
PSYCHIATRIC DISORDERS	7 (50,0)
Anxiety	1 (7,1)
Attention deficit hyperactivity disorder	1 (7,1)
Depression	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.
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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Insomnia	4 (28,6)
Irritability	1 (7,1)
Suicidal ideation	1 (7,1)
NERVOUS SYSTEM DISORDERS	9 (64,3)
Aphasia	1 (7,1)
Disturbance in attention	1 (7,1)
Dizziness	2 (14,3)
Encephalomalacia	1 (7,1)
Headache	6 (42,9)
Lethargy	1 (7,1)
Neuralgia	1 (7,1)
Paraesthesia	2 (14,3)
Presyncope	1 (7,1)
Seizure	1 (7,1)
Syncope	2 (14,3)
EYE DISORDERS	6 (42,9)
Cataract	1 (7,1)
Eye oedema	1 (7,1)
Eye pain	3 (21,4)
Eye pruritus	1 (7,1)
Eyelid skin dryness	1 (7,1)
Lacrimation increased	2 (14,3)
Vision blurred	2 (14,3)
EAR AND LABYRINTH DISORDERS	2 (14,3)
Ear pain	1 (7,1)
Hypoacusis	1 (7,1)
Vertigo	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
CARDIAC DISORDERS	4 (28,6)
Sinus tachycardia	4 (28,6)
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)
Cough	6 (42,9)
Dysphonia	1 (7,1)
Dyspnoea	3 (21,4)
Epistaxis	3 (21,4)
Hypoxia	3 (21,4)
Increased bronchial secretion	1 (7,1)
Nasal congestion	6 (42,9)
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)
Cheilitis	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
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)
Nausea	10 (71,4)
Oesophageal stenosis	1 (7,1)
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	11 (78,6)
Dry skin	9 (64,3)
Ecchymosis	1 (7,1)
Eczema	2 (14,3)
Erythema	2 (14,3)
Exfoliative rash	1 (7,1)
Hair colour changes	2 (14,3)
Pain of skin	1 (7,1)
Photosensitivity reaction	1 (7,1)
Pityriasis alba	1 (7,1)
Pruritus	7 (50,0)
Rash erythematous	1 (7,1)
Rash maculo-papular	6 (42,9)
Skin exfoliation	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Skin hyperpigmentation	1 (7,1)
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	10 (71,4)
Arthralgia	1 (7,1)
Axillary mass	1 (7,1)
Back pain	4 (28,6)
Neck pain	2 (14,3)
Pain in extremity	5 (35,7)
Sever's disease	1 (7,1)
RENAL AND URINARY DISORDERS	9 (64,3)
Haematuria	7 (50,0)
Haemoglobinuria	1 (7,1)
Nephrolithiasis	1 (7,1)
Proteinuria	3 (21,4)
Urinary incontinence	2 (14,3)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	4 (28,6)
Dysmenorrhoea	2 (14,3)
Ovarian cyst	1 (7,1)
Vulvovaginal inflammation	1 (7,1)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	13 (92,9)
Facial pain	1 (7,1)
Fatigue	6 (42,9)

[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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Influenza like illness	1 (7,1)
Localised oedema	2 (14,3)
Medical device site erythema	1 (7,1)
Oedema peripheral	3 (21,4)
Pain	4 (28,6)
Peripheral swelling	1 (7,1)
Pyrexia	9 (64,3)
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	9 (64,3)
Blood creatinine increased	6 (42,9)
Ejection fraction decreased	6 (42,9)
Electrocardiogram QT prolonged	1 (7,1)
Haemoglobin increased	1 (7,1)
Lipase increased	4 (28,6)
Lymphocyte count decreased	4 (28,6)
Neutrophil count decreased	2 (14,3)
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	8 (57,1)
Arthropod bite	1 (7,1)
Arthropod sting	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.
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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Contusion	1 (7,1)
Fall	3 (21,4)
Fracture	2 (14,3)
Joint dislocation	1 (7,1)
Joint injury	1 (7,1)
Post procedural haemorrhage	1 (7,1)
Procedural hypotension	1 (7,1)
Procedural pain	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).

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3.1.3.3 Subgruppenanalysen zu den schweren unerwünschten Ereignissen nach SOC und PT

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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Patients with Any Severe AE (CTCAE >=3)	23 (76,7)
INFECTIONS AND INFESTATIONS	9 (30,0)
Clostridium difficile colitis	1 (3,3)
Influenza	1 (3,3)
Osteomyelitis	1 (3,3)
Paronychia	4 (13,3)
Skin infection	2 (6,7)
Urinary tract infection	1 (3,3)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	2 (6,7)
Neurofibrosarcoma	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	3 (10,0)
Dehydration	1 (3,3)
Hyperkalaemia	1 (3,3)
Hyperuricaemia	1 (3,3)
Hypocalcaemia	2 (6,7)
Hypokalaemia	2 (6,7)
PSYCHIATRIC DISORDERS	1 (3,3)
Insomnia	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
NERVOUS SYSTEM DISORDERS	2 (6,7)
Headache	1 (3,3)
Syncope	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)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (3,3)
Scoliosis	1 (3,3)
RENAL AND URINARY DISORDERS	2 (6,7)
Acute kidney injury	1 (3,3)
Haematuria	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.
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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	3 (10,0)
Influenza like illness	1 (3,3)
Pyrexia	3 (10,0)
INVESTIGATIONS	7 (23,3)
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	4 (13,3)
Fracture	3 (10,0)
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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Patients with Any Severe AE (CTCAE >=3)	11 (55,0)
INFECTIONS AND INFESTATIONS	1 (5,0)
Pneumonia	1 (5,0)
Tracheitis	1 (5,0)
PSYCHIATRIC DISORDERS	1 (5,0)
Depression	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)

[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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Pyrexia	1 (5,0)
INVESTIGATIONS	5 (25,0)
Alanine aminotransferase increased	1 (5,0)
Aspartate aminotransferase increased	1 (5,0)
Blood creatine phosphokinase increased	1 (5,0)
Lipase increased	1 (5,0)
Neutrophil count decreased	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Patients with Any Severe AE (CTCAE >=3)	14 (66,7)
INFECTIONS AND INFESTATIONS	5 (23,8)
Clostridium difficile colitis	1 (4,8)
Paronychia	4 (19,0)
Skin infection	1 (4,8)
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)

[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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Eczema	2 (9,5)
Rash maculo-papular	1 (4,8)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (4,8)
Scoliosis	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Patients with Any Severe AE (CTCAE >=3)	11 (73,3)
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	2 (13,3)
Dehydration	1 (6,7)
Hyperkalaemia	1 (6,7)
Hyperuricaemia	1 (6,7)
Hypocalcaemia	2 (13,3)
Hypokalaemia	1 (6,7)
PSYCHIATRIC DISORDERS	1 (6,7)
Depression	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)

[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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Hypoxia	1 (6,7)
GASTROINTESTINAL DISORDERS	3 (20,0)
Dental caries	1 (6,7)
Diarrhoea	1 (6,7)
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)
Fracture	2 (13,3)

[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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Patients with Any Severe AE (CTCAE >=3)	9 (64,3)
INFECTIONS AND INFESTATIONS	2 (14,3)
Osteomyelitis	1 (7,1)
Pneumonia	1 (7,1)
Tracheitis	1 (7,1)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (7,1)
Neurofibrosarcoma	1 (7,1)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (7,1)
Anaemia	1 (7,1)
NERVOUS SYSTEM DISORDERS	2 (14,3)
Syncope	2 (14,3)
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	2 (14,3)
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).

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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, data cut-off: 31 March 2021 (DC02)

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)
Neutrophil count decreased	1 (7,1)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	2 (14,3)
Fracture	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).

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3.1.3.4 Subgruppenanalysen zu den schwerwiegenden unerwünschten Ereignissen nach SOC und PT

Table 3.1.3.1 Serious Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Patients with Any SAE	14 (46,7)
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	2 (6,7)
Urinary tract infection	1 (3,3)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (3,3)
Neurofibrosarcoma	1 (3,3)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	2 (6,7)
Anaemia	2 (6,7)
METABOLISM AND NUTRITION DISORDERS	2 (6,7)
Dehydration	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	4 (13,3)
Abdominal pain	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).

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Table 3.1.3.1 Serious Adverse events by system organ class and preferred term
- Gender = Male (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=30)
Constipation	1 (3,3)
Diarrhoea	2 (6,7)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (3,3)
Skin ulcer	1 (3,3)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (3,3)
Flank pain	1 (3,3)
RENAL AND URINARY DISORDERS	2 (6,7)
Acute kidney injury	1 (3,3)
Haematuria	1 (3,3)
Proteinuria	1 (3,3)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	2 (6,7)
Oedema peripheral	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	3 (10,0)
Fracture	2 (6,7)
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).

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Table 3.1.3.2 Serious Adverse events by system organ class and preferred term
- Gender = Female (Safety analysis set)
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=20)
Patients with Any SAE	1 (5,0)
PSYCHIATRIC DISORDERS	1 (5,0)
Depression	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=21)
Patients with Any SAE	4 (19,0)
INFECTIONS AND INFESTATIONS	1 (4,8)
Clostridium difficile colitis	1 (4,8)
Skin infection	1 (4,8)
GASTROINTESTINAL DISORDERS	1 (4,8)
Diarrhoea	1 (4,8)
RENAL AND URINARY DISORDERS	1 (4,8)
Haematuria	1 (4,8)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (4,8)
Oedema peripheral	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
Patients with Any SAE	6 (40,0)
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	2 (13,3)
Dehydration	1 (6,7)
Hyperkalaemia	1 (6,7)
Hyperuricaemia	1 (6,7)
Hypocalcaemia	1 (6,7)
PSYCHIATRIC DISORDERS	1 (6,7)
Depression	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	2 (13,3)
Abdominal pain	1 (6,7)
Constipation	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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=15)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (6,7)
Flank pain	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)
Pyrexia	1 (6,7)
INVESTIGATIONS	1 (6,7)
Blood creatinine increased	1 (6,7)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (6,7)
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).

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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, data cut-off: 31 March 2021 (DC02)

System organ class / Preferred term	Number (%) of patients [a] Selumetinib 25 mg/m² BID (N=14)
Patients with Any SAE	5 (35,7)
INFECTIONS AND INFESTATIONS	1 (7,1)
Osteomyelitis	1 (7,1)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (7,1)
Neurofibrosarcoma	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	2 (14,3)
Fracture	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).

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3.1.3.5 Subgruppenanalysen zu den unerwünschten Ereignissen, die zum Abbruch der Studienmedikation geführt haben nach SOC und PT

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, data cut-off: 31 March 2021 (DC02)

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)
Neurofibrosarcoma	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).

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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, data cut-off: 31 March 2021 (DC02)

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).

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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, data cut-off: 31 March 2021 (DC02)

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).

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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, data cut-off: 31 March 2021 (DC02)

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).

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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, data cut-off: 31 March 2021 (DC02)

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)
Neurofibrosarcoma	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).

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3.1.3.6 Subgruppenanalysen zu den unerwünschten Ereignissen von besonderem Interesse

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Table 3.1.6.1 Adverse Events of Special Interest
Sex = Male
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

	Number (%) of patients [a] Selumetinib 25 mg/m^2 BID (N=30)			
Adverse Event of Special Interest	Any AESI	Any Serious AESI	Any non-severe AESI (CTCAE <= 2)	Any severe AESI (CTCAE >=3)
Any AE of Special Interest	30 (100.0%)	4 (13.3%)	30 (100.0%)	11 (36.7%)
Cardiac failure effects	13 (43.3%)	1 (3.3%)	13 (43.3%)	0 (0.0%)
Erythropenia effects	20 (66.7%)	2 (6.7%)	19 (63.3%)	2 (6.7%)
Leucopenic effects	18 (60.0%)	0 (0.0%)	18 (60.0%)	1 (3.3%)
Muscle related effects	27 (90.0%)	2 (6.7%)	27 (90.0%)	4 (13.3%)
Nail disorders	19 (63.3%)	0 (0.0%)	19 (63.3%)	4 (13.3%)
Oral mucositis effects	14 (46.7%)	0 (0.0%)	14 (46.7%)	0 (0.0%)
Physeal Dysplasia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash acneiform	15 (50.0%)	0 (0.0%)	15 (50.0%)	3 (10.0%)
Rash, non-acneiform	22 (73.3%)	0 (0.0%)	22 (73.3%)	0 (0.0%)
Retinal effects	7 (23.3%)	0 (0.0%)	7 (23.3%)	0 (0.0%)
Thrombocytopenia effects	5 (16.7%)	0 (0.0%)	5 (16.7%)	0 (0.0%)

[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.

Number (%) of patients with AESIs, sorted alphabetically

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).

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Table 3.1.6.2 Adverse Events of Special Interest
Sex = Female
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

	Number (%) of patients [a] Selumetinib 25 mg/m^2 BID (N=20)			
Adverse Event of Special Interest	Any AESI	Any Serious AESI	Any non-severe AESI (CTCAE <= 2)	Any severe AESI (CTCAE >=3)
Any AE of Special Interest	19 (95.0%)	0 (0.0%)	19 (95.0%)	3 (15.0%)
Cardiac failure effects	8 (40.0%)	0 (0.0%)	8 (40.0%)	0 (0.0%)
Erythropenia effects	7 (35.0%)	0 (0.0%)	7 (35.0%)	0 (0.0%)
Leucopenic effects	11 (55.0%)	0 (0.0%)	11 (55.0%)	1 (5.0%)
Muscle related effects	17 (85.0%)	0 (0.0%)	17 (85.0%)	1 (5.0%)
Nail disorders	9 (45.0%)	0 (0.0%)	9 (45.0%)	0 (0.0%)
Oral mucositis effects	14 (70.0%)	0 (0.0%)	14 (70.0%)	0 (0.0%)
Physeal Dysplasia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash acneiform	13 (65.0%)	0 (0.0%)	13 (65.0%)	0 (0.0%)
Rash, non-acneiform	16 (80.0%)	0 (0.0%)	16 (80.0%)	1 (5.0%)
Retinal effects	3 (15.0%)	0 (0.0%)	3 (15.0%)	0 (0.0%)
Thrombocytopenia effects	1 (5.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)

[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.

Number (%) of patients with AESIs, sorted alphabetically

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).

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Table 3.1.6.3 Adverse Events of Special Interest
PN status at enrollment = Progressive
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

	Number (%) of patients [a] Selumetinib 25 mg/m^2 BID (N=21)			
Adverse Event of Special Interest	**Any AESI**	**Any Serious AESI**	**Any non-severe AESI (CTCAE <= 2)**	**Any severe AESI (CTCAE >=3)**
Any AE of Special Interest	21 (100.0%)	2 (9.5%)	21 (100.0%)	7 (33.3%)
Cardiac failure effects	5 (23.8%)	1 (4.8%)	5 (23.8%)	0 (0.0%)
Erythropenia effects	11 (52.4%)	0 (0.0%)	11 (52.4%)	0 (0.0%)
Leucopenic effects	15 (71.4%)	0 (0.0%)	15 (71.4%)	0 (0.0%)
Muscle related effects	19 (90.5%)	1 (4.8%)	19 (90.5%)	2 (9.5%)
Nail disorders	14 (66.7%)	0 (0.0%)	14 (66.7%)	4 (19.0%)
Oral mucositis effects	12 (57.1%)	0 (0.0%)	12 (57.1%)	0 (0.0%)
Physeal Dysplasia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash acneiform	7 (33.3%)	0 (0.0%)	7 (33.3%)	2 (9.5%)
Rash, non-acneiform	18 (85.7%)	0 (0.0%)	18 (85.7%)	1 (4.8%)
Retinal effects	5 (23.8%)	0 (0.0%)	5 (23.8%)	0 (0.0%)
Thrombocytopenia effects	3 (14.3%)	0 (0.0%)	3 (14.3%)	0 (0.0%)

[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.

Number (%) of patients with AESIs, sorted alphabetically

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).

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Table 3.1.6.4 Adverse Events of Special Interest
PN status at enrollment = Non-Progressive
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

	Number (%) of patients [a] Selumetinib 25 mg/m^2 BID (N=15)			
Adverse Event of Special Interest	**Any AESI**	**Any Serious AESI**	**Any non-severe AESI (CTCAE <= 2)**	**Any severe AESI (CTCAE >=3)**
Any AE of Special Interest	14 (93.3%)	1 (6.7%)	14 (93.3%)	4 (26.7%)
Cardiac failure effects	7 (46.7%)	0 (0.0%)	7 (46.7%)	0 (0.0%)
Erythropenia effects	8 (53.3%)	1 (6.7%)	7 (46.7%)	1 (6.7%)
Leucopenic effects	8 (53.3%)	0 (0.0%)	8 (53.3%)	1 (6.7%)
Muscle related effects	13 (86.7%)	1 (6.7%)	13 (86.7%)	3 (20.0%)
Nail disorders	8 (53.3%)	0 (0.0%)	8 (53.3%)	0 (0.0%)
Oral mucositis effects	7 (46.7%)	0 (0.0%)	7 (46.7%)	0 (0.0%)
Physeal Dysplasia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash acneiform	10 (66.7%)	0 (0.0%)	10 (66.7%)	0 (0.0%)
Rash, non-acneiform	11 (73.3%)	0 (0.0%)	11 (73.3%)	0 (0.0%)
Retinal effects	3 (20.0%)	0 (0.0%)	3 (20.0%)	0 (0.0%)
Thrombocytopenia effects	2 (13.3%)	0 (0.0%)	2 (13.3%)	0 (0.0%)

[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.

Number (%) of patients with AESIs, sorted alphabetically

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).

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Table 3.1.6.5 Adverse Events of Special Interest
PN status at enrollment = Unknown
Phase II Stratum 1, data cut-off: 31 March 2021 (DC02)

	Number (%) of patients [a] Selumetinib 25 mg/m^2 BID (N=14)			
Adverse Event of Special Interest	**Any AESI**	**Any Serious AESI**	**Any non-severe AESI (CTCAE <= 2)**	**Any severe AESI (CTCAE >=3)**
Any AE of Special Interest	14 (100.0%)	1 (7.1%)	14 (100.0%)	3 (21.4%)
Cardiac failure effects	9 (64.3%)	0 (0.0%)	9 (64.3%)	0 (0.0%)
Erythropenia effects	8 (57.1%)	1 (7.1%)	8 (57.1%)	1 (7.1%)
Leucopenic effects	6 (42.9%)	0 (0.0%)	6 (42.9%)	1 (7.1%)
Muscle related effects	12 (85.7%)	0 (0.0%)	12 (85.7%)	0 (0.0%)
Nail disorders	6 (42.9%)	0 (0.0%)	6 (42.9%)	0 (0.0%)
Oral mucositis effects	9 (64.3%)	0 (0.0%)	9 (64.3%)	0 (0.0%)
Physeal Dysplasia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash acneiform	11 (78.6%)	0 (0.0%)	11 (78.6%)	1 (7.1%)
Rash, non-acneiform	9 (64.3%)	0 (0.0%)	9 (64.3%)	0 (0.0%)
Retinal effects	2 (14.3%)	0 (0.0%)	2 (14.3%)	0 (0.0%)
Thrombocytopenia effects	1 (7.1%)	0 (0.0%)	1 (7.1%)	0 (0.0%)

[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.

Number (%) of patients with AESIs, sorted alphabetically

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).

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