表 2.7.4.2-13 治験薬の減量に至った有害事象の一覧（SP）（NPC-25-3 試験 ）

Group	Patient No ID		Reported Term System Organ Class Preferred Term	Datetime of Onset (Duration) [1)] Datetime of Outcome (Duration) [1)]	Action Taken with Study Treatment Other Action Taken Outcome	Serious Event Serious Event Type Severity	Relationship with Study Treatment Reason for No Relation
NPC-25	[redacted]	1	nausea Gastrointestinal disorders Nausea	20[redacted] (30) 20[redacted] (58)	Dose Reduced N Recovered/Resolved	N - Mild	Related
	[redacted]	2	Decrease in serum copper Investigations Blood copper decreased	20[redacted] (64) 20[redacted] (148)	Dose Reduced N Recovering/Resolving	N - Moderate	Related
	[redacted]	1	Lipase increased Investigations Lipase increased	20[redacted] (173) 20[redacted] (194)	Dose Reduced N Not Recovered/Not Resolved	N - Mild	Related
		2	Amylase increased Investigations Amylase increased	20[redacted] (173) 20[redacted] (194)	Dose Reduced N Not Recovered/Not Resolved	N - Mild	Related
	[redacted]	1	Stomach discomfort Gastrointestinal disorders Abdominal discomfort	20[redacted] (1) 20[redacted] (12)	Dose Reduced N Recovered/Resolved	N - Mild	Related
		3	Gastralgia Gastrointestinal disorders Abdominal pain upper	20[redacted] (339) 20[redacted] (341)	Dose Reduced Y Recovered/Resolved	N - Mild	Related
	[redacted]	1	nausea Gastrointestinal disorders Nausea	20[redacted] (4) 20[redacted] (4)	Dose Reduced N Recovered/Resolved	N - Mild	Related
		3	nausea Gastrointestinal disorders Nausea	20[redacted] (41) 20[redacted] (42)	Dose Reduced N Recovered/Resolved	N - Mild	Related
		4	diarrhea Gastrointestinal disorders Diarrhoea	20[redacted] (41) 20[redacted] (42)	Dose Reduced N Recovered/Resolved	N - Mild	Related

表 2.7.4.2-13 治験薬の減量に至った有害事象の一覧（SP）（NPC-25-3 試験 ）（続き）

Group	Patient No ID	Reported Term System Organ Class Preferred Term	Datetime of Onset (Duration) [1)] Datetime of Outcome (Duration) [1)]	Action Taken with Study Treatment Other Action Taken Outcome	Serious Event Serious Event Type Severity	Relationship with Study Treatment Reason for No Relation
NOBELZIN	[redacted] 4	Nausea Gastrointestinal disorders Nausea	20[redacted] (152) 20[redacted] (169)	Dose Reduced N Recovered/Resolved	N - Mild	Related
	[redacted] 1	Nausea Gastrointestinal disorders Nausea	20[redacted] (32) 20[redacted] (65)	Dose Reduced N Recovered/Resolved	N - Mild	Related
	[redacted] 1	nausea Gastrointestinal disorders Nausea	20[redacted] (2) 20[redacted] (27)	Dose Reduced N Recovered/Resolved	N - Mild	Related
	[redacted] 1	Stomach discomfort Gastrointestinal disorders Abdominal discomfort	20[redacted] (35) 20[redacted] (51)	Dose Reduced Y Recovered/Resolved	N - Mild	Related

1) : Number of days from first study treatment
MedDRA: Version 24.1

2.7.4.2.1.5 器官別又は症候群別有害事象の解析

NPC-25-3 試験における器官別の有害事象を表 2.7.4.2-14 に、副作用を表 2.7.4.2-15 に示した。

(1) 有害事象

本剤群で発現した器官別の有害事象の発現率は、「感染症および寄生虫症」30.8%で最も高く、次いで、「胃腸障害」23.4%、「臨床検査」16.8%、「神経系障害」、「皮膚および皮下組織障害」、「一般・全身障害および投与部位の状態」、「筋骨格系および結合組織障害」が各 11.2%、「傷害、中毒および処置合併症」10.3%、「代謝および栄養障害」8.4%、「肝胆道系障害」5.6%、「眼障害」、「呼吸器、胸郭および縦隔障害」、「血液およびリンパ系障害」が各 4.7%、「腎および尿路障害」、「血管障害」が各 2.8%の順であった。その他の器官別の有害事象の発現率は 2%未満であった。

(2) 副作用

本剤群で発現した器官別の副作用の発現率は、「臨床検査」12.1%で最も高く、次いで、「胃腸障害」10.3%、「血液およびリンパ系障害」3.7%であった。その他の器官別の副作用の発現率は 2%未満であった。

表 2.7.4.2-14 器官別の有害事象（SP）（NPC-25-3 試験）

System Organ Class	NPC-25 N = 107	
	n Events	n (%) Patients
Gastrointestinal disorders	40	25 (23.4)
Infections and infestations	38	33 (30.8)
Investigations	27	18 (16.8)
Nervous system disorders	16	12 (11.2)
Skin and subcutaneous tissue disorders	16	12 (11.2)
General disorders and administration site conditions	14	12 (11.2)
Musculoskeletal and connective tissue disorders	14	12 (11.2)
Metabolism and nutrition disorders	13	9 (8.4)
Injury, poisoning and procedural complications	12	11 (10.3)
Eye disorders	7	5 (4.7)
Hepatobiliary disorders	7	6 (5.6)
Respiratory, thoracic and mediastinal disorders	7	5 (4.7)
Blood and lymphatic system disorders	5	5 (4.7)
Renal and urinary disorders	4	3 (2.8)
Vascular disorders	3	3 (2.8)
Cardiac disorders	2	2 (1.9)
Psychiatric disorders	1	1 (0.9)
Reproductive system and breast disorders	1	1 (0.9)
Social circumstances	1	1 (0.9)
Surgical and medical procedures	1	1 (0.9)

MedDRA: Version 24.1

表 2.7.4.2-15 器官別の副作用（SP）（NPC-25-3 試験）

System Organ Class	NPC-25 N = 107	
	n Events	n (%) Patients
Investigations	17	13 (12.1)
Gastrointestinal disorders	16	11 (10.3)
Blood and lymphatic system disorders	4	4 (3.7)
Nervous system disorders	3	2 (1.9)
Hepatobiliary disorders	1	1 (0.9)
Metabolism and nutrition disorders	1	1 (0.9)
Psychiatric disorders	1	1 (0.9)
Respiratory, thoracic and mediastinal disorders	1	1 (0.9)

MedDRA: Version 24.1

2.7.4.2.2 個別有害事象の文章による説明

「2.7.4.2.1.3 その他の重篤な有害事象」に関する詳細記載は，治験総括報告書（5.3.5.1-2）に記述した。

2.7.4.3 臨床検査値の評価

NPC-25-3 試験における本剤群とノベルジン錠群の血液学的検査及び血液生化学的検査の要約統計量をそれぞれ表 2.7.4.7-1 及び表 2.7.4.7-2 に示した。また、本剤群とノベルジン錠群の尿検査値の推移（シフトテーブル）を表 2.7.4.7-3 に示した。

治験責任（分担）医師は、2.7.4.1.1.1 に示す基準に従って一般臨床検査値の基準値外変動を判定し、異常変動は有害事象として取り扱った。

本剤群の血液学的検査項目に関する有害事象は、認められなかった。

本剤群の血液生化学的検査項目に関する本剤群の有害事象は、血中銅減少 4.7%（5/107 例）、アミラーゼ増加、リパーゼ増加が各 3.7%（4/107 例）、肝機能検査異常 1.9%（2/107 例）、アラニンアミノトランスフェラーゼ増加、アスパラギン酸アミノトランスフェラーゼ増加、血中鉄減少、血中カリウム減少が各 0.9%（1/107 例）であった。そのうち本剤との因果関係ありと判定されたのは、血中銅減少 4.7%（5/107 例）、リパーゼ増加 3.7%（4/107 例）、アミラーゼ増加 2.8%（3/107 例）、肝機能検査異常 1.9%（2/107 例）であった。

本剤群の尿検査項目に関する本剤群の有害事象は、尿中蛋白陽性 0.9%（1/107 例）であったが、因果関係は否定された。

治験実施計画書で規定した表 2.7.4.1-2 に示した一般臨床検査項目以外の本剤群の臨床検査の有害事象は、血中アルドステロン増加、眼圧上昇が各 0.9%（1/107 例）であったが、いずれも因果関係は否定された。

なお、上記、臨床検査の有害事象のうち、血中銅減少、血中鉄減少の各 0.9%（1/107 例）が中等度であり、その他の有害事象はいずれも軽度と判定された。

血液学的検査の中央値及び平均値の推移では、特筆すべき変化は認められなかった。

血液生化学的検査の中央値及び平均値の推移では、血中銅の経時的な減少傾向及びリパーゼの経時的な増加傾向が、投与開始後 24 週まで本剤群及びノベルジン錠群のいずれにおいても同程度に認められたが、それ以上の悪化傾向は認められなかった。その他特筆すべき変化は認められなかった。

尿検査項目の推移（シフトテーブル）では、特筆すべき変化は認められなかった。

2.7.4.4 バイタルサイン、身体的所見及び安全性に関連する他の観察項目

NPC-25-3 試験におけるノベルジン錠群を含めたバイタルサイン及び体重の推移（要約統計量）を、表 2.7.4.4-1～表 2.7.4.4-5 に示した。治験責任（分担）医師は、2.7.4.1.1.1 に示す基準に従って体重、体温、血圧及び脈拍における治験薬投与前の値からの変動を判定し、異常変動は有害事象として取り扱った。本剤群のバイタルサインに関する有害事象は、血圧上昇、体重減少が各 0.9%（1/107 例）であった。そのうち本剤との因果関係ありと判定されたのは、体重減少 0.9%（1/107 例）であった。その他、体重、体温、脈拍、血圧について、特筆すべき変化は認められなかった。

表 2.7.4.4-1 バイタルサイン（収縮期血圧 [mmHg]）（SP）（NPC-25-3 試験）

Parameter	Treatment Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Systolic Blood Pressure (mmHg)	NPC-25	Start of Administration	107	132.9	15.71	87	131.0	175	-	-	-	-	-	-
		Week 4	104	127.3	16.68	90	128.5	168	104	-5.7	14.52	-57	-5.0	22
		Week 8	100	128.1	16.40	88	127.5	179	100	-5.0	14.76	-56	-4.0	28
		Week 12	99	125.7	13.76	94	126.0	163	99	-7.2	13.54	-60	-7.0	32
		Week 16	77	126.6	16.19	94	128.0	160	77	-5.9	17.32	-71	-5.0	32
		Week 20	67	129.6	17.01	98	130.0	184	67	-3.7	13.64	-43	-5.0	32
		Week 24	57	127.7	14.76	96	127.0	168	57	-4.1	13.88	-36	-4.0	34
		Week 28	51	126.4	15.94	95	127.0	163	51	-5.7	14.54	-44	-5.0	24
		Week 32	35	130.3	19.02	95	127.0	176	35	-1.0	15.79	-33	-1.0	43
		Week 36	31	126.3	15.85	101	124.0	159	31	-4.9	12.41	-31	-6.0	32
		Week 40	30	128.2	18.30	93	130.0	165	30	-3.1	16.64	-50	-1.0	32
		Week 44	30	129.8	17.30	96	129.5	175	30	-1.5	14.14	-25	-2.5	50
		Week 48	29	130.5	21.89	94	129.0	184	29	-1.5	20.35	-33	-2.0	59
		Week 52	28	130.0	19.52	103	126.5	189	28	-2.4	18.93	-28	-8.5	64
		Discontinuation	14	126.4	12.09	108	124.0	146	14	-0.3	16.23	-41	0.0	25
	NOBELZIN	Start of Administration	109	125.5	20.55	78	124.0	192	-	-	-	-	-	-
		Week 4	107	123.7	19.01	82	123.0	181	107	-1.9	14.60	-50	-1.0	35
		Week 8	104	120.9	19.23	73	122.5	176	104	-4.7	15.09	-52	-4.0	40
		Week 12	104	119.4	19.22	73	118.0	181	104	-6.1	13.84	-59	-6.0	27
		Week 16	62	117.6	18.04	79	114.0	164	62	-8.1	15.27	-46	-7.5	46
		Week 20	30	112.9	14.09	87	112.5	138	30	-7.3	13.28	-41	-7.0	20
		Week 24	17	109.9	16.80	72	109.0	141	17	-7.6	17.19	-36	-8.0	28
		Discontinuation	10	117.6	15.61	95	115.0	144	10	-4.1	21.84	-59	-1.5	25

表 2.7.4.4-2 バイタルサイン（拡張期血圧 [mmHg]）（SP）（NPC-25-3 試験）

Parameter	Treatment Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Diastolic Blood Pressure (mmHg)	NPC-25	Start of Administration	107	75.9	10.21	47	75.0	107	-	-	-	-	-	-
		Week 4	104	73.0	11.37	45	72.0	97	104	-3.1	8.49	-24	-2.5	22
		Week 8	100	73.7	10.28	50	74.0	99	100	-2.4	9.23	-36	-2.0	28
		Week 12	99	73.5	9.88	51	73.0	101	99	-2.6	9.85	-26	-2.0	33
		Week 16	77	72.0	11.05	41	72.0	95	77	-2.9	10.80	-32	-4.0	30
		Week 20	67	73.6	10.95	49	72.0	103	67	-1.9	10.26	-23	-3.0	34
		Week 24	57	73.3	11.13	48	75.0	98	57	-2.0	9.61	-23	-3.0	21
		Week 28	51	73.0	10.58	45	71.0	96	51	-2.0	9.86	-27	-2.0	27
		Week 32	35	75.0	12.50	43	75.0	100	35	-0.6	8.93	-21	0.0	30
		Week 36	31	75.8	12.78	53	75.0	113	31	0.3	9.85	-15	-1.0	28
		Week 40	30	75.9	11.50	48	75.5	97	30	0.2	11.75	-22	1.5	28
		Week 44	30	76.5	12.73	45	75.5	101	30	0.8	13.17	-33	1.0	32
		Week 48	29	75.6	12.34	52	74.0	110	29	-0.5	12.16	-18	0.0	41
		Week 52	28	74.1	12.32	55	71.5	105	28	-1.5	10.84	-32	-1.5	36
		Discontinuation	14	71.0	12.50	51	70.0	94	14	-1.6	12.06	-21	-1.0	17
	NOBELZIN	Start of Administration	109	73.4	12.81	47	73.0	115	-	-	-	-	-	-
		Week 4	107	71.0	12.37	41	71.0	98	107	-2.6	10.23	-39	-4.0	23
		Week 8	104	70.5	11.74	43	71.0	96	104	-3.2	9.82	-52	-2.5	21
		Week 12	104	69.5	12.71	39	69.0	101	104	-3.9	8.85	-38	-4.0	14
		Week 16	62	67.9	12.73	41	67.0	96	62	-5.0	10.99	-32	-4.5	24
		Week 20	30	69.1	13.45	50	67.0	102	30	-4.0	11.11	-30	-3.5	19
		Week 24	17	66.5	15.50	38	65.0	90	17	-4.4	14.03	-26	-8.0	31
		Discontinuation	10	73.0	8.92	61	70.0	90	10	0.4	13.24	-29	1.5	16

表 2.7.4.4-3 バイタルサイン（脈拍数 [回／分]）（SP）（NPC-25-3 試験）

Parameter	Treatment Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Pulse Rate (beats/min)	NPC-25	Start of Administration	107	76.3	12.50	48	75.0	118	-	-	-	-	-	-
		Week 4	104	77.1	13.14	52	77.0	124	104	0.5	9.22	-22	1.0	37
		Week 8	100	76.1	10.83	49	76.0	98	100	-0.9	8.00	-22	-1.0	23
		Week 12	99	74.8	11.88	47	74.0	120	99	-2.1	9.77	-36	-2.0	33
		Week 16	77	74.8	12.20	48	73.0	109	77	-2.0	8.79	-31	-1.0	14
		Week 20	67	74.4	12.29	49	73.0	110	67	-2.6	9.78	-25	-4.0	24
		Week 24	57	73.9	10.99	47	73.0	101	57	-2.8	8.88	-24	-3.0	17
		Week 28	51	74.0	10.86	53	71.0	101	51	-2.7	10.08	-23	-3.0	18
		Week 32	35	73.1	13.84	53	71.0	116	35	-4.8	12.83	-47	-3.0	30
		Week 36	31	79.3	13.29	56	77.0	122	31	0.7	13.18	-21	0.0	36
		Week 40	30	77.8	12.22	57	77.5	104	30	-1.2	11.67	-23	-2.0	21
		Week 44	30	76.3	13.81	51	73.5	113	30	-2.7	12.80	-28	-3.0	21
		Week 48	29	76.4	11.50	52	76.0	98	29	-2.2	11.11	-20	-2.0	24
		Week 52	28	74.1	11.43	51	73.0	100	28	-5.4	11.97	-41	-6.5	15
		Discontinuation	14	76.9	12.20	56	74.5	102	14	4.9	11.95	-22	8.0	24
	NOBELZIN	Start of Administration	109	76.0	11.39	42	75.0	106	-	-	-	-	-	-
		Week 4	107	75.0	11.96	40	75.0	105	107	-1.1	9.33	-33	0.0	23
		Week 8	104	75.1	12.12	41	74.5	103	104	-0.9	8.68	-40	0.0	21
		Week 12	104	74.9	11.54	40	74.5	106	104	-0.8	9.40	-26	0.0	22
		Week 16	62	72.8	9.65	55	72.0	102	62	-1.0	8.99	-22	0.0	17
		Week 20	30	73.4	8.09	58	74.0	90	30	0.1	7.29	-15	-1.5	14
		Week 24	17	73.4	10.25	55	74.0	90	17	1.8	10.49	-13	0.0	30
		Discontinuation	10	82.5	13.11	65	80.5	111	10	4.2	7.96	-6	4.0	16

表 2.7.4.4-4 バイタルサイン（体温[度]）（SP）（NPC-25-3 試験）

Parameter	Treatment Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Temperature (C)	NPC-25	Start of Administration	107	36.29	0.405	35.3	36.30	37.4	-	-	-	-	-	-
		Week 4	104	36.36	0.369	35.0	36.40	37.0	104	0.06	0.421	-0.9	0.05	1.1
		Week 8	100	36.31	0.399	35.0	36.40	37.6	100	0.00	0.421	-1.4	0.00	1.1
		Week 12	99	36.32	0.400	35.1	36.40	37.1	99	0.00	0.409	-1.3	0.00	1.1
		Week 16	77	36.33	0.475	35.2	36.40	37.2	77	-0.01	0.458	-1.1	0.00	0.8
		Week 20	67	36.33	0.437	35.1	36.40	37.2	67	-0.01	0.417	-1.1	0.00	1.0
		Week 24	57	36.29	0.391	34.9	36.40	36.9	57	-0.01	0.377	-1.2	0.00	0.7
		Week 28	51	36.27	0.432	35.3	36.30	37.1	51	-0.05	0.412	-0.9	-0.10	1.0
		Week 32	35	36.29	0.436	35.2	36.40	37.0	35	-0.04	0.396	-1.2	0.00	0.9
		Week 36	31	36.20	0.452	35.2	36.20	37.3	31	-0.14	0.398	-0.8	-0.10	1.0
		Week 40	30	36.21	0.494	35.2	36.30	37.0	30	-0.12	0.413	-1.0	-0.10	0.6
		Week 44	30	36.18	0.412	35.4	36.15	37.0	30	-0.15	0.413	-0.9	-0.10	0.5
		Week 48	29	36.23	0.444	35.3	36.40	37.1	29	-0.08	0.464	-1.0	0.00	0.7
		Week 52	28	36.21	0.493	35.3	36.25	37.0	28	-0.11	0.394	-1.1	0.00	0.6
		Discontinuation	14	36.28	0.336	35.2	36.40	36.5	14	0.24	0.560	-1.1	0.20	1.1
	NOBELZIN	Start of Administration	109	36.34	0.442	34.7	36.40	37.4	-	-	-	-	-	-
		Week 4	108	36.37	0.403	35.1	36.40	37.1	108	0.03	0.410	-1.0	0.00	1.1
		Week 8	104	36.36	0.401	35.0	36.40	37.1	104	0.01	0.401	-1.0	0.00	1.2
		Week 12	104	36.44	0.362	35.0	36.50	37.2	104	0.09	0.425	-0.8	0.00	1.7
		Week 16	62	36.38	0.409	35.3	36.50	37.3	62	0.07	0.377	-0.9	0.10	0.9
		Week 20	30	36.34	0.428	35.6	36.35	37.2	30	-0.02	0.413	-0.8	0.00	0.8
		Week 24	17	36.48	0.334	35.9	36.50	37.3	17	0.10	0.412	-0.6	0.20	0.6
		Discontinuation	11	36.55	0.401	35.9	36.60	37.1	11	0.24	0.398	-0.5	0.20	0.8

表 2.7.4.4-5 体重[kg]（SP）（NPC-25-3 試験）

Parameter	Treatment Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Weight (kg)	NPC-25	Start of Administration	107	58.65	13.137	34.2	57.10	116.9	-	-	-	-	-	-
		Week 4	104	58.69	13.168	32.9	56.60	116.6	104	0.06	1.076	-3.2	0.10	3.2
		Week 8	100	58.31	13.057	33.1	56.45	115.7	100	-0.16	1.494	-6.4	-0.10	4.1
		Week 12	99	57.80	12.813	34.2	55.90	117.9	99	-0.38	1.911	-7.2	-0.30	4.2
		Week 16	77	58.52	13.267	34.4	55.60	115.7	77	-0.40	2.084	-7.9	-0.30	5.3
		Week 20	67	57.80	12.124	34.6	56.30	95.0	67	-0.56	2.237	-7.6	-0.50	6.8
		Week 24	57	58.18	12.160	35.2	56.50	96.1	57	-0.29	2.545	-10.1	-0.50	8.0
		Week 28	51	58.19	12.588	35.0	57.30	96.6	51	-0.03	2.423	-10.1	-0.10	7.2
		Week 32	35	57.85	13.600	33.9	55.90	96.7	35	-0.27	2.821	-11.7	-0.10	7.2
		Week 36	31	57.25	14.226	34.9	53.00	97.3	31	-0.09	2.441	-9.0	-0.30	5.8
		Week 40	30	57.45	14.397	33.7	54.55	94.6	30	-0.20	2.663	-6.3	-0.85	7.7
		Week 44	30	57.25	13.455	34.9	54.10	85.2	30	-0.40	3.597	-11.0	-0.65	9.2
		Week 48	29	57.28	13.635	34.5	53.20	87.2	29	-0.44	3.764	-10.4	-0.30	9.3
		Week 52	28	56.90	13.584	34.3	53.70	87.0	28	-0.32	3.966	-9.7	-0.30	9.6
		Discontinuation	14	61.60	14.207	34.8	65.05	86.6	14	-0.46	2.460	-5.9	-0.50	4.2
	NOBELZIN	Start of Administration	109	58.46	13.066	32.4	55.30	97.1	-	-	-	-	-	-
		Week 4	107	58.47	13.021	32.2	56.10	97.5	107	-0.30	1.232	-4.2	-0.30	3.3
		Week 8	104	58.63	13.035	32.1	56.55	97.9	104	-0.43	1.415	-4.4	-0.40	4.4
		Week 12	104	58.18	13.085	31.7	55.55	98.0	104	-0.79	1.740	-8.4	-0.65	2.4
		Week 16	62	60.50	13.138	33.4	60.75	94.0	62	-0.92	1.881	-4.9	-0.80	3.3
		Week 20	30	60.34	13.209	33.3	61.45	90.2	30	-1.21	2.055	-6.1	-0.65	1.6
		Week 24	17	57.21	10.793	39.4	60.70	76.4	17	-0.59	1.440	-2.2	-1.00	2.6
		Discontinuation	10	57.31	12.872	39.6	54.80	76.2	10	-0.59	1.935	-4.6	-0.65	2.6

Change From Baseline : Each visit - Start of Administration

2.7.4.5 特別な患者集団及び状況下における安全性

2.7.4.5.1 内因性要因

内因性要因として性別、年齢、体重及び投与前の血清亜鉛濃度が本剤の安全性に及ぼす影響を検討した。

2.7.4.5.1.1 性別

NPC-25-3 試験における「男女」別の有害事象発現率を表 2.7.4.5-1 に、副作用発現率を表 2.7.4.5-2 に示した。

(1) 有害事象

本剤群の有害事象の発現率は男性で 82.6%（38/46 例）、女性で 70.5%（43/61 例）であり、女性に比べて男性で発現率が高い傾向があった。2.7.4.2.1.1.1 項に示した発現率が 2%以上の有害事象のうち、男女間における発現率に 5%以上の差異が認められた有害事象は、貧血、背部痛であった。

貧血の発現率は、男性 8.7%（4/46 例）、女性 0.0%（0/61 例）であり、女性に比べて男性で高かった。

背部痛の発現率は、男性 8.7%（4/46 例）、女性 0.0%（0/61 例）であり、女性に比べて男性で高かった。

(2) 副作用

本剤群の副作用の発現率は男性で 23.9%（11/46 例）、女性で 24.6%（15/61 例）であり、発現率に大きな差はなかった。2.7.4.2.1.1.1 項に示した発現率が 2%以上の副作用について、男女間における発現率に 5%以上の差異が認められた副作用は、貧血であった。

貧血の発現率は、男性 6.5%（3/46 例）、女性 0.0%（0/61 例）であり、女性に比べて男性で高かった。

表 2.7.4.5-1 男女別の有害事象発現率（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25			
	Male		Female	
	N = 46		N = 61	
	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Events	106	38 (82.6)	123	43 (70.5)
Blood and lymphatic system disorders	4	4 (8.7)	1	1 (1.6)
Anaemia	4	4 (8.7)	0	0 (0.0)
Iron deficiency anaemia	0	0 (0.0)	1	1 (1.6)
Cardiac disorders	1	1 (2.2)	1	1 (1.6)
Prinzmetal angina	0	0 (0.0)	1	1 (1.6)
Tachycardia	1	1 (2.2)	0	0 (0.0)
Eye disorders	3	2 (4.3)	4	3 (4.9)
Asthenopia	1	1 (2.2)	0	0 (0.0)
Blepharitis	1	1 (2.2)	0	0 (0.0)
Conjunctivitis allergic	0	0 (0.0)	1	1 (1.6)
Dry eye	0	0 (0.0)	2	2 (3.3)
Eye discharge	1	1 (2.2)	0	0 (0.0)
Vitreous floaters	0	0 (0.0)	1	1 (1.6)
Gastrointestinal disorders	19	11 (23.9)	21	14 (23.0)
Abdominal discomfort	1	1 (2.2)	2	2 (3.3)
Abdominal pain	1	1 (2.2)	0	0 (0.0)
Abdominal pain lower	1	1 (2.2)	0	0 (0.0)
Abdominal pain upper	0	0 (0.0)	1	1 (1.6)
Abnormal faeces	1	1 (2.2)	0	0 (0.0)
Angular cheilitis	2	2 (4.3)	0	0 (0.0)
Aphthous ulcer	0	0 (0.0)	1	1 (1.6)
Chronic gastritis	0	0 (0.0)	1	1 (1.6)
Constipation	2	2 (4.3)	2	2 (3.3)
Crohn's disease	1	1 (2.2)	0	0 (0.0)
Dental caries	0	0 (0.0)	1	1 (1.6)

表 2.7.4.5-1 男女別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25			
	Male		Female	
	N = 46		N = 61	
	n Events	n (%) Patients	n Events	n (%) Patients
Diarrhoea	1	1 (2.2)	2	2 (3.3)
Duodenal ulcer	0	0 (0.0)	1	1 (1.6)
Duodenitis	0	0 (0.0)	1	1 (1.6)
Enterocolitis	1	1 (2.2)	0	0 (0.0)
Gastric ulcer	0	0 (0.0)	1	1 (1.6)
Gastrooesophageal reflux disease	1	1 (2.2)	0	0 (0.0)
Haemorrhoids	1	1 (2.2)	0	0 (0.0)
Large intestine polyp	0	0 (0.0)	1	1 (1.6)
Melaena	1	1 (2.2)	0	0 (0.0)
Nausea	4	2 (4.3)	2	2 (3.3)
Pancreatic cyst	0	0 (0.0)	1	1 (1.6)
Stomatitis	1	1 (2.2)	1	1 (1.6)
Tooth disorder	0	0 (0.0)	1	1 (1.6)
Vomiting	0	0 (0.0)	2	2 (3.3)
General disorders and administration site conditions	5	4 (8.7)	9	8 (13.1)
Malaise	1	1 (2.2)	0	0 (0.0)
Oedema peripheral	0	0 (0.0)	3	3 (4.9)
Pyrexia	4	4 (8.7)	6	5 (8.2)
Hepatobiliary disorders	4	3 (6.5)	3	3 (4.9)
Cirrhosis alcoholic	1	1 (2.2)	0	0 (0.0)
Drug-induced liver injury	2	2 (4.3)	0	0 (0.0)
Hepatic function abnormal	1	1 (2.2)	2	2 (3.3)
Non-alcoholic steatohepatitis	0	0 (0.0)	1	1 (1.6)
Infections and infestations	15	13 (28.3)	23	20 (32.8)
Abscess limb	1	1 (2.2)	0	0 (0.0)

表 2.7.4.5-1 男女別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25			
	Male		Female	
	N = 46		N = 61	
	n Events	n (%) Patients	n Events	n (%) Patients
Bronchitis	0	0 (0.0)	1	1 (1.6)
COVID-19	3	3 (6.5)	5	5 (8.2)
Coronavirus infection	1	1 (2.2)	1	1 (1.6)
Cystitis	0	0 (0.0)	2	2 (3.3)
Dermatophytosis of nail	0	0 (0.0)	1	1 (1.6)
Folliculitis	1	1 (2.2)	0	0 (0.0)
Gastroenteritis	0	0 (0.0)	1	1 (1.6)
Gingivitis	2	2 (4.3)	0	0 (0.0)
Herpes zoster	0	0 (0.0)	2	2 (3.3)
Influenza	0	0 (0.0)	1	1 (1.6)
Nasopharyngitis	4	3 (6.5)	5	5 (8.2)
Paronychia	1	1 (2.2)	0	0 (0.0)
Tinea pedis	0	0 (0.0)	3	3 (4.9)
Tonsillitis	1	1 (2.2)	0	0 (0.0)
Upper respiratory tract infection	0	0 (0.0)	1	1 (1.6)
Urinary tract infection	1	1 (2.2)	0	0 (0.0)
Injury, poisoning and procedural complications	6	6 (13.0)	6	5 (8.2)
Arthropod sting	0	0 (0.0)	3	3 (4.9)
Contusion	1	1 (2.2)	1	1 (1.6)
Foot fracture	1	1 (2.2)	0	0 (0.0)
Ligament sprain	2	2 (4.3)	2	2 (3.3)
Skin abrasion	1	1 (2.2)	0	0 (0.0)
Spinal compression fracture	1	1 (2.2)	0	0 (0.0)
Investigations	10	8 (17.4)	17	10 (16.4)
Alanine aminotransferase increased	0	0 (0.0)	1	1 (1.6)

表 2.7.4.5-1 男女別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25			
	Male		Female	
	N = 46		N = 61	
	n Events	n (%) Patients	n Events	n (%) Patients
Amylase increased	1	1 (2.2)	3	3 (4.9)
Aspartate aminotransferase increased	0	0 (0.0)	2	1 (1.6)
Blood aldosterone increased	0	0 (0.0)	1	1 (1.6)
Blood copper decreased	2	2 (4.3)	4	3 (4.9)
Blood iron decreased	1	1 (2.2)	0	0 (0.0)
Blood potassium decreased	0	0 (0.0)	1	1 (1.6)
Blood pressure increased	0	0 (0.0)	1	1 (1.6)
Intraocular pressure increased	1	1 (2.2)	0	0 (0.0)
Lipase increased	1	1 (2.2)	4	3 (4.9)
Liver function test abnormal	2	2 (4.3)	0	0 (0.0)
Protein urine present	1	1 (2.2)	0	0 (0.0)
Weight decreased	1	1 (2.2)	0	0 (0.0)
Metabolism and nutrition disorders	5	4 (8.7)	8	5 (8.2)
Decreased appetite	2	2 (4.3)	0	0 (0.0)
Dehydration	0	0 (0.0)	1	1 (1.6)
Diabetes mellitus	0	0 (0.0)	1	1 (1.6)
Hyperammonaemia	0	0 (0.0)	1	1 (1.6)
Hyperglycaemia	0	0 (0.0)	1	1 (1.6)
Hypertriglyceridaemia	1	1 (2.2)	0	0 (0.0)
Hyperuricaemia	1	1 (2.2)	0	0 (0.0)
Hypocalcaemia	0	0 (0.0)	1	1 (1.6)
Hypoglycaemia	0	0 (0.0)	2	1 (1.6)
Type 2 diabetes mellitus	1	1 (2.2)	1	1 (1.6)
Musculoskeletal and connective tissue disorders	9	7 (15.2)	5	5 (8.2)
Arthralgia	2	1 (2.2)	2	2 (3.3)

表 2.7.4.5-1 男女別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25			
	Male		Female	
	N = 46		N = 61	
	n Events	n (%) Patients	n Events	n (%) Patients
Back pain	4	4 (8.7)	0	0 (0.0)
Osteoarthritis	0	0 (0.0)	1	1 (1.6)
Osteoporosis	1	1 (2.2)	0	0 (0.0)
Periarthritis	0	0 (0.0)	1	1 (1.6)
Rheumatoid arthritis	1	1 (2.2)	0	0 (0.0)
Tendonitis	0	0 (0.0)	1	1 (1.6)
Trigger finger	1	1 (2.2)	0	0 (0.0)
Nervous system disorders	10	9 (19.6)	6	3 (4.9)
Cerebellar ataxia	1	1 (2.2)	0	0 (0.0)
Cerebral haemorrhage	1	1 (2.2)	0	0 (0.0)
Cerebral infarction	2	1 (2.2)	0	0 (0.0)
Dizziness	3	3 (6.5)	2	2 (3.3)
Headache	2	2 (4.3)	2	2 (3.3)
Hypoaesthesia	0	0 (0.0)	1	1 (1.6)
Sciatica	1	1 (2.2)	0	0 (0.0)
Somnolence	0	0 (0.0)	1	1 (1.6)
Psychiatric disorders	0	0 (0.0)	1	1 (1.6)
Insomnia	0	0 (0.0)	1	1 (1.6)
Renal and urinary disorders	2	2 (4.3)	2	1 (1.6)
Haematuria	1	1 (2.2)	0	0 (0.0)
Hypertonic bladder	0	0 (0.0)	1	1 (1.6)
Nephrolithiasis	0	0 (0.0)	1	1 (1.6)
Renal impairment	1	1 (2.2)	0	0 (0.0)
Reproductive system and breast disorders	1	1 (2.2)	0	0 (0.0)
Prostatitis	1	1 (2.2)	0	0 (0.0)

表 2.7.4.5-1 男女別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25			
	Male		Female	
	N = 46		N = 61	
	n Events	n (%) Patients	n Events	n (%) Patients
Respiratory, thoracic and mediastinal disorders	3	2 (4.3)	4	3 (4.9)
Epistaxis	0	0 (0.0)	2	1 (1.6)
Interstitial lung disease	0	0 (0.0)	1	1 (1.6)
Laryngeal discomfort	1	1 (2.2)	0	0 (0.0)
Oropharyngeal discomfort	1	1 (2.2)	0	0 (0.0)
Oropharyngeal pain	1	1 (2.2)	0	0 (0.0)
Rhinitis allergic	0	0 (0.0)	1	1 (1.6)
Skin and subcutaneous tissue disorders	7	5 (10.9)	9	7 (11.5)
Blister	1	1 (2.2)	0	0 (0.0)
Dermatitis	2	1 (2.2)	0	0 (0.0)
Dermatitis acneiform	0	0 (0.0)	1	1 (1.6)
Drug eruption	0	0 (0.0)	2	2 (3.3)
Eczema	1	1 (2.2)	2	2 (3.3)
Eczema asteatotic	1	1 (2.2)	0	0 (0.0)
Haemorrhage subcutaneous	0	0 (0.0)	1	1 (1.6)
Pruritus	2	2 (4.3)	2	2 (3.3)
Rash	0	0 (0.0)	1	1 (1.6)
Social circumstances	0	0 (0.0)	1	1 (1.6)
Overwork	0	0 (0.0)	1	1 (1.6)
Surgical and medical procedures	1	1 (2.2)	0	0 (0.0)
Large intestinal polypectomy	1	1 (2.2)	0	0 (0.0)
Vascular disorders	1	1 (2.2)	2	2 (3.3)
Hypertension	1	1 (2.2)	1	1 (1.6)
White coat hypertension	0	0 (0.0)	1	1 (1.6)

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表 2.7.4.5-2 男女別の副作用発現率（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25			
	Male		Female	
	N = 46		N = 61	
	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Drug Reactions	19	11 (23.9)	25	15 (24.6)
Blood and lymphatic system disorders	3	3 (6.5)	1	1 (1.6)
Anaemia	3	3 (6.5)	0	0 (0.0)
Iron deficiency anaemia	0	0 (0.0)	1	1 (1.6)
Gastrointestinal disorders	7	4 (8.7)	9	7 (11.5)
Abdominal discomfort	0	0 (0.0)	2	2 (3.3)
Abdominal pain lower	1	1 (2.2)	0	0 (0.0)
Abdominal pain upper	0	0 (0.0)	1	1 (1.6)
Constipation	0	0 (0.0)	1	1 (1.6)
Diarrhoea	1	1 (2.2)	2	2 (3.3)
Gastric ulcer	0	0 (0.0)	1	1 (1.6)
Gastrooesophageal reflux disease	1	1 (2.2)	0	0 (0.0)
Nausea	4	2 (4.3)	1	1 (1.6)
Vomiting	0	0 (0.0)	1	1 (1.6)
Hepatobiliary disorders	0	0 (0.0)	1	1 (1.6)
Hepatic function abnormal	0	0 (0.0)	1	1 (1.6)
Investigations	7	6 (13.0)	10	7 (11.5)
Amylase increased	1	1 (2.2)	2	2 (3.3)
Blood copper decreased	2	2 (4.3)	4	3 (4.9)
Lipase increased	1	1 (2.2)	4	3 (4.9)
Liver function test abnormal	2	2 (4.3)	0	0 (0.0)
Weight decreased	1	1 (2.2)	0	0 (0.0)
Metabolism and nutrition disorders	1	1 (2.2)	0	0 (0.0)
Decreased appetite	1	1 (2.2)	0	0 (0.0)

表 2.7.4.5-2 男女別の副作用発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25			
	Male		Female	
	N = 46		N = 61	
	n Events	n (%) Patients	n Events	n (%) Patients
Nervous system disorders	1	1 (2.2)	2	1 (1.6)
Dizziness	1	1 (2.2)	1	1 (1.6)
Headache	0	0 (0.0)	1	1 (1.6)
Psychiatric disorders	0	0 (0.0)	1	1 (1.6)
Insomnia	0	0 (0.0)	1	1 (1.6)
Respiratory, thoracic and mediastinal disorders	0	0 (0.0)	1	1 (1.6)
Interstitial lung disease	0	0 (0.0)	1	1 (1.6)

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2.7.4.5.1.2 年齢

NPC-25-3 試験における「年齢」別の有害事象発現率を表 2.7.4.5-3 に、副作用発現率を表 2.7.4.5-4 に示した。

(1) 有害事象

本剤群の有害事象の発現率は 10～11 歳で 100.0%（2/2 例）、12～18 歳で 50.0%（1/2 例）、19～64 歳で 81.8%（27/33 例）、65 歳以上で 72.9%（51/70 例）であり、症例数が 10 例以上の 19～64 歳と 65 歳以上の年齢区分間における発現率に大きな差はなかった。10～11 歳及び 12～18 歳で認められた有害事象はアレルギー性結膜炎、下痢、悪心、発熱、ＣＯＶＩＤ－１９、インフルエンザ、上咽頭炎、足骨折、アレルギー性鼻炎が各 1 例であった。2.7.4.2.1.1.1 項に示した発現率が 2%以上の有害事象について、19～64 歳と 65 歳以上の年齢区分間における発現率に 5%以上の差異が認められた有害事象は、発熱、上咽頭炎、リパーゼ増加、背部痛であった。

発熱の発現率は、19～64 歳 12.1%（4/33 例）、65 歳以上 5.7%（4/70 例）であり、65 歳以上に比べて 19～64 歳で高かった。

上咽頭炎の発現率は、19～64 歳 15.2%（5/33 例）、65 歳以上 2.9%（2/70 例）であり、65 歳以上に比べて 19～64 歳で高かった。

リパーゼ増加の発現率は、19～64 歳 0.0%（0/33 例）、65 歳以上 5.7%（4/70 例）であり、19～64 歳に比べて 65 歳以上で高かった。

背部痛の発現率は、19～64 歳 0.0%（0/33 例）、65 歳以上 5.7%（4/70 例）であり、19～64 歳に比べて 65 歳以上で高かった。

(2) 副作用

本剤群の副作用の発現率は 10～11 歳で 50.0%（1/2 例）、12～18 歳で 0.0%（0/2 例）、19～64 歳で 30.3%（10/33 例）、65 歳以上で 21.4%（15/70 例）であり、症例数が 10 例以上の 19～64 歳と 65 歳以上の年齢区分間における発現率に大きな差はなかった。10～11 歳及び 12～18 歳で認められた副作用は下痢、悪心が各 1 例であった。2.7.4.2.1.1.1 項に示した発現率が 2%以上の副作用について、19～64 歳と 65 歳以上の年齢区分間における発現率に 5%以上の差異が認められた副作用は、リパーゼ増加であった。

リパーゼ増加の発現率は、19～64 歳 0.0%（0/33 例）、65 歳以上 5.7%（4/70 例）であり、19～64 歳に比べて 65 歳以上で高かった。

表 2.7.4.5-3 年齢別の有害事象発現率（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25							
	<= 11		12 <= <= 18		19 <= <= 64		>= 65	
	N = 2		N = 2		N = 33		N = 70	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Events	8	2 (100.0)	2	1 (50.0)	73	27 (81.8)	146	51 (72.9)
Blood and lymphatic system disorders	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	4	4 (5.7)
Anaemia	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	3	3 (4.3)
Iron deficiency anaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Cardiac disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Prinzmetal angina	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Tachycardia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Eye disorders	1	1 (50.0)	0	0 (0.0)	3	2 (6.1)	3	2 (2.9)
Asthenopia	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Blepharitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Conjunctivitis allergic	1	1 (50.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dry eye	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	1	1 (1.4)
Eye discharge	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Vitreous floaters	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Gastrointestinal disorders	3	1 (50.0)	0	0 (0.0)	12	8 (24.2)	25	16 (22.9)
Abdominal discomfort	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	2	2 (2.9)
Abdominal pain	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Abdominal pain lower	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Abdominal pain upper	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Abnormal faeces	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Angular cheilitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Aphthous ulcer	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Chronic gastritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Constipation	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	3	3 (4.3)
Crohn's disease	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Dental caries	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)

表 2.7.4.5-3 年齢別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25							
	<= 11		12 <= <= 18		19 <= <= 64		>= 65	
	N = 2		N = 2		N = 33		N = 70	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Diarrhoea	1	1 (50.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Duodenal ulcer	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Duodenitis	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Enterocolitis	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Gastric ulcer	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Gastrooesophageal reflux disease	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Haemorrhoids	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Large intestine polyp	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Melaena	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Nausea	2	1 (50.0)	0	0 (0.0)	2	1 (3.0)	2	2 (2.9)
Pancreatic cyst	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Stomatitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Tooth disorder	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Vomiting	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
General disorders and administration site conditions	0	0 (0.0)	1	1 (50.0)	5	4 (12.1)	8	7 (10.0)
Malaise	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Oedema peripheral	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	3	3 (4.3)
Pyrexia	0	0 (0.0)	1	1 (50.0)	4	4 (12.1)	5	4 (5.7)
Hepatobiliary disorders	0	0 (0.0)	0	0 (0.0)	2	2 (6.1)	5	4 (5.7)
Cirrhosis alcoholic	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Drug-induced liver injury	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Hepatic function abnormal	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	2	2 (2.9)
Non-alcoholic steatohepatitis	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Infections and infestations	2	1 (50.0)	1	1 (50.0)	15	13 (39.4)	20	18 (25.7)
Abscess limb	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)

表 2.7.4.5-3 年齢別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25							
	<= 11		12 <= <= 18		19 <= <= 64		>= 65	
	N = 2		N = 2		N = 33		N = 70	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Bronchitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
COVID-19	1	1 (50.0)	0	0 (0.0)	3	3 (9.1)	4	4 (5.7)
Coronavirus infection	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	1	1 (1.4)
Cystitis	0	0 (0.0)	0	0 (0.0)	2	2 (6.1)	0	0 (0.0)
Dermatophytosis of nail	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Folliculitis	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Gastroenteritis	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Gingivitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Herpes zoster	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Influenza	1	1 (50.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Nasopharyngitis	0	0 (0.0)	1	1 (50.0)	6	5 (15.2)	2	2 (2.9)
Paronychia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Tinea pedis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	3	3 (4.3)
Tonsillitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Upper respiratory tract infection	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Urinary tract infection	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Injury, poisoning and procedural complications	1	1 (50.0)	0	0 (0.0)	1	1 (3.0)	10	9 (12.9)
Arthropod sting	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	3	3 (4.3)
Contusion	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Foot fracture	1	1 (50.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Ligament sprain	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	3	3 (4.3)
Skin abrasion	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Spinal compression fracture	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Investigations	0	0 (0.0)	0	0 (0.0)	11	9 (27.3)	16	9 (12.9)
Alanine aminotransferase increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)

表 2.7.4.5-3 年齢別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25							
	<= 11		12 <= <= 18		19 <= <= 64		>= 65	
	N = 2		N = 2		N = 33		N = 70	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Amylase increased	0	0 (0.0)	0	0 (0.0)	2	2 (6.1)	2	2 (2.9)
Aspartate aminotransferase increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	1 (1.4)
Blood aldosterone increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Blood copper decreased	0	0 (0.0)	0	0 (0.0)	3	2 (6.1)	3	3 (4.3)
Blood iron decreased	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Blood potassium decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Blood pressure increased	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Intraocular pressure increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Lipase increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	5	4 (5.7)
Liver function test abnormal	0	0 (0.0)	0	0 (0.0)	2	2 (6.1)	0	0 (0.0)
Protein urine present	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Weight decreased	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Metabolism and nutrition disorders	0	0 (0.0)	0	0 (0.0)	4	3 (9.1)	9	6 (8.6)
Decreased appetite	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Dehydration	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Diabetes mellitus	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Hyperammonaemia	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Hyperglycaemia	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Hypertriglyceridaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Hyperuricaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Hypocalcaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Hypoglycaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	1 (1.4)
Type 2 diabetes mellitus	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	1	1 (1.4)
Musculoskeletal and connective tissue disorders	0	0 (0.0)	0	0 (0.0)	4	2 (6.1)	10	10 (14.3)
Arthralgia	0	0 (0.0)	0	0 (0.0)	2	1 (3.0)	2	2 (2.9)

表 2.7.4.5-3 年齢別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25							
	<= 11		12 <= <= 18		19 <= <= 64		>= 65	
	N = 2		N = 2		N = 33		N = 70	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Back pain	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	4	4 (5.7)
Osteoarthritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Osteoporosis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Periarthritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Rheumatoid arthritis	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Tendonitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Trigger finger	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Nervous system disorders	0	0 (0.0)	0	0 (0.0)	3	3 (9.1)	13	9 (12.9)
Cerebellar ataxia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Cerebral haemorrhage	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Cerebral infarction	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	1 (1.4)
Dizziness	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	4	4 (5.7)
Headache	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	3	3 (4.3)
Hypoaesthesia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Sciatica	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Somnolence	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Psychiatric disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Insomnia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Renal and urinary disorders	0	0 (0.0)	0	0 (0.0)	3	2 (6.1)	1	1 (1.4)
Haematuria	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Hypertonic bladder	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Nephrolithiasis	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Renal impairment	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Reproductive system and breast disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Prostatitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)

表 2.7.4.5-3 年齢別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25							
	<= 11		12 <= <= 18		19 <= <= 64		>= 65	
	N = 2		N = 2		N = 33		N = 70	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Respiratory, thoracic and mediastinal disorders	1	1 (50.0)	0	0 (0.0)	3	2 (6.1)	3	2 (2.9)
Epistaxis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	1 (1.4)
Interstitial lung disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Laryngeal discomfort	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Oropharyngeal discomfort	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Oropharyngeal pain	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Rhinitis allergic	1	1 (50.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Skin and subcutaneous tissue disorders	0	0 (0.0)	0	0 (0.0)	5	3 (9.1)	11	9 (12.9)
Blister	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Dermatitis	0	0 (0.0)	0	0 (0.0)	2	1 (3.0)	0	0 (0.0)
Dermatitis acneiform	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Drug eruption	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Eczema	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	3	3 (4.3)
Eczema asteatotic	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Haemorrhage subcutaneous	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Pruritus	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	3	3 (4.3)
Rash	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Social circumstances	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Overwork	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Surgical and medical procedures	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Large intestinal polypectomy	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Vascular disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	3	3 (4.3)
Hypertension	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
White coat hypertension	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)

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表 2.7.4.5-4 年齢別の副作用発現率（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25							
	<= 11		12 <= <= 18		19 <= <= 64		>= 65	
	N = 2		N = 2		N = 33		N = 70	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Drug Reactions	3	1 (50.0)	0	0 (0.0)	15	10 (30.3)	26	15 (21.4)
Blood and lymphatic system disorders	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	3	3 (4.3)
Anaemia	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	2	2 (2.9)
Iron deficiency anaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Gastrointestinal disorders	3	1 (50.0)	0	0 (0.0)	6	4 (12.1)	7	6 (8.6)
Abdominal discomfort	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	1	1 (1.4)
Abdominal pain lower	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Abdominal pain upper	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Constipation	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Diarrhoea	1	1 (50.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Gastric ulcer	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Gastrooesophageal reflux disease	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Nausea	2	1 (50.0)	0	0 (0.0)	2	1 (3.0)	1	1 (1.4)
Vomiting	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Hepatobiliary disorders	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Hepatic function abnormal	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Investigations	0	0 (0.0)	0	0 (0.0)	7	6 (18.2)	10	7 (10.0)
Amylase increased	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	2	2 (2.9)
Blood copper decreased	0	0 (0.0)	0	0 (0.0)	3	2 (6.1)	3	3 (4.3)
Lipase increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	5	4 (5.7)
Liver function test abnormal	0	0 (0.0)	0	0 (0.0)	2	2 (6.1)	0	0 (0.0)
Weight decreased	0	0 (0.0)	0	0 (0.0)	1	1 (3.0)	0	0 (0.0)
Metabolism and nutrition disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Decreased appetite	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)

表 2.7.4.5-4 年齢別の副作用発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25							
	<= 11		12 <= <= 18		19 <= <= 64		>= 65	
	N = 2		N = 2		N = 33		N = 70	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Nervous system disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	3	2 (2.9)
Dizziness	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (2.9)
Headache	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Psychiatric disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Insomnia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Respiratory, thoracic and mediastinal disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)
Interstitial lung disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.4)

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2.7.4.5.1.3 体重

NPC-25-3 試験における「体重」別の有害事象発現率を表 2.7.4.5-5 に、副作用発現率を表 2.7.4.5-6 に示した。

(1) 有害事象

本剤群の有害事象の発現率は 30 kg 以上 50 kg 未満で 77.8%（21/27 例）、50 kg 以上 70 kg 未満で 67.7%（42/62 例）、70 kg以上で 100.0%（18/18 例）であり、一定の傾向は認められなかった。2.7.4.2.1.1.1 項に示した発現率が 2%以上の有害事象について、体重区分間における発現率に 5%以上かつ 2 例以上の差異が認められた有害事象は、貧血、下痢、悪心、末梢性浮腫、上咽頭炎、足部白癬、節足動物刺傷、アミラーゼ増加、血中銅減少、リパーゼ増加であった。

貧血の発現率は、30 kg 以上 50 kg 未満で 0.0%（0/27 例）、50 kg 以上 70 kg 未満で 3.2%（2/62 例）、70 kg以上で 11.1%（2/18 例）であり、体重が重くなるにつれて、発現率が高かった。

下痢の発現率は、30 kg 以上 50 kg 未満で 7.4%（2/27 例）、50 kg 以上 70 kg 未満で 1.6%（1/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

悪心の発現率は、30 kg 以上 50 kg 未満で 7.4%（2/27 例）、50 kg 以上 70 kg 未満で 3.2%（2/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

末梢性浮腫の発現率は、30 kg 以上 50 kg 未満で 7.4%（2/27 例）、50 kg 以上 70 kg 未満で 1.6%（1/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

上咽頭炎の発現率は、30 kg 以上 50 kg 未満で 0.0%（0/27 例）、50 kg 以上 70 kg 未満で 8.1%（5/62 例）、70 kg以上で 16.7%（3/18 例）であり、体重が重くなるにつれて、発現率が高かった。

足部白癬の発現率は、30 kg 以上 50 kg 未満で 7.4%（2/27 例）、50 kg 以上 70 kg 未満で 1.6%（1/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

節足動物刺傷の発現率は、30 kg 以上 50 kg 未満で 11.1%（3/27 例）、50 kg 以上 70 kg 未満で 0.0%（0/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

アミラーゼ増加の発現率は、30 kg 以上 50 kg 未満で 11.1%（3/27 例）、50 kg 以上 70 kg 未満で 1.6%（1/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

血中銅減少の発現率は、30 kg 以上 50 kg 未満で 0.0%（0/27 例）、50 kg 以上 70 kg 未満で 4.8%（3/62 例）、70 kg以上で 11.1%（2/18 例）であり、体重が重くなるにつれて、発現率が高かった。

リバーゼ増加の発現率は、30 kg 以上 50 kg 未満で 11.1%（3/27 例）、50 kg 以上 70 kg 未満で 1.6%（1/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

(2) 副作用

本剤群の副作用の発現率は 30 kg 以上 50 kg 未満で 37.0%（10/27 例）、50 kg 以上 70 kg 未満で 16.1%（10/62 例）、70 kg以上で 33.3%（6/18 例）であり、一定の傾向は認められなかった。2.7.4.2.1.1.1 項に示した発現率が 2%以上の副作用について、体重区分間における発現率に 5%以上かつ 2 例以上の差異が認められた副作用は、貧血、下痢、悪心、アミラーゼ増加、血中銅減少、リパーゼ増加であった。

貧血の発現率は、30 kg 以上 50 kg 未満で 0.0%（0/27 例）、50 kg 以上 70 kg 未満で 1.6%（1/62 例）、70 kg以上で 11.1%（2/18 例）であり、体重が重くなるにつれて、発現率が高かった。

下痢の発現率は、30 kg 以上 50 kg 未満で 7.4%（2/27 例）、50 kg 以上 70 kg 未満で 1.6%（1/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

悪心の発現率は、30 kg 以上 50 kg 未満で 7.4%（2/27 例）、50 kg 以上 70 kg 未満で 1.6%（1/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

アミラーゼ増加の発現率は、30 kg 以上 50 kg 未満で 11.1%（3/27 例）、50 kg 以上 70 kg 未満で 0.0%（0/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

血中銅減少の発現率は、30 kg 以上 50 kg 未満で 0.0%（0/27 例）、50 kg 以上 70 kg 未満で 4.8%（3/62 例）、70 kg以上で 11.1%（2/18 例）であり、体重が重くなるにつれて、発現率が高かった。

リパーゼ増加の発現率は、30 kg 以上 50 kg 未満で 11.1%（3/27 例）、50 kg 以上 70 kg 未満で 1.6%（1/62 例）、70 kg以上で 0.0%（0/18 例）であり、体重が重くなるにつれて、発現率が低下した。

表 2.7.4.5-5 体重別の有害事象発現率（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25					
	30.0 <= < 50.0		50.0 <= < 70.0		>= 70.0	
	N = 27		N = 62		N = 18	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Events	68	21 (77.8)	100	42 (67.7)	61	18 (100.0)
Blood and lymphatic system disorders	0	0 (0.0)	3	3 (4.8)	2	2 (11.1)
Anaemia	0	0 (0.0)	2	2 (3.2)	2	2 (11.1)
Iron deficiency anaemia	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Cardiac disorders	0	0 (0.0)	1	1 (1.6)	1	1 (5.6)
Prinzmetal angina	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Tachycardia	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Eye disorders	1	1 (3.7)	3	2 (3.2)	3	2 (11.1)
Asthenopia	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Blepharitis	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Conjunctivitis allergic	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Dry eye	0	0 (0.0)	2	2 (3.2)	0	0 (0.0)
Eye discharge	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Vitreous floaters	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Gastrointestinal disorders	12	7 (25.9)	18	11 (17.7)	10	7 (38.9)
Abdominal discomfort	0	0 (0.0)	2	2 (3.2)	1	1 (5.6)
Abdominal pain	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Abdominal pain lower	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Abdominal pain upper	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Abnormal faeces	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Angular cheilitis	0	0 (0.0)	1	1 (1.6)	1	1 (5.6)
Aphthous ulcer	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Chronic gastritis	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Constipation	1	1 (3.7)	1	1 (1.6)	2	2 (11.1)
Crohn's disease	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Dental caries	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.5-5 体重別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	30.0 <= < 50.0		50.0 <= < 70.0		>= 70.0	
	N = 27		N = 62		N = 18	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Diarrhoea	2	2 (7.4)	1	1 (1.6)	0	0 (0.0)
Duodenal ulcer	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Duodenitis	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Enterocolitis	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Gastric ulcer	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Gastrooesophageal reflux disease	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Haemorrhoids	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Large intestine polyp	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Melaena	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Nausea	3	2 (7.4)	3	2 (3.2)	0	0 (0.0)
Pancreatic cyst	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Stomatitis	0	0 (0.0)	1	1 (1.6)	1	1 (5.6)
Tooth disorder	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Vomiting	0	0 (0.0)	2	2 (3.2)	0	0 (0.0)
General disorders and administration site conditions	6	5 (18.5)	4	4 (6.5)	4	3 (16.7)
Malaise	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Oedema peripheral	2	2 (7.4)	1	1 (1.6)	0	0 (0.0)
Pyrexia	4	3 (11.1)	3	3 (4.8)	3	3 (16.7)
Hepatobiliary disorders	0	0 (0.0)	3	3 (4.8)	4	3 (16.7)
Cirrhosis alcoholic	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Drug-induced liver injury	0	0 (0.0)	0	0 (0.0)	2	2 (11.1)
Hepatic function abnormal	0	0 (0.0)	3	3 (4.8)	0	0 (0.0)
Non-alcoholic steatohepatitis	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Infections and infestations	9	7 (25.9)	18	17 (27.4)	11	9 (50.0)
Abscess limb	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)

表 2.7.4.5-5 体重別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	30.0 <= < 50.0		50.0 <= < 70.0		>= 70.0	
	N = 27		N = 62		N = 18	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Bronchitis	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
COVID-19	2	2 (7.4)	5	5 (8.1)	1	1 (5.6)
Coronavirus infection	1	1 (3.7)	1	1 (1.6)	0	0 (0.0)
Cystitis	0	0 (0.0)	1	1 (1.6)	1	1 (5.6)
Dermatophytosis of nail	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Folliculitis	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Gastroenteritis	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Gingivitis	0	0 (0.0)	2	2 (3.2)	0	0 (0.0)
Herpes zoster	1	1 (3.7)	1	1 (1.6)	0	0 (0.0)
Influenza	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Nasopharyngitis	0	0 (0.0)	5	5 (8.1)	4	3 (16.7)
Paronychia	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Tinea pedis	2	2 (7.4)	1	1 (1.6)	0	0 (0.0)
Tonsillitis	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Upper respiratory tract infection	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Urinary tract infection	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Injury, poisoning and procedural complications	5	4 (14.8)	5	5 (8.1)	2	2 (11.1)
Arthropod sting	3	3 (11.1)	0	0 (0.0)	0	0 (0.0)
Contusion	0	0 (0.0)	1	1 (1.6)	1	1 (5.6)
Foot fracture	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Ligament sprain	1	1 (3.7)	2	2 (3.2)	1	1 (5.6)
Skin abrasion	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Spinal compression fracture	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Investigations	13	7 (25.9)	9	7 (11.3)	5	4 (22.2)
Alanine aminotransferase increased	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.5-5 体重別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	30.0 <= < 50.0		50.0 <= < 70.0		>= 70.0	
	N = 27		N = 62		N = 18	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Amylase increased	3	3 (11.1)	1	1 (1.6)	0	0 (0.0)
Aspartate aminotransferase increased	2	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Blood aldosterone increased	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Blood copper decreased	0	0 (0.0)	4	3 (4.8)	2	2 (11.1)
Blood iron decreased	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Blood potassium decreased	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Blood pressure increased	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Intraocular pressure increased	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Lipase increased	4	3 (11.1)	1	1 (1.6)	0	0 (0.0)
Liver function test abnormal	0	0 (0.0)	1	1 (1.6)	1	1 (5.6)
Protein urine present	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Weight decreased	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Metabolism and nutrition disorders	3	1 (3.7)	6	5 (8.1)	4	3 (16.7)
Decreased appetite	0	0 (0.0)	1	1 (1.6)	1	1 (5.6)
Dehydration	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Diabetes mellitus	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Hyperammonaemia	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Hyperglycaemia	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Hypertriglyceridaemia	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Hyperuricaemia	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Hypocalcaemia	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Hypoglycaemia	2	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Type 2 diabetes mellitus	0	0 (0.0)	1	1 (1.6)	1	1 (5.6)
Musculoskeletal and connective tissue disorders	2	2 (7.4)	9	8 (12.9)	3	2 (11.1)
Arthralgia	1	1 (3.7)	1	1 (1.6)	2	1 (5.6)

表 2.7.4.5-5 体重別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	30.0 <= < 50.0		50.0 <= < 70.0		>= 70.0	
	N = 27		N = 62		N = 18	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Back pain	0	0 (0.0)	3	3 (4.8)	1	1 (5.6)
Osteoarthritis	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Osteoporosis	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Periarthritis	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Rheumatoid arthritis	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Tendonitis	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Trigger finger	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Nervous system disorders	5	2 (7.4)	8	7 (11.3)	3	3 (16.7)
Cerebellar ataxia	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Cerebral haemorrhage	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Cerebral infarction	0	0 (0.0)	2	1 (1.6)	0	0 (0.0)
Dizziness	2	2 (7.4)	1	1 (1.6)	2	2 (11.1)
Headache	2	2 (7.4)	1	1 (1.6)	1	1 (5.6)
Hypoaesthesia	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Sciatica	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Somnolence	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Psychiatric disorders	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Insomnia	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Renal and urinary disorders	0	0 (0.0)	1	1 (1.6)	3	2 (11.1)
Haematuria	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Hypertonic bladder	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Nephrolithiasis	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Renal impairment	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Reproductive system and breast disorders	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Prostatitis	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)

表 2.7.4.5-5 体重別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	30.0 <= < 50.0		50.0 <= < 70.0		>= 70.0	
	N = 27		N = 62		N = 18	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Respiratory, thoracic and mediastinal disorders	2	2 (7.4)	3	2 (3.2)	2	1 (5.6)
Epistaxis	0	0 (0.0)	2	1 (1.6)	0	0 (0.0)
Interstitial lung disease	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Laryngeal discomfort	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Oropharyngeal discomfort	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Oropharyngeal pain	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Rhinitis allergic	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Skin and subcutaneous tissue disorders	7	5 (18.5)	6	5 (8.1)	3	2 (11.1)
Blister	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Dermatitis	0	0 (0.0)	0	0 (0.0)	2	1 (5.6)
Dermatitis acneiform	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Drug eruption	2	2 (7.4)	0	0 (0.0)	0	0 (0.0)
Eczema	1	1 (3.7)	2	2 (3.2)	0	0 (0.0)
Eczema asteatotic	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Haemorrhage subcutaneous	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Pruritus	1	1 (3.7)	2	2 (3.2)	1	1 (5.6)
Rash	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Social circumstances	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Overwork	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Surgical and medical procedures	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Large intestinal polypectomy	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Vascular disorders	2	2 (7.4)	1	1 (1.6)	0	0 (0.0)
Hypertension	1	1 (3.7)	1	1 (1.6)	0	0 (0.0)
White coat hypertension	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)

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表 2.7.4.5-6 体重別の副作用発現率（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25					
	30.0 <= < 50.0		50.0 <= < 70.0		>= 70.0	
	N = 27		N = 62		N = 18	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Drug Reactions	18	10 (37.0)	16	10 (16.1)	10	6 (33.3)
Blood and lymphatic system disorders	0	0 (0.0)	2	2 (3.2)	2	2 (11.1)
Anaemia	0	0 (0.0)	1	1 (1.6)	2	2 (11.1)
Iron deficiency anaemia	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Gastrointestinal disorders	7	5 (18.5)	7	4 (6.5)	2	2 (11.1)
Abdominal discomfort	0	0 (0.0)	2	2 (3.2)	0	0 (0.0)
Abdominal pain lower	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Abdominal pain upper	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Constipation	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Diarrhoea	2	2 (7.4)	1	1 (1.6)	0	0 (0.0)
Gastric ulcer	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Gastrooesophageal reflux disease	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Nausea	3	2 (7.4)	2	1 (1.6)	0	0 (0.0)
Vomiting	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Hepatobiliary disorders	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Hepatic function abnormal	0	0 (0.0)	1	1 (1.6)	0	0 (0.0)
Investigations	7	5 (18.5)	6	4 (6.5)	4	4 (22.2)
Amylase increased	3	3 (11.1)	0	0 (0.0)	0	0 (0.0)
Blood copper decreased	0	0 (0.0)	4	3 (4.8)	2	2 (11.1)
Lipase increased	4	3 (11.1)	1	1 (1.6)	0	0 (0.0)
Liver function test abnormal	0	0 (0.0)	1	1 (1.6)	1	1 (5.6)
Weight decreased	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Metabolism and nutrition disorders	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Decreased appetite	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)

表 2.7.4.5-6 体重別の副作用発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	30.0 <= < 50.0		50.0 <= < 70.0		>= 70.0	
	N = 27		N = 62		N = 18	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Nervous system disorders	2	1 (3.7)	0	0 (0.0)	1	1 (5.6)
Dizziness	1	1 (3.7)	0	0 (0.0)	1	1 (5.6)
Headache	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Psychiatric disorders	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Insomnia	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Respiratory, thoracic and mediastinal disorders	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)
Interstitial lung disease	1	1 (3.7)	0	0 (0.0)	0	0 (0.0)

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2.7.4.5.1.4 投与前の血清亜鉛濃度

NPC-25-3 試験における「投与前の血清亜鉛濃度」別の有害事象発現率を表 2.7.4.5-7 に、副作用発現率を表 2.7.4.5-8 に示した。

(1) 有害事象

本剤群の有害事象の発現率は 50 μg/dL 未満で 100%（4/4 例）、50～59 μg/dL で 81.6%（31/38 例）、60 μg/dL 以上で 70.8%（46/65 例）であり、症例数が 10 例以上の 50～59 μg/dL と 60 μg/dL 以上の投与前の血清亜鉛濃度区分間の発現率に大きな差はなかった。50 μg/dL 未満で認められた有害事象は血中銅減少 2 例、貧血、腹部不快感、下腹部痛、上腹部痛、メレナ、倦怠感、発熱、アルコール性肝硬変、薬物性肝障害、上咽頭炎、血中鉄減少、リパーゼ増加、肝機能検査異常、関節痛が各 1 例であった。2.7.4.2.1.1.1 項に示した発現率が 2%以上の有害事象について、50～59 μg/dL と 60 μg/dL 以上の投与前の血清亜鉛濃度区分間の発現率に 5%以上の差異が認められた有害事象は、発熱、背部痛、そう痒症であった。

発熱の発現率は、50～59 μg/dL 2.6%（1/38 例）、60 μg/dL 以上 10.8%（7/65 例）であり、50～59 μg/dL に比べて 60 μg/dL 以上で高かった。

背部痛の発現率は、50～59 μg/dL 7.9%（3/38 例）、60 μg/dL 以上 1.5%（1/65 例）であり、50～59 μg/dL に比べて 60 μg/dL 以上で低下した。

そう痒症の発現率は、50～59 μg/dL 0.0%（0/38 例）、60 μg/dL 以上 6.2%（4/65 例）であり、50～59 μg/dL に比べて 60 μg/dL 以上で高かった。

(2) 副作用

本剤群の副作用の発現率は 50 μg/dL 未満で 100%（4/4 例）、50～59 μg/dL で 21.1%（8/38 例）、60 μg/dL 以上で 21.5%（14/65 例）であり、症例数が 10 例以上の 50～59 μg/dL と 60 μg/dL 以上の投与前の血清亜鉛濃度区分間の発現率に大きな差はなかった。50 μg/dL 未満で認められた副作用は血中銅減少 2 例、貧血、腹部不快感、下腹部痛、上腹部痛、リパーゼ増加、肝機能検査異常が各 1 例であった。2.7.4.2.1.1.1 項に示した発現率が 2%以上の副作用について、50～59 μg/dL と 60 μg/dL 以上の投与前の血清亜鉛濃度区分間の発現率に 5%以上の差異が認められた副作用はなかった。

表 2.7.4.5-7 投与前の血清亜鉛濃度別の有害事象発現率（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25					
	< 50 *		50 <= <= 59 *		>= 60 *	
	N = 4		N = 38		N = 65	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Events	16	4 (100.0)	78	31 (81.6)	135	46 (70.8)
Blood and lymphatic system disorders	1	1 (25.0)	1	1 (2.6)	3	3 (4.6)
Anaemia	1	1 (25.0)	1	1 (2.6)	2	2 (3.1)
Iron deficiency anaemia	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Cardiac disorders	0	0 (0.0)	1	1 (2.6)	1	1 (1.5)
Prinzmetal angina	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Tachycardia	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Eye disorders	0	0 (0.0)	3	2 (5.3)	4	3 (4.6)
Asthenopia	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Blepharitis	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Conjunctivitis allergic	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Dry eye	0	0 (0.0)	1	1 (2.6)	1	1 (1.5)
Eye discharge	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Vitreous floaters	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Gastrointestinal disorders	4	2 (50.0)	13	10 (26.3)	23	13 (20.0)
Abdominal discomfort	1	1 (25.0)	1	1 (2.6)	1	1 (1.5)
Abdominal pain	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Abdominal pain lower	1	1 (25.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain upper	1	1 (25.0)	0	0 (0.0)	0	0 (0.0)
Abnormal faeces	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Angular cheilitis	0	0 (0.0)	1	1 (2.6)	1	1 (1.5)
Aphthous ulcer	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Chronic gastritis	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Constipation	0	0 (0.0)	2	2 (5.3)	2	2 (3.1)
Crohn's disease	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Dental caries	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)

表 2.7.4.5-7 投与前の血清亜鉛濃度別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	<50 *		50 <= <= 59 *		>= 60 *	
	N = 4		N = 38		N = 65	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Diarrhoea	0	0 (0.0)	1	1 (2.6)	2	2 (3.1)
Duodenal ulcer	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Duodenitis	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Enterocolitis	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Gastric ulcer	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Gastrooesophageal reflux disease	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Haemorrhoids	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Large intestine polyp	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Melaena	1	1 (25.0)	0	0 (0.0)	0	0 (0.0)
Nausea	0	0 (0.0)	2	1 (2.6)	4	3 (4.6)
Pancreatic cyst	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Stomatitis	0	0 (0.0)	0	0 (0.0)	2	2 (3.1)
Tooth disorder	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Vomiting	0	0 (0.0)	1	1 (2.6)	1	1 (1.5)
General disorders and administration site conditions	2	1 (25.0)	3	2 (5.3)	9	9 (13.8)
Malaise	1	1 (25.0)	0	0 (0.0)	0	0 (0.0)
Oedema peripheral	0	0 (0.0)	1	1 (2.6)	2	2 (3.1)
Pyrexia	1	1 (25.0)	2	1 (2.6)	7	7 (10.8)
Hepatobiliary disorders	2	1 (25.0)	1	1 (2.6)	4	4 (6.2)
Cirrhosis alcoholic	1	1 (25.0)	0	0 (0.0)	0	0 (0.0)
Drug-induced liver injury	1	1 (25.0)	1	1 (2.6)	0	0 (0.0)
Hepatic function abnormal	0	0 (0.0)	0	0 (0.0)	3	3 (4.6)
Non-alcoholic steatohepatitis	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Infections and infestations	1	1 (25.0)	16	13 (34.2)	21	19 (29.2)
Abscess limb	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)

表 2.7.4.5-7 投与前の血清亜鉛濃度別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	<50 *		50 <= <= 59 *		>= 60 *	
	N = 4		N = 38		N = 65	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Bronchitis	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
COVID-19	0	0 (0.0)	4	4 (10.5)	4	4 (6.2)
Coronavirus infection	0	0 (0.0)	1	1 (2.6)	1	1 (1.5)
Cystitis	0	0 (0.0)	0	0 (0.0)	2	2 (3.1)
Dermatophytosis of nail	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Folliculitis	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Gastroenteritis	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Gingivitis	0	0 (0.0)	1	1 (2.6)	1	1 (1.5)
Herpes zoster	0	0 (0.0)	0	0 (0.0)	2	2 (3.1)
Influenza	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Nasopharyngitis	1	1 (25.0)	4	3 (7.9)	4	4 (6.2)
Paronychia	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Tinea pedis	0	0 (0.0)	1	1 (2.6)	2	2 (3.1)
Tonsillitis	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Upper respiratory tract infection	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Urinary tract infection	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Injury, poisoning and procedural complications	0	0 (0.0)	4	4 (10.5)	8	7 (10.8)
Arthropod sting	0	0 (0.0)	1	1 (2.6)	2	2 (3.1)
Contusion	0	0 (0.0)	2	2 (5.3)	0	0 (0.0)
Foot fracture	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Ligament sprain	0	0 (0.0)	1	1 (2.6)	3	3 (4.6)
Skin abrasion	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Spinal compression fracture	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Investigations	5	3 (75.0)	8	3 (7.9)	14	12 (18.5)
Alanine aminotransferase increased	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)

表 2.7.4.5-7 投与前の血清亜鉛濃度別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	<50 *		50 <= <= 59 *		>= 60 *	
	N = 4		N = 38		N = 65	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Amylase increased	0	0 (0.0)	1	1 (2.6)	3	3 (4.6)
Aspartate aminotransferase increased	0	0 (0.0)	2	1 (2.6)	0	0 (0.0)
Blood aldosterone increased	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Blood copper decreased	2	2 (50.0)	0	0 (0.0)	4	3 (4.6)
Blood iron decreased	1	1 (25.0)	0	0 (0.0)	0	0 (0.0)
Blood potassium decreased	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Blood pressure increased	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Intraocular pressure increased	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Lipase increased	1	1 (25.0)	3	2 (5.3)	1	1 (1.5)
Liver function test abnormal	1	1 (25.0)	0	0 (0.0)	1	1 (1.5)
Protein urine present	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Weight decreased	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Metabolism and nutrition disorders	0	0 (0.0)	4	3 (7.9)	9	6 (9.2)
Decreased appetite	0	0 (0.0)	0	0 (0.0)	2	2 (3.1)
Dehydration	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Diabetes mellitus	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Hyperammonaemia	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Hyperglycaemia	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Hypertriglyceridaemia	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Hyperuricaemia	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Hypocalcaemia	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Hypoglycaemia	0	0 (0.0)	0	0 (0.0)	2	1 (1.5)
Type 2 diabetes mellitus	0	0 (0.0)	2	2 (5.3)	0	0 (0.0)
Musculoskeletal and connective tissue disorders	1	1 (25.0)	8	6 (15.8)	5	5 (7.7)
Arthralgia	1	1 (25.0)	2	1 (2.6)	1	1 (1.5)

表 2.7.4.5-7 投与前の血清亜鉛濃度別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	<50 *		50 <= <= 59 *		>= 60 *	
	N = 4		N = 38		N = 65	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Back pain	0	0 (0.0)	3	3 (7.9)	1	1 (1.5)
Osteoarthritis	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Osteoporosis	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Periarthritis	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Rheumatoid arthritis	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Tendonitis	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Trigger finger	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Nervous system disorders	0	0 (0.0)	5	4 (10.5)	11	8 (12.3)
Cerebellar ataxia	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Cerebral haemorrhage	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Cerebral infarction	0	0 (0.0)	2	1 (2.6)	0	0 (0.0)
Dizziness	0	0 (0.0)	1	1 (2.6)	4	4 (6.2)
Headache	0	0 (0.0)	1	1 (2.6)	3	3 (4.6)
Hypoaesthesia	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Sciatica	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Somnolence	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Psychiatric disorders	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Insomnia	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Renal and urinary disorders	0	0 (0.0)	1	1 (2.6)	3	2 (3.1)
Haematuria	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Hypertonic bladder	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Nephrolithiasis	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Renal impairment	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Reproductive system and breast disorders	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Prostatitis	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)

表 2.7.4.5-7 投与前の血清亜鉛濃度別の有害事象発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	< 50 *		50 <= <= 59 *		>= 60 *	
	N = 4		N = 38		N = 65	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Respiratory, thoracic and mediastinal disorders	0	0 (0.0)	4	3 (7.9)	3	2 (3.1)
Epistaxis	0	0 (0.0)	0	0 (0.0)	2	1 (1.5)
Interstitial lung disease	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Laryngeal discomfort	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Oropharyngeal discomfort	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Oropharyngeal pain	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Rhinitis allergic	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Skin and subcutaneous tissue disorders	0	0 (0.0)	4	3 (7.9)	12	9 (13.8)
Blister	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Dermatitis	0	0 (0.0)	2	1 (2.6)	0	0 (0.0)
Dermatitis acneiform	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Drug eruption	0	0 (0.0)	0	0 (0.0)	2	2 (3.1)
Eczema	0	0 (0.0)	0	0 (0.0)	3	3 (4.6)
Eczema asteatotic	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Haemorrhage subcutaneous	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Pruritus	0	0 (0.0)	0	0 (0.0)	4	4 (6.2)
Rash	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Social circumstances	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Overwork	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Surgical and medical procedures	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Large intestinal polypectomy	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Vascular disorders	0	0 (0.0)	0	0 (0.0)	3	3 (4.6)
Hypertension	0	0 (0.0)	0	0 (0.0)	2	2 (3.1)
White coat hypertension	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)

MedDRA: Version 24.1
* Serum Zinc Concentrations at Enrollment.

表 2.7.4.5-8 投与前の血清亜鉛濃度別の副作用発現率（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25					
	< 50 *		50 <= <= 59 *		>= 60 *	
	N = 4		N = 38		N = 65	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Drug Reactions	8	4 (100.0)	14	8 (21.1)	22	14 (21.5)
Blood and lymphatic system disorders	1	1 (25.0)	1	1 (2.6)	2	2 (3.1)
Anaemia	1	1 (25.0)	1	1 (2.6)	1	1 (1.5)
Iron deficiency anaemia	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Gastrointestinal disorders	3	2 (50.0)	6	4 (10.5)	7	5 (7.7)
Abdominal discomfort	1	1 (25.0)	0	0 (0.0)	1	1 (1.5)
Abdominal pain lower	1	1 (25.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain upper	1	1 (25.0)	0	0 (0.0)	0	0 (0.0)
Constipation	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Diarrhoea	0	0 (0.0)	1	1 (2.6)	2	2 (3.1)
Gastric ulcer	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Gastrooesophageal reflux disease	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Nausea	0	0 (0.0)	2	1 (2.6)	3	2 (3.1)
Vomiting	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Hepatobiliary disorders	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Hepatic function abnormal	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Investigations	4	3 (75.0)	5	3 (7.9)	8	7 (10.8)
Amylase increased	0	0 (0.0)	1	1 (2.6)	2	2 (3.1)
Blood copper decreased	2	2 (50.0)	0	0 (0.0)	4	3 (4.6)
Lipase increased	1	1 (25.0)	3	2 (5.3)	1	1 (1.5)
Liver function test abnormal	1	1 (25.0)	0	0 (0.0)	1	1 (1.5)
Weight decreased	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Metabolism and nutrition disorders	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Decreased appetite	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)

表 2.7.4.5-8 投与前の血清亜鉛濃度別の副作用発現率（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25					
	< 50 *		50 <= <= 59 *		>= 60 *	
	N = 4		N = 38		N = 65	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Nervous system disorders	0	0 (0.0)	0	0 (0.0)	3	2 (3.1)
Dizziness	0	0 (0.0)	0	0 (0.0)	2	2 (3.1)
Headache	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)
Psychiatric disorders	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Insomnia	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Respiratory, thoracic and mediastinal disorders	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)
Interstitial lung disease	0	0 (0.0)	1	1 (2.6)	0	0 (0.0)

MedDRA: Version 24.1
* Serum Zinc Concentrations at Enrollment.

2.7.4.5.2 外因性要因

外因性要因の検討は実施していない。

2.7.4.5.3 薬物相互作用

本剤の臨床試験では、薬物相互作用が疑われる有害事象は認められなかった。

2.7.4.5.4 妊娠及び授乳時の使用

本剤の臨床試験では、妊婦及び授乳婦は対象から除外しており、妊婦及び授乳婦への使用は検討していない。

2.7.4.5.5 過量投与

本剤の臨床試験では、1 例について、1 日分のみ、1 日 1 回 100 mg/日投与のところ、誤って 1 日 2 回 200 mg/日服薬した可能性はあったが、過量投与の疑いがあった時期に有害事象は認められなかった。

2.7.4.5.6 薬物乱用

本剤の臨床試験では、薬物乱用が疑われる有害事象は認められなかった。

2.7.4.5.7 離脱症状及び反跳現象

本剤の臨床試験では、投与終了後に発現した有害事象は、下痢（1 件、因果関係あり）、メレナ（1 件、因果関係なし）、悪心（1 件、因果関係あり）、リパーゼ増加（1 件、因果関係あり）、脱水（1 件、因果関係なし）、低血糖（1 件、因果関係なし）、小脳性運動失調（1 件、因果関係なし）であった。いずれも発現件数は 1 件であり、本剤の投与中止に伴う離脱症状及び反跳現象はないものと考えられた。

2.7.4.5.8 自動車運転及び機械操作に対する影響又は精神機能の障害

本剤の臨床試験では、自動車運転及び機械操作に対する影響又は精神機能の障害に関する検討は実施していない。

2.7.4.6 市販後データ

該当しない。

2.7.4.7 付録

2.7.4.3 項の付録として、NPC-25-3 試験における本剤群とノベルジン錠群の血液学的検査及び血液生化学的検査の要約統計量をそれぞれ表 2.7.4.7-1 及び表 2.7.4.7-2 に示した。また、本剤群とノベルジン錠群の尿検査値の推移（シフトテーブル）を表 2.7.4.7-3 に示した。

表 2.7.4.7-1 血液学的検査の要約統計量（SP）（NPC-25-3 試験）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Leukocytes (10^9/L)	NPC-25	Start of Administration	107	5.976	1.8694	1.60	5.900	12.40	-	-	-	-	-	-
		Week 4	104	5.875	2.0872	2.02	5.395	13.90	104	-0.091	1.4018	-6.56	-0.100	5.74
		Week 8	100	5.745	1.8786	1.59	5.635	12.00	100	-0.198	1.2377	-6.50	-0.230	2.90
		Week 12	99	5.893	1.8411	1.73	5.720	11.10	99	-0.064	1.2486	-5.61	-0.100	2.90
		Week 16	77	5.810	1.7978	1.76	5.700	12.20	77	-0.190	1.1165	-3.50	-0.100	3.20
		Week 20	67	5.948	1.8489	2.07	5.800	11.36	67	-0.164	1.2461	-4.10	-0.100	2.60
		Week 24	57	5.640	1.6794	2.20	5.500	10.40	57	-0.322	1.2595	-4.60	-0.400	2.57
		Week 28	53	5.758	1.7650	2.30	5.700	10.50	53	-0.258	1.2823	-3.90	-0.490	2.10
		Week 32	35	5.903	1.9317	2.21	5.700	10.30	35	0.095	1.4980	-2.80	0.100	5.60
		Week 36	31	6.435	2.1792	3.20	6.000	13.40	31	0.381	1.5644	-2.40	0.330	4.80
		Week 40	30	6.092	1.8378	3.40	5.650	10.10	30	0.037	1.1451	-2.30	0.035	2.70
		Week 44	30	6.118	1.9062	3.10	6.100	11.50	30	0.063	1.0889	-1.80	0.100	3.50
		Week 48	29	6.172	1.8855	3.00	5.900	11.40	29	0.070	1.0667	-1.80	0.000	2.10
		Week 52	28	5.994	1.5498	3.50	5.750	9.00	28	-0.151	1.1761	-3.40	-0.150	2.00
		Discontinuation	14	5.532	2.0957	2.40	5.750	9.40	14	-0.476	1.7274	-5.10	-0.150	1.70
	NOBELZIN	Start of Administration	109	5.717	1.7874	2.20	5.500	11.10	-	-	-	-	-	-
		Week 4	108	5.853	1.9325	2.42	5.600	12.50	108	0.125	1.2180	-3.15	0.100	4.60
		Week 8	105	5.723	1.7009	1.80	5.800	10.41	105	-0.016	1.0818	-3.50	0.070	2.30
		Week 12	104	5.720	1.8405	1.60	5.730	12.01	104	0.013	1.2459	-5.26	0.100	3.10
		Week 16	62	5.695	1.8515	2.10	5.620	12.27	62	0.253	1.1559	-2.80	0.220	2.40
		Week 20	30	5.416	1.8896	2.50	5.400	12.21	30	0.172	0.9957	-2.00	0.140	2.30
		Week 24	17	5.427	2.4012	2.50	5.450	12.97	17	0.313	0.8348	-0.90	0.100	1.87
		Discontinuation	11	5.522	1.7299	1.40	5.500	7.70	11	0.085	1.2236	-2.20	0.400	2.00

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Erythrocytes (10^12/L)	NPC-25	Start of Administration	107	4.206	0.4964	2.56	4.270	5.47	-	-	-	-	-	-
		Week 4	104	4.197	0.4886	2.38	4.165	5.33	104	-0.002	0.1817	-0.58	0.000	0.48
		Week 8	100	4.180	0.4744	2.20	4.155	5.44	100	-0.030	0.2152	-0.40	-0.060	0.71
		Week 12	99	4.171	0.5070	2.76	4.160	5.38	99	-0.039	0.2304	-0.52	-0.060	0.73
		Week 16	77	4.164	0.4808	3.02	4.180	5.35	77	-0.075	0.2603	-0.55	-0.130	0.54
		Week 20	67	4.176	0.4798	2.82	4.200	5.29	67	-0.082	0.2436	-0.55	-0.100	0.57
		Week 24	57	4.184	0.5048	2.88	4.160	5.62	57	-0.106	0.2343	-0.59	-0.120	0.59
		Week 28	53	4.204	0.5657	2.18	4.170	5.53	53	-0.085	0.2858	-1.11	-0.070	0.50
		Week 32	35	4.345	0.5429	3.65	4.240	5.71	35	0.022	0.2715	-0.43	0.030	0.53
		Week 36	31	4.410	0.5769	3.56	4.370	5.69	31	0.056	0.2796	-0.52	0.050	0.66
		Week 40	30	4.439	0.5712	3.44	4.460	5.69	30	0.071	0.3061	-0.49	0.080	0.65
		Week 44	30	4.406	0.5770	3.43	4.440	5.74	30	0.038	0.2977	-0.65	0.095	0.68
		Week 48	29	4.423	0.5902	3.31	4.330	5.76	29	0.044	0.3259	-0.87	0.070	0.70
		Week 52	28	4.473	0.5434	3.58	4.415	5.58	28	0.088	0.2685	-0.46	0.100	0.52
		Discontinuation	14	4.093	0.6045	3.13	4.280	4.76	14	-0.043	0.3146	-0.87	-0.100	0.57
	NOBELZIN	Start of Administration	109	4.140	0.5369	2.90	4.090	6.15	-	-	-	-	-	-
		Week 4	108	4.119	0.5642	2.12	4.115	5.44	108	-0.018	0.2597	-1.27	0.015	0.59
		Week 8	105	4.160	0.5368	2.87	4.120	5.47	105	0.016	0.2399	-0.80	0.030	0.69
		Week 12	104	4.123	0.5443	2.67	4.040	5.50	104	-0.013	0.2825	-0.80	-0.010	0.88
		Week 16	62	4.075	0.5481	2.84	4.045	5.40	62	-0.031	0.2621	-0.82	-0.045	0.64
		Week 20	30	4.126	0.5066	3.14	4.070	5.35	30	-0.060	0.2218	-0.66	-0.030	0.36
		Week 24	17	4.098	0.5034	3.10	4.050	5.04	17	-0.053	0.2297	-0.70	-0.020	0.20
		Discontinuation	11	3.699	0.7737	2.12	3.930	4.53	11	-0.317	0.4684	-1.29	-0.090	0.08

表 2.7.4.7-1 血液学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Hemoglobin (g/L)	NPC-25	Start of Administration	107	127.4	16.79	75	130.0	170	-	-	-	-	-	-
		Week 4	104	127.1	16.31	72	127.5	165	104	0.0	5.57	-18	0.0	16
		Week 8	100	126.5	16.03	67	128.0	168	100	-1.2	6.54	-15	-1.5	22
		Week 12	99	126.4	16.27	76	126.0	167	99	-1.4	7.43	-20	-2.0	36
		Week 16	77	126.4	16.21	75	126.0	166	77	-2.5	7.85	-18	-3.0	29
		Week 20	67	126.7	16.59	74	127.0	165	67	-3.0	8.03	-18	-3.0	31
		Week 24	57	126.9	18.28	72	128.0	167	57	-3.4	7.75	-24	-4.0	18
		Week 28	53	126.8	18.76	68	128.0	168	53	-2.8	8.58	-41	-2.0	14
		Week 32	35	128.1	18.45	73	127.0	172	35	-0.9	7.66	-16	0.0	14
		Week 36	31	130.7	17.52	95	128.0	173	31	0.8	7.56	-12	1.0	18
		Week 40	30	131.4	18.29	91	131.0	169	30	1.2	8.65	-17	1.0	18
		Week 44	30	129.5	18.35	85	131.5	172	30	-0.6	8.05	-22	0.5	14
		Week 48	29	130.3	17.74	86	128.0	172	29	-1.0	9.62	-35	0.0	14
		Week 52	28	130.3	18.10	84	129.5	167	28	-0.3	8.18	-18	-0.5	15
		Discontinuation	14	119.9	18.03	86	121.0	144	14	-2.2	14.05	-35	-3.5	31
	NOBELZIN	Start of Administration	109	126.3	16.65	88	128.0	181	-	-	-	-	-	-
		Week 4	108	126.1	17.92	66	127.0	164	108	-0.3	7.74	-37	0.0	25
		Week 8	105	127.4	17.88	84	128.0	194	105	0.8	9.71	-31	0.0	56
		Week 12	104	125.9	16.44	80	127.5	168	104	-0.5	10.29	-27	0.0	34
		Week 16	62	129.7	38.64	87	126.0	399	62	3.8	35.98	-28	-1.5	270
		Week 20	30	126.9	14.38	91	127.0	157	30	-3.0	9.17	-28	-2.0	21
		Week 24	17	124.5	16.86	88	127.0	152	17	-5.2	11.30	-31	-4.0	8
		Discontinuation	11	112.2	21.81	66	118.0	137	11	-9.7	13.65	-34	-2.0	3

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Hematocrit (fraction of 1)	NPC-25	Start of Administration	107	0.3907	0.04699	0.251	0.3960	0.515	-	-	-	-	-	-
		Week 4	104	0.3886	0.04477	0.224	0.3905	0.492	104	-0.0014	0.01799	-0.055	-0.0015	0.058
		Week 8	100	0.3880	0.04552	0.210	0.3890	0.497	100	-0.0035	0.02184	-0.043	-0.0040	0.070
		Week 12	99	0.3866	0.04672	0.269	0.3870	0.504	99	-0.0050	0.02344	-0.066	-0.0090	0.107
		Week 16	77	0.3866	0.04427	0.268	0.3840	0.501	77	-0.0086	0.02346	-0.052	-0.0110	0.075
		Week 20	67	0.3863	0.04426	0.266	0.3850	0.487	67	-0.0105	0.02259	-0.063	-0.0160	0.078
		Week 24	57	0.3895	0.05014	0.253	0.3910	0.502	57	-0.0107	0.02306	-0.070	-0.0130	0.058
		Week 28	53	0.3895	0.05319	0.225	0.3840	0.507	53	-0.0092	0.02617	-0.107	-0.0050	0.054
		Week 32	35	0.3968	0.05300	0.261	0.3950	0.530	35	-0.0008	0.02571	-0.053	0.0000	0.047
		Week 36	31	0.4039	0.05141	0.310	0.3970	0.520	31	0.0037	0.02434	-0.044	0.0040	0.057
		Week 40	30	0.4056	0.05411	0.303	0.4050	0.530	30	0.0048	0.02652	-0.048	0.0070	0.062
		Week 44	30	0.4025	0.05388	0.284	0.4035	0.532	30	0.0016	0.02704	-0.064	0.0025	0.059
		Week 48	29	0.4047	0.05448	0.268	0.3980	0.536	29	0.0008	0.03157	-0.099	0.0080	0.063
		Week 52	28	0.4043	0.05318	0.282	0.4055	0.515	28	0.0016	0.02689	-0.053	-0.0005	0.049
		Discontinuation	14	0.3680	0.05233	0.268	0.3670	0.444	14	-0.0051	0.03775	-0.099	-0.0075	0.078
	NOBELZIN	Start of Administration	109	0.3847	0.04958	0.178	0.3880	0.511	-	-	-	-	-	-
		Week 4	108	0.3877	0.05215	0.206	0.3865	0.508	108	0.0028	0.03627	-0.105	0.0010	0.297
		Week 8	105	0.3900	0.04688	0.278	0.3900	0.516	105	0.0048	0.03649	-0.076	0.0010	0.296
		Week 12	104	0.3860	0.04680	0.247	0.3870	0.508	104	0.0015	0.03915	-0.080	-0.0010	0.285
		Week 16	62	0.3815	0.04884	0.270	0.3845	0.495	62	-0.0041	0.02941	-0.075	-0.0040	0.107
		Week 20	30	0.3880	0.04499	0.297	0.3810	0.499	30	-0.0090	0.02713	-0.076	-0.0115	0.051
		Week 24	17	0.3825	0.04885	0.282	0.3800	0.462	17	-0.0118	0.03197	-0.080	-0.0080	0.035
		Discontinuation	11	0.3469	0.06673	0.206	0.3640	0.416	11	-0.0334	0.04234	-0.114	-0.0120	0.011

表 2.7.4.7-1 血液学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Platelets (10^9/L)	NPC-25	Start of Administration	107	219.9	87.44	52	216.0	567	-	-	-	-	-	-
		Week 4	104	222.5	91.76	48	220.5	591	104	1.0	29.20	-55	2.5	215
		Week 8	100	217.7	81.64	44	215.0	524	100	-3.0	34.58	-109	-2.0	184
		Week 12	99	214.6	76.14	44	213.0	509	99	-7.2	32.62	-128	-7.0	101
		Week 16	77	209.7	76.23	43	212.0	445	77	-5.6	34.10	-110	-6.0	87
		Week 20	67	218.4	84.43	45	213.0	553	67	-4.1	34.54	-97	-6.0	75
		Week 24	57	215.0	76.76	48	210.0	486	57	-9.5	29.90	-96	-7.0	64
		Week 28	53	222.6	84.46	46	214.0	496	53	-4.0	36.82	-109	-4.0	94
		Week 32	35	227.9	96.46	48	226.0	553	35	-9.0	37.14	-124	-6.0	60
		Week 36	31	251.8	80.96	113	236.0	507	31	3.1	36.11	-55	-2.0	118
		Week 40	30	247.5	72.83	131	232.0	443	30	7.0	34.45	-59	8.5	82
		Week 44	30	242.9	70.39	113	239.5	378	30	2.4	44.23	-84	-6.0	86
		Week 48	29	241.2	72.35	120	238.0	406	29	0.2	33.31	-72	-1.0	67
		Week 52	28	235.4	65.37	122	234.0	375	28	-5.1	32.13	-88	-5.5	58
		Discontinuation	14	191.0	127.59	48	178.5	542	14	-0.6	34.33	-96	-0.5	40
	NOBELZIN	Start of Administration	109	225.5	94.12	32	228.0	554	-	-	-	-	-	-
		Week 4	108	213.6	81.92	36	217.0	435	108	-11.7	45.05	-357	-7.5	72
		Week 8	105	210.3	81.26	35	211.0	407	105	-15.5	52.49	-384	-7.0	93
		Week 12	104	209.8	80.28	33	220.5	397	104	-16.0	54.05	-363	-4.0	104
		Week 16	62	193.4	85.02	37	194.5	445	62	-19.2	34.44	-142	-10.0	41
		Week 20	30	198.6	92.87	43	201.0	398	30	-12.4	36.36	-115	-10.5	56
		Week 24	17	191.4	97.72	45	197.0	396	17	-23.0	41.82	-117	-1.0	16
		Discontinuation	11	190.3	51.03	76	185.0	250	11	-20.9	61.87	-194	-1.0	30

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Ery. Mean Corpuscular Volume (fL)	NPC-25	Start of Administration	107	93.11	6.690	71.4	93.70	105.4	-	-	-	-	-	-
		Week 4	104	92.85	6.590	71.6	93.00	104.4	104	-0.29	1.906	-4.4	-0.30	6.0
		Week 8	100	93.00	6.417	73.0	92.75	103.5	100	-0.17	2.440	-7.1	0.00	8.1
		Week 12	99	92.98	6.509	72.6	92.60	106.5	99	-0.23	3.222	-8.4	-0.20	11.4
		Week 16	77	93.10	6.703	71.8	92.20	106.2	77	-0.29	3.149	-8.4	0.00	10.4
		Week 20	67	92.73	6.576	71.7	92.50	105.1	67	-0.61	2.836	-8.4	-0.40	7.1
		Week 24	57	93.23	6.725	69.9	93.40	103.1	57	-0.17	2.820	-8.5	0.50	5.9
		Week 28	53	92.88	6.544	70.1	93.20	103.7	53	-0.18	2.819	-9.0	0.00	5.7
		Week 32	35	91.43	6.535	70.4	91.10	102.5	35	-0.56	2.665	-8.3	-0.60	5.9
		Week 36	31	91.75	5.243	79.0	91.90	102.5	31	-0.27	2.426	-6.2	-0.10	6.4
		Week 40	30	91.43	4.924	80.0	91.20	101.4	30	-0.45	2.075	-5.8	-0.65	3.7
		Week 44	30	91.50	5.653	76.0	91.15	102.3	30	-0.38	2.694	-6.4	-0.35	7.3
		Week 48	29	91.62	5.012	81.0	91.00	101.5	29	-0.77	2.797	-6.8	-0.50	6.7
		Week 52	28	90.46	5.919	70.0	90.80	101.5	28	-1.50	2.559	-8.3	-1.30	3.0
		Discontinuation	14	90.47	8.951	70.8	91.65	105.1	14	-0.36	3.515	-6.8	-0.85	7.1
	NOBELZIN	Start of Administration	109	94.00	6.695	72.8	94.70	113.3	-	-	-	-	-	-
		Week 4	108	94.38	6.249	74.1	94.95	113.5	108	0.25	1.997	-5.2	0.10	7.2
		Week 8	105	94.08	6.101	78.0	94.10	112.5	105	0.00	2.425	-5.4	-0.30	9.8
		Week 12	104	93.93	6.108	76.0	94.40	112.4	104	-0.17	3.076	-9.7	-0.35	11.9
		Week 16	62	93.85	5.676	79.8	93.55	112.4	62	-0.29	4.013	-14.9	-0.45	12.7
		Week 20	30	94.23	5.329	81.1	94.70	107.0	30	-0.97	3.866	-13.6	-1.20	10.4
		Week 24	17	93.54	6.770	77.9	94.00	107.1	17	-1.78	4.938	-16.8	-0.60	5.2
		Discontinuation	11	94.48	8.665	82.1	92.50	110.4	11	-0.85	1.468	-3.5	-1.00	1.0

表 2.7.4.7-1 血液学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Ery. Mean Corpuscular HGB Concentration (g/L)	NPC-25	Start of Administration	107	325.7	11.34	279	326.0	353	-	-	-	-	-	-
		Week 4	104	326.3	12.40	288	326.0	368	104	0.7	7.28	-29	2.0	23
		Week 8	100	325.3	12.19	287	327.0	351	100	-0.5	9.09	-29	0.0	29
		Week 12	99	326.4	12.35	278	327.0	358	99	0.6	8.02	-25	1.0	20
		Week 16	77	326.8	12.78	280	329.0	354	77	1.0	8.51	-22	1.0	26
		Week 20	67	326.5	14.70	276	327.0	358	67	0.1	10.67	-39	0.0	23
		Week 24	57	325.4	11.55	285	325.0	353	57	0.4	7.97	-17	0.0	22
		Week 28	53	325.0	11.42	286	327.0	349	53	0.3	8.00	-26	0.0	17
		Week 32	35	322.2	11.31	280	325.0	343	35	-1.5	6.93	-19	-1.0	9
		Week 36	31	322.3	11.21	282	322.0	346	31	-2.0	8.69	-33	-2.0	11
		Week 40	30	323.7	10.66	300	323.5	345	30	-0.5	7.66	-15	-1.5	18
		Week 44	30	321.5	9.97	299	323.0	336	30	-2.7	8.21	-21	-2.5	14
		Week 48	29	320.8	9.22	297	323.0	336	29	-4.3	10.33	-37	-5.0	12
		Week 52	28	321.9	9.84	298	320.0	344	28	-2.0	7.07	-14	-1.0	12
		Discontinuation	14	325.7	13.12	288	329.5	344	14	-1.9	9.45	-19	-3.0	17
	NOBELZIN	Start of Administration	109	325.0	11.26	293	325.0	351	-	-	-	-	-	-
		Week 4	108	324.9	11.08	299	325.0	350	108	0.0	7.89	-16	-0.5	34
		Week 8	105	324.6	12.58	290	325.0	349	105	-0.6	8.99	-35	0.0	34
		Week 12	104	325.7	12.31	295	326.0	360	104	0.4	9.63	-18	0.0	27
		Week 16	62	328.4	10.29	304	328.5	350	62	2.5	9.72	-12	0.0	33
		Week 20	30	327.3	11.19	301	328.5	355	30	0.8	11.06	-19	0.0	35
		Week 24	17	325.4	10.61	305	326.0	343	17	-2.0	12.13	-17	-3.0	37
		Discontinuation	11	323.5	7.12	310	324.0	332	11	2.6	8.79	-15	6.0	12

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Reticulocytes/Erythrocytes (fraction of 1)	NPC-25	Start of Administration	107	0.01540	0.006213	0.0040	0.01500	0.0497	-	-	-	-	-	-
		Week 4	104	0.01537	0.005791	0.0030	0.01450	0.0398	104	0.00010	0.003324	-0.0099	0.00000	0.0080
		Week 8	100	0.01558	0.006042	0.0050	0.01485	0.0430	100	0.00037	0.005218	-0.0100	0.00000	0.0320
		Week 12	99	0.01553	0.007330	0.0050	0.01400	0.0598	99	0.00045	0.005966	-0.0173	0.00100	0.0330
		Week 16	77	0.01664	0.008152	0.0040	0.01500	0.0600	77	0.00108	0.007754	-0.0167	0.00100	0.0500
		Week 20	67	0.01546	0.005683	0.0060	0.01500	0.0426	67	0.00027	0.003780	-0.0130	0.00100	0.0080
		Week 24	57	0.01510	0.004735	0.0050	0.01400	0.0270	57	0.00082	0.004203	-0.0115	0.00100	0.0110
		Week 28	53	0.01607	0.007079	0.0050	0.01380	0.0510	53	0.00179	0.007561	-0.0120	0.00100	0.0470
		Week 32	35	0.01445	0.004786	0.0070	0.01400	0.0310	35	-0.00025	0.004071	-0.0120	0.00040	0.0090
		Week 36	31	0.01421	0.003579	0.0090	0.01400	0.0250	31	-0.00020	0.002886	-0.0060	0.00000	0.0080
		Week 40	30	0.01390	0.003274	0.0080	0.01300	0.0220	30	-0.00052	0.003413	-0.0110	0.00000	0.0050
		Week 44	30	0.01367	0.004218	0.0060	0.01345	0.0230	30	-0.00075	0.004097	-0.0150	0.00000	0.0060
		Week 48	29	0.01426	0.004168	0.0070	0.01380	0.0270	29	-0.00038	0.003885	-0.0130	0.00000	0.0100
		Week 52	28	0.01355	0.003845	0.0050	0.01345	0.0200	28	-0.00104	0.003174	-0.0090	-0.00050	0.0060
		Discontinuation	14	0.01905	0.009201	0.0103	0.01700	0.0426	14	-0.00101	0.005282	-0.0080	-0.00075	0.0090
	NOBELZIN	Start of Administration	109	0.01568	0.006722	0.0020	0.01400	0.0534	-	-	-	-	-	-
		Week 4	108	0.01646	0.009701	0.0051	0.01500	0.0890	108	0.00076	0.008052	-0.0100	0.00000	0.0700
		Week 8	105	0.01624	0.005982	0.0050	0.01600	0.0391	105	0.00038	0.004704	-0.0143	0.00100	0.0215
		Week 12	104	0.01531	0.005492	0.0050	0.01400	0.0376	104	-0.00056	0.004633	-0.0158	0.00000	0.0150
		Week 16	62	0.01621	0.006080	0.0050	0.01485	0.0380	62	0.00061	0.005093	-0.0150	0.00100	0.0140
		Week 20	30	0.01598	0.005256	0.0080	0.01450	0.0302	30	0.00010	0.003665	-0.0081	0.00000	0.0102
		Week 24	17	0.01565	0.006126	0.0080	0.01500	0.0337	17	-0.00035	0.003756	-0.0090	0.00000	0.0040
		Discontinuation	11	0.01504	0.006217	0.0040	0.01680	0.0268	11	0.00094	0.006859	-0.0180	0.00100	0.0083

Change From Baseline : Each visit - Start of Administration

表 2.7.4.7-2 血液生化学的検査の要約統計量（SP）（NPC-25-3 試験）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Aspartate Aminotransferase (ukat/L)	NPC-25	Start of Administration	107	0.43810	0.225559	0.1503	0.40080	1.8036	-	-	-	-	-	-
		Week 4	104	0.42874	0.201578	0.2004	0.38410	1.4362	104	-0.00145	0.145905	-0.6513	0.00000	0.8517
		Week 8	100	0.42201	0.143578	0.2338	0.40080	0.9853	100	-0.00484	0.126680	-0.9519	0.00000	0.4008
		Week 12	99	0.43808	0.265381	0.2004	0.38410	2.4549	99	0.01383	0.269090	-1.2024	0.00000	2.1376
		Week 16	77	0.45198	0.238529	0.1837	0.38410	1.5197	77	0.01323	0.155704	-0.3674	0.00000	0.8517
		Week 20	67	0.47408	0.262943	0.2171	0.40080	1.7368	67	0.03240	0.169259	-0.2672	0.00000	0.7849
		Week 24	57	0.47844	0.307407	0.2338	0.40080	2.0541	57	0.06241	0.260490	-0.1503	0.01670	1.7368
		Week 28	53	0.47926	0.288316	0.1837	0.38410	1.8370	53	0.05829	0.237614	-0.2505	0.00000	1.1022
		Week 32	35	0.49146	0.297315	0.2171	0.40080	1.7702	35	0.05201	0.223753	-0.2505	0.00000	1.0354
		Week 36	31	0.44228	0.164242	0.2338	0.40080	0.8350	31	0.01185	0.110287	-0.3173	0.00000	0.2672
		Week 40	30	0.42474	0.157008	0.2505	0.37575	0.8684	30	-0.00724	0.125867	-0.3674	0.00000	0.3340
		Week 44	30	0.43977	0.207489	0.2505	0.35070	1.1857	30	0.00779	0.174311	-0.2839	0.00000	0.6513
		Week 48	29	0.42787	0.215184	0.2338	0.38410	1.3026	29	-0.00288	0.176345	-0.2672	-0.01670	0.7682
		Week 52	28	0.42525	0.171726	0.2338	0.36740	0.9185	28	-0.01491	0.128905	-0.3173	-0.00835	0.3674
		Discontinuation	14	0.51651	0.266433	0.3006	0.45925	1.2692	14	-0.05845	0.110339	-0.3841	-0.03340	0.0334
	NOBELZIN	Start of Administration	109	0.42960	0.204139	0.1837	0.40080	1.3360	-	-	-	-	-	-
		Week 4	108	0.43807	0.223689	0.2004	0.38410	1.5364	108	0.00711	0.127331	-0.7515	0.00000	0.5344
		Week 8	105	0.43738	0.205932	0.1837	0.40080	1.4028	105	0.00461	0.119990	-0.7181	0.00000	0.4676
		Week 12	104	0.44962	0.259256	0.1837	0.38410	2.3380	104	0.01461	0.163455	-0.7181	0.01670	1.2191
		Week 16	62	0.45790	0.147972	0.2004	0.41750	0.8684	62	0.00620	0.125782	-0.4509	0.01670	0.3507
		Week 20	30	0.52271	0.333370	0.2505	0.44255	2.0541	30	0.04342	0.179361	-0.2505	0.03340	0.7348
		Week 24	17	0.45286	0.148419	0.2338	0.38410	0.7348	17	0.00098	0.115621	-0.1837	0.00000	0.2672
		Discontinuation	11	0.54655	0.529687	0.2171	0.36740	2.0541	11	0.11386	0.244963	-0.0501	0.00000	0.7348

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Alanine Aminotransferase (ukat/L)	NPC-25	Start of Administration	107	0.32510	0.196868	0.0835	0.26720	1.1022	-	-	-	-	-	-
		Week 4	104	0.34315	0.241545	0.0835	0.28390	1.7702	104	0.02457	0.155740	-0.1837	0.00000	0.9853
		Week 8	100	0.34085	0.201285	0.1169	0.28390	1.1523	100	0.02605	0.111771	-0.2505	0.01670	0.5511
		Week 12	99	0.38343	0.463129	0.1002	0.28390	4.4756	99	0.07135	0.443504	-0.4175	0.01670	4.2084
		Week 16	77	0.37933	0.273523	0.1169	0.30060	1.6700	77	0.05747	0.167537	-0.3507	0.03340	0.9686
		Week 20	67	0.40205	0.319031	0.1336	0.31730	2.1543	67	0.08250	0.211018	-0.2338	0.03340	1.4529
		Week 24	57	0.41516	0.363001	0.1002	0.30060	2.1710	57	0.10079	0.254738	-0.1503	0.03340	1.4696
		Week 28	53	0.43294	0.419062	0.1336	0.31730	2.3714	53	0.11469	0.310120	-0.2505	0.05010	1.6700
		Week 32	35	0.46760	0.477237	0.1503	0.31730	2.2211	35	0.12406	0.343045	-0.3006	0.05010	1.5197
		Week 36	31	0.40242	0.308517	0.1670	0.28390	1.5698	31	0.07704	0.219683	-0.1837	0.05010	0.8684
		Week 40	30	0.36406	0.210757	0.1336	0.30895	1.0187	30	0.03618	0.144332	-0.2505	0.02505	0.4843
		Week 44	30	0.39802	0.335296	0.1503	0.30060	1.8537	30	0.07014	0.244119	-0.2672	0.01670	1.1523
		Week 48	29	0.36682	0.216295	0.1336	0.30060	1.0020	29	0.03513	0.166004	-0.3173	0.01670	0.5845
		Week 52	28	0.36919	0.254867	0.1670	0.28390	1.3861	28	0.03340	0.211826	-0.3340	0.01670	0.9853
		Discontinuation	14	0.41273	0.229954	0.1837	0.38410	1.0688	14	-0.01074	0.106350	-0.2338	0.00000	0.1503
	NOBELZIN	Start of Administration	109	0.31868	0.192663	0.0668	0.28390	1.0521	-	-	-	-	-	-
		Week 4	108	0.32874	0.187827	0.0835	0.28390	1.2692	108	0.00835	0.128051	-0.6513	0.01670	0.4676
		Week 8	105	0.33623	0.166599	0.1169	0.30060	0.9018	105	0.01288	0.137970	-0.5344	0.01670	0.5010
		Week 12	104	0.35279	0.182875	0.1169	0.31730	0.9853	104	0.02794	0.139673	-0.5010	0.03340	0.4509
		Week 16	62	0.37737	0.174614	0.1169	0.34235	0.9519	62	0.03340	0.129358	-0.3841	0.04175	0.3340
		Week 20	30	0.41305	0.223234	0.1670	0.35905	1.1189	30	0.04175	0.169046	-0.4676	0.05010	0.5678
		Week 24	17	0.35659	0.106269	0.2171	0.33400	0.5845	17	0.04519	0.115666	-0.1837	0.06680	0.2338
		Discontinuation	11	0.37347	0.280269	0.1503	0.26720	1.1189	11	0.09716	0.118044	-0.0501	0.06680	0.3507

表 2.7.4.7-2 血液生化学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Alkaline Phosphatase (ukat/L)	NPC-25	Start of Administration	107	1.54092	0.978444	0.5177	1.31930	6.3126	-	-	-	-	-	-
		Week 4	104	1.76213	1.467793	0.5678	1.39445	11.1055	104	0.21354	0.674497	-0.4342	0.10020	6.3460
		Week 8	100	1.68769	1.128930	0.5845	1.41950	7.8824	100	0.15797	0.339633	-0.7014	0.10020	1.5698
		Week 12	99	1.85453	1.942075	0.5678	1.41950	17.1676	99	0.32471	1.550881	-1.0187	0.15030	15.1636
		Week 16	77	1.77140	1.340528	0.5511	1.40280	8.0995	77	0.24499	0.509276	-0.8851	0.13360	3.0561
		Week 20	67	1.76920	1.341032	0.6012	1.38610	8.7675	67	0.23430	0.581325	-1.1857	0.13360	3.7241
		Week 24	57	1.75379	1.198099	0.5678	1.41950	7.2812	57	0.24083	0.398106	-0.6680	0.15030	1.6199
		Week 28	53	1.77902	1.194859	0.6179	1.51970	6.8303	53	0.26184	0.413119	-0.8183	0.20040	1.2692
		Week 32	35	1.72487	1.184576	0.6179	1.50300	7.0641	35	0.22044	0.441056	-0.8016	0.13360	1.9706
		Week 36	31	1.75296	1.176511	0.6680	1.38610	6.4462	31	0.22141	0.354443	-0.5678	0.21710	1.3527
		Week 40	30	1.86483	1.257686	0.6513	1.55310	6.2625	30	0.31730	0.501595	-0.3841	0.22545	2.2879
		Week 44	30	1.81306	1.097975	0.6346	1.48630	6.1456	30	0.26553	0.502808	-1.0855	0.20875	1.8704
		Week 48	29	1.72010	0.996548	0.5511	1.48630	5.5945	29	0.15030	0.381367	-1.2358	0.11690	0.8851
		Week 52	28	1.76424	1.114587	0.6346	1.48630	6.2124	28	0.17296	0.369257	-0.8183	0.13360	1.1189
		Discontinuation	14	2.81276	2.623366	0.8684	1.46960	8.7675	14	0.40915	1.051962	-0.3173	0.09185	3.7241
	NOBELZIN	Start of Administration	109	1.49560	0.837382	0.5010	1.25250	5.1436	-	-	-	-	-	-
		Week 4	108	1.62417	1.077065	0.5010	1.34435	8.4001	108	0.15662	0.403234	-0.6196	0.10020	3.2565
		Week 8	105	1.70553	1.166324	0.4676	1.45290	10.0200	105	0.24743	0.550384	-1.1573	0.18370	4.8764
		Week 12	104	1.72185	1.174288	0.5344	1.49465	9.5190	104	0.26418	0.517001	-0.6313	0.16700	4.3754
		Week 16	62	1.67388	0.759632	0.5845	1.50300	3.9913	62	0.22887	0.276182	-0.5728	0.20875	1.2191
		Week 20	30	1.64334	0.708611	0.6012	1.48630	3.1730	30	0.20953	0.258879	-0.6780	0.20875	0.7181
		Week 24	17	1.60124	0.730682	0.6179	1.43620	3.4569	17	0.19549	0.253458	-0.2338	0.16700	1.0020
		Discontinuation	11	1.77779	0.790401	0.8684	1.58650	3.5070	11	0.01518	0.507826	-1.0187	0.08350	1.0688

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Gamma Glutamyl Transferase (ukat/L)	NPC-25	Start of Administration	107	0.61072	0.938105	0.1336	0.31730	7.4983	-	-	-	-	-	-
		Week 4	104	0.69931	1.353509	0.1336	0.33400	11.6232	104	0.08222	0.911110	-2.8724	0.00000	8.5170
		Week 8	100	0.61924	1.013794	0.1336	0.31730	8.4001	100	0.01937	0.650617	-4.3253	0.00000	3.6573
		Week 12	99	0.75099	2.296487	0.1336	0.31730	22.5951	99	0.15671	2.317470	-5.0434	0.00000	22.2945
		Week 16	77	0.58905	0.838883	0.1336	0.30060	4.3253	77	0.01757	0.570366	-3.6072	-0.01670	2.4382
		Week 20	67	0.66974	1.109228	0.1169	0.31730	6.8804	67	0.07577	0.490390	-0.6179	-0.01670	2.8223
		Week 24	57	0.62171	1.046347	0.1336	0.28390	6.5631	57	0.14092	0.780829	-0.2171	-0.01670	5.4943
		Week 28	53	0.60656	0.902025	0.1336	0.31730	4.9933	53	0.10902	0.616637	-0.9853	0.00000	3.9245
		Week 32	35	0.54633	0.681778	0.1169	0.30060	3.4569	35	0.06632	0.295078	-0.2338	-0.01670	1.1523
		Week 36	31	0.45359	0.481047	0.1336	0.30060	2.1877	31	-0.00054	0.238815	-0.7014	-0.01670	0.6012
		Week 40	30	0.45090	0.451337	0.1169	0.26720	1.8203	30	-0.00835	0.314385	-1.0688	-0.01670	1.1857
		Week 44	30	0.44979	0.399645	0.1336	0.28390	1.6366	30	-0.00946	0.302440	-1.2525	-0.00835	0.7515
		Week 48	29	0.44226	0.389472	0.1503	0.28390	1.8370	29	-0.02649	0.250162	-1.0521	-0.01670	0.4843
		Week 52	28	0.38649	0.354223	0.1169	0.25885	1.8036	28	-0.07396	0.224304	-1.0855	-0.01670	0.1503
		Discontinuation	14	1.06403	1.754368	0.2004	0.39245	6.7134	14	0.26481	0.988850	-0.3006	0.00000	3.6072
	NOBELZIN	Start of Administration	109	0.70232	1.384415	0.1002	0.35070	13.5270	-	-	-	-	-	-
		Week 4	108	0.69058	1.338386	0.1169	0.35070	12.7755	108	-0.01670	0.148810	-0.7515	-0.00835	0.7181
		Week 8	105	0.67993	1.191311	0.1002	0.36740	10.7381	105	-0.04199	0.347745	-2.7889	0.00000	0.9519
		Week 12	104	0.68438	1.304689	0.1002	0.35905	12.2411	104	-0.03966	0.317152	-1.2859	0.00000	1.8370
		Week 16	62	0.72780	1.499609	0.1336	0.35905	11.8403	62	-0.09266	0.317274	-1.6867	-0.00835	0.3841
		Week 20	30	1.06546	2.578971	0.1169	0.45090	14.4789	30	-0.01447	0.310165	-0.9352	0.00000	0.9519
		Week 24	17	0.52752	0.345091	0.2004	0.41750	1.3527	17	-0.05894	0.343626	-1.2358	-0.03340	0.2672
		Discontinuation	11	1.63660	4.268188	0.1670	0.21710	14.4789	11	0.13512	0.288814	-0.0334	0.01670	0.9519

表 2.7.4.7-2 血液生化学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Protein (g/L)	NPC-25	Start of Administration	107	70.8	5.03	56	71.0	94	-	-	-	-	-	-
		Week 4	104	70.7	4.86	56	70.0	85	104	0.0	3.20	-13	0.0	7
		Week 8	100	70.3	5.28	49	69.5	89	100	-0.4	3.40	-12	0.0	11
		Week 12	99	70.5	5.30	56	70.0	86	99	-0.1	4.04	-17	0.0	11
		Week 16	77	69.9	4.54	61	70.0	82	77	-0.5	3.49	-13	-1.0	8
		Week 20	67	70.4	4.31	59	70.0	80	67	-0.1	3.99	-15	0.0	10
		Week 24	57	70.0	4.55	63	69.0	86	57	-0.7	4.14	-13	-1.0	15
		Week 28	53	70.4	5.14	58	70.0	81	53	-0.5	3.71	-13	0.0	7
		Week 32	35	71.1	4.32	65	70.0	83	35	-0.8	4.65	-20	0.0	6
		Week 36	31	71.5	4.34	64	71.0	82	31	-0.6	4.52	-19	0.0	8
		Week 40	30	72.0	3.94	65	72.0	80	30	-0.4	3.99	-17	0.0	5
		Week 44	30	72.3	4.00	64	72.0	81	30	-0.1	4.85	-20	0.0	7
		Week 48	29	71.4	4.31	64	71.0	81	29	-1.0	5.05	-21	-1.0	7
		Week 52	28	71.7	3.94	65	72.0	80	28	-0.8	5.00	-22	-0.5	6
		Discontinuation	14	70.2	5.21	59	69.5	79	14	-0.6	3.86	-9	1.0	3
	NOBELZIN	Start of Administration	109	70.3	5.29	58	70.0	88	-	-	-	-	-	-
		Week 4	108	69.9	4.88	56	69.5	89	108	-0.4	3.74	-15	0.0	9
		Week 8	105	70.3	5.08	56	70.0	94	105	-0.1	3.62	-10	0.0	10
		Week 12	104	70.1	4.76	60	69.0	90	104	-0.3	3.82	-11	0.0	9
		Week 16	62	69.9	5.22	59	69.0	87	62	-0.2	3.29	-8	0.0	7
		Week 20	30	69.9	4.18	60	69.5	79	30	-0.1	3.37	-8	0.0	5
		Week 24	17	68.7	4.93	61	67.0	79	17	-0.7	3.58	-6	-1.0	10
		Discontinuation	11	67.5	4.68	61	67.0	76	11	-2.5	4.32	-13	-2.0	2

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Albumin (g/L)	NPC-25	Start of Administration	107	39.7	3.36	28	41.0	46	-	-	-	-	-	-
		Week 4	104	39.7	3.27	28	40.0	46	104	-0.1	1.92	-6	0.0	4
		Week 8	100	39.8	3.37	25	40.0	46	100	-0.2	2.27	-6	0.0	5
		Week 12	99	40.0	3.39	28	40.0	49	99	0.0	2.44	-5	0.0	8
		Week 16	77	39.8	3.33	30	40.0	48	77	-0.3	2.48	-8	0.0	7
		Week 20	67	40.3	3.63	29	41.0	48	67	0.0	2.72	-6	0.0	7
		Week 24	57	40.2	2.96	30	41.0	47	57	-0.3	2.60	-7	0.0	6
		Week 28	53	40.4	3.65	25	40.0	47	53	0.0	2.93	-11	0.0	6
		Week 32	35	40.7	2.78	34	41.0	45	35	0.1	2.86	-7	0.0	5
		Week 36	31	40.9	2.77	36	41.0	47	31	0.0	2.76	-5	0.0	6
		Week 40	30	41.3	2.29	35	41.5	45	30	0.4	2.29	-5	0.0	4
		Week 44	30	41.0	2.56	35	41.0	46	30	0.0	2.82	-4	-1.0	7
		Week 48	29	40.6	2.55	34	41.0	47	29	-0.3	3.10	-6	0.0	8
		Week 52	28	41.1	2.83	34	41.0	46	28	0.0	2.49	-4	0.0	4
		Discontinuation	14	36.8	4.49	29	38.0	45	14	-0.4	2.56	-5	0.5	3
	NOBELZIN	Start of Administration	109	39.5	4.28	29	40.0	50	-	-	-	-	-	-
		Week 4	108	39.5	4.73	24	40.0	49	108	0.0	2.06	-6	0.0	6
		Week 8	105	39.4	4.44	26	40.0	48	105	-0.1	1.87	-5	0.0	4
		Week 12	104	39.4	4.30	24	40.0	51	104	-0.1	2.52	-7	0.0	7
		Week 16	62	38.5	4.30	28	38.0	49	62	-0.1	2.41	-5	0.0	6
		Week 20	30	39.0	4.26	29	39.5	46	30	-0.3	1.98	-5	0.0	3
		Week 24	17	38.6	5.55	27	40.0	49	17	-0.9	2.41	-5	-1.0	5
		Discontinuation	11	36.8	4.35	29	37.0	44	11	-1.6	1.63	-4	-1.0	0

表 2.7.4.7-2 血液生化学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Bilirubin (umol/L)	NPC-25	Start of Administration	107	13.008631	11.2112855	3.42080	10.262400	82.44128	-	-	-	-	-	-
		Week 4	104	12.747414	9.5828339	3.42080	10.262400	69.27120	104	-0.210511	3.8399295	-13.68320	0.000000	11.97280
		Week 8	100	12.255016	9.2497914	3.42080	10.262400	65.16624	100	-0.667056	4.2345421	-17.27504	0.000000	8.55200
		Week 12	99	12.142112	8.7981242	3.42080	10.262400	68.75808	99	-0.799914	4.6767139	-22.23520	0.000000	8.03888
		Week 16	77	12.074980	8.6577626	3.42080	10.262400	63.45584	77	-1.041789	5.1223539	-25.48496	0.000000	7.18368
		Week 20	67	13.004146	12.7656858	3.42080	10.262400	99.37424	67	-0.232308	4.7746320	-17.10400	0.000000	16.93296
		Week 24	57	10.538465	4.7956337	3.42080	10.262400	27.70848	57	-1.230288	5.7754670	-34.03696	0.000000	5.13120
		Week 28	53	10.930424	6.2308515	3.42080	8.552000	37.62880	53	-0.658343	4.6143502	-24.11664	0.000000	6.84160
		Week 32	35	10.081586	5.3151971	3.42080	8.552000	25.48496	35	-1.202167	6.7901557	-36.26048	0.000000	5.13120
		Week 36	31	9.578240	5.8362831	3.42080	8.552000	27.36640	31	-1.506255	7.0624429	-34.89216	0.000000	6.84160
		Week 40	30	9.304576	5.0508705	3.42080	8.552000	27.36640	30	-1.864336	8.2637282	-41.56272	0.000000	6.84160
		Week 44	30	9.350187	5.4781314	3.42080	8.380960	29.07680	30	-1.818725	7.8584083	-40.02336	0.000000	6.84160
		Week 48	29	9.501567	5.0245324	3.42080	8.552000	25.82704	29	-1.757583	7.8190721	-35.91840	-1.368320	5.13120
		Week 52	28	9.724846	6.1646002	3.42080	8.552000	34.20800	28	-1.447731	8.1002394	-40.36544	0.000000	6.84160
		Discontinuation	14	17.934766	23.9088129	3.42080	11.972800	99.37424	14	-0.256560	6.4640205	-11.63072	0.000000	16.93296
	NOBELZIN	Start of Administration	109	12.881352	9.1341130	3.42080	10.262400	57.81152	-	-	-	-	-	-
		Week 4	108	12.615784	9.0783619	1.71040	10.262400	65.67936	108	-0.337329	3.9354458	-13.85424	0.000000	11.28864
		Week 8	105	12.582028	8.0818027	3.42080	10.262400	53.53552	105	-0.415383	4.1692717	-13.68320	0.000000	13.68320
		Week 12	104	12.878983	8.3825994	3.42080	10.262400	44.47040	104	-0.111834	4.5689402	-17.78816	0.000000	13.68320
		Week 16	62	12.883174	8.0686108	3.42080	10.176880	41.04960	62	-0.275871	2.9334371	-10.43344	0.000000	6.84160
		Week 20	30	14.287541	7.6692576	5.13120	11.716240	31.81344	30	0.119728	4.0882521	-8.89408	0.000000	11.97280
		Week 24	17	14.156075	7.7416928	5.13120	11.972800	32.49760	17	-1.971991	5.0728276	-15.56464	-1.710400	5.13120
		Discontinuation	11	10.448989	5.6574978	3.42080	8.552000	23.94560	11	-0.746356	4.4518218	-4.78912	-1.710400	11.97280

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Lipase (ukat/L)	NPC-25	Start of Administration	107	0.633102	0.3544084	0.11690	0.584500	1.73680	-	-	-	-	-	-
		Week 4	104	0.679818	0.3865565	0.11690	0.675515	1.95390	104	0.049666	0.1844348	-0.45758	0.033400	0.86840
		Week 8	100	0.748661	0.4866636	0.16700	0.701400	3.40680	100	0.118687	0.2943811	-0.62792	0.083500	2.17100
		Week 12	99	0.766985	0.4384531	0.18370	0.751500	2.55510	99	0.141275	0.2467420	-0.54442	0.113560	1.21910
		Week 16	77	0.814049	0.4596100	0.20040	0.701400	2.38810	77	0.174656	0.2603983	-0.51770	0.150300	1.10220
		Week 20	67	0.865932	0.4845798	0.21710	0.751500	2.80560	67	0.178391	0.2918560	-0.44589	0.133600	1.56980
		Week 24	57	0.933354	0.7429847	0.23380	0.768200	4.37540	57	0.273353	0.6111829	-0.31730	0.163660	3.72410
		Week 28	53	0.971247	0.7236560	0.20040	0.751500	3.47360	53	0.314685	0.5565405	-0.40080	0.167000	2.80560
		Week 32	35	0.983105	0.8459997	0.30060	0.833330	4.97660	35	0.347074	0.7539041	-0.25050	0.183700	4.32530
		Week 36	31	0.950876	0.6280501	0.28390	0.835000	2.88910	31	0.312990	0.4640505	-0.23380	0.200400	2.23780
		Week 40	29	0.848187	0.4788793	0.26720	0.784900	2.43820	29	0.202588	0.3011224	-0.55110	0.167000	1.03540
		Week 44	30	0.909705	0.6380607	0.23380	0.776550	3.55710	30	0.266142	0.4553050	-0.40080	0.225450	2.32130
		Week 48	29	0.932839	0.6244418	0.36740	0.768200	3.25650	29	0.280906	0.4217161	-0.31730	0.200400	2.02070
		Week 52	28	0.906810	0.5425872	0.31730	0.801600	2.55510	28	0.255450	0.3288562	-0.35070	0.217100	1.31930
		Discontinuation	14	0.759611	0.4249444	0.28390	0.592850	1.50300	14	0.118928	0.2731114	-0.15030	0.083500	0.86840
	NOBELZIN	Start of Administration	109	0.643639	0.3768452	0.08350	0.561120	2.45490	-	-	-	-	-	-
		Week 4	108	0.721564	0.4548607	0.10020	0.650465	2.88910	108	0.075212	0.3421676	-1.33600	0.033400	2.07080
		Week 8	105	0.745663	0.4297409	0.10020	0.651300	2.42150	105	0.101679	0.2757505	-1.28590	0.066800	1.25250
		Week 12	104	0.825558	0.5848037	0.13360	0.674680	3.65730	104	0.179236	0.3837050	-0.43420	0.100200	2.53840
		Week 16	62	0.961247	0.7208679	0.11690	0.793250	4.59250	62	0.252332	0.5890476	-0.95190	0.133600	3.64060
		Week 20	30	1.194885	1.2253261	0.16700	0.831660	6.42950	30	0.422621	1.1430714	-0.83500	0.133600	5.47760
		Week 24	17	1.158292	1.0723889	0.20040	0.751500	4.44220	17	0.364649	0.9064855	-0.25050	0.150300	3.77420
		Discontinuation	11	0.805699	0.4315839	0.35070	0.668000	1.73680	11	0.204195	0.3424910	-0.05010	0.096860	0.95190

表 2.7.4.7-2 血液生化学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Amylase (ukat/L)	NPC-25	Start of Administration	107	1.60133	0.829056	0.4342	1.41950	6.5297	-	-	-	-	-	-
		Week 4	104	1.62151	0.864931	0.3674	1.43620	6.4295	104	0.01670	0.264132	-0.8350	0.00000	0.9352
		Week 8	100	1.59869	0.643013	0.7348	1.46125	4.4088	100	0.05361	0.318149	-1.0855	0.05010	0.7849
		Week 12	99	1.64689	0.668408	0.6847	1.45290	4.3754	99	0.09345	0.319596	-1.4529	0.06680	0.8851
		Week 16	77	1.62055	0.680542	0.6179	1.41950	4.4255	77	0.05552	0.288140	-1.0688	0.05010	0.9853
		Week 20	67	1.68944	0.766595	0.6346	1.45290	4.7428	67	0.10793	0.464402	-1.1189	0.08350	2.8557
		Week 24	57	1.80506	1.054768	0.8517	1.51970	6.9639	57	0.18311	0.565550	-0.5511	0.05010	3.0394
		Week 28	53	1.75318	0.898723	0.6680	1.51970	6.0955	53	0.15534	0.467756	-1.2692	0.10020	2.1710
		Week 32	35	1.85990	1.240227	0.7849	1.53640	7.7488	35	0.17511	0.680944	-0.8851	0.05010	3.8243
		Week 36	31	1.83538	0.978544	0.7014	1.61990	5.4776	31	0.15461	0.366690	-0.7014	0.11690	1.5531
		Week 40	30	1.78412	0.776221	0.5845	1.59485	4.1583	30	0.11078	0.393230	-1.3360	0.19205	0.7849
		Week 44	30	1.96670	1.236451	0.8684	1.62825	7.2478	30	0.29336	1.049145	-1.3026	0.15030	5.3941
		Week 48	29	1.78805	0.800057	0.8016	1.53640	4.4923	29	0.11172	0.389024	-1.0020	0.10020	1.1022
		Week 52	28	1.89485	0.810474	0.9352	1.52805	4.7762	28	0.20279	0.505469	-1.0354	0.14195	1.7535
		Discontinuation	14	1.52447	0.714504	0.8016	1.27755	3.4569	14	0.09066	0.285949	-0.4342	0.09185	0.8684
	NOBELZIN	Start of Administration	109	1.65253	0.686325	0.6346	1.50300	4.7261	-	-	-	-	-	-
		Week 4	108	1.70015	0.780457	0.6346	1.52805	5.6947	108	0.04206	0.598739	-2.6553	0.05010	3.5905
		Week 8	105	1.73076	0.819839	0.7348	1.58650	6.9973	105	0.07173	0.647480	-2.9559	0.05010	5.0935
		Week 12	104	1.71528	0.678635	0.6346	1.55310	3.8243	104	0.05733	0.459308	-2.9225	0.10020	1.4529
		Week 16	62	1.86744	0.790576	0.8350	1.67835	4.3253	62	0.15111	0.502853	-0.8183	0.10020	2.4716
		Week 20	30	1.89712	0.883731	0.7181	1.53640	4.0247	30	0.18036	0.606827	-0.6680	0.08350	2.8891
		Week 24	17	1.95979	1.017501	0.8350	1.68670	4.3420	17	0.10413	0.275014	-0.2672	0.03340	0.8684
		Discontinuation	11	1.62901	0.724263	0.6346	1.48630	3.2565	11	0.16548	0.513723	-0.3674	-0.05010	1.4028

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Cholesterol (mmol/L)	NPC-25	Start of Administration	107	5.04687	1.190999	2.9008	4.97280	11.6809	-	-	-	-	-	-
		Week 4	104	4.98973	1.195154	2.8231	4.80445	11.4478	104	-0.06824	0.400218	-1.1914	-0.06475	0.9583
		Week 8	100	5.00362	1.142929	2.2792	4.92100	10.8262	100	-0.06812	0.510087	-1.2173	-0.05180	1.7871
		Week 12	99	4.91027	1.209702	2.6418	4.84330	10.4895	99	-0.15174	0.561389	-1.2432	-0.12950	1.7871
		Week 16	77	4.79890	1.181661	2.8749	4.61020	9.7902	77	-0.24790	0.623987	-1.8907	-0.25900	1.7094
		Week 20	67	4.87577	1.116793	3.0303	4.71380	9.2722	67	-0.19290	0.732358	-2.4087	-0.15540	1.7094
		Week 24	57	4.76696	1.191203	1.5540	4.76560	8.7024	57	-0.25218	0.896729	-3.6519	-0.20720	2.0979
		Week 28	53	4.89021	1.077614	2.7972	4.81740	8.6765	53	-0.16029	0.753193	-3.0044	-0.07770	1.4245
		Week 32	35	4.92766	0.984207	2.9267	4.92100	7.2779	35	-0.34188	0.903291	-4.4030	-0.20720	0.8806
		Week 36	31	5.10898	0.780731	3.6260	4.92100	6.3455	31	-0.29827	1.163789	-5.5685	-0.15540	1.7094
		Week 40	29	5.17286	0.940889	3.3152	5.10230	6.7599	29	-0.27418	1.215203	-5.4908	-0.10360	1.5799
		Week 44	30	5.07726	0.868579	3.1080	5.20590	6.7858	30	-0.34447	1.302021	-6.2678	-0.10360	1.4245
		Week 48	29	5.15142	0.888545	3.2375	5.28360	6.7340	29	-0.24828	1.345670	-6.2160	-0.12950	2.0979
		Week 52	28	5.12265	0.953853	2.6936	5.10230	6.7599	28	-0.33855	1.388168	-6.6304	-0.12950	0.9324
		Discontinuation	14	4.34195	0.809499	3.0044	4.33825	5.6462	14	-0.33855	0.374427	-1.0101	-0.41440	0.4144
	NOBELZIN	Start of Administration	109	4.96520	0.940098	2.9267	4.94690	7.4592	-	-	-	-	-	-
		Week 4	108	4.90181	0.989950	2.5382	4.84330	7.9254	108	-0.06547	0.443180	-1.2950	-0.07770	1.2950
		Week 8	105	4.85391	0.958439	2.3051	4.79150	7.5628	105	-0.13468	0.447945	-1.5022	-0.05180	1.1914
		Week 12	104	4.87667	1.009921	1.8907	4.86920	7.4074	104	-0.11232	0.531866	-1.8907	-0.11655	1.5022
		Week 16	62	4.68665	0.967345	1.8648	4.71380	7.0448	62	-0.28657	0.473824	-1.4763	-0.27195	1.5799
		Week 20	30	4.82517	0.814758	3.3411	4.67495	6.3196	30	-0.20547	0.562895	-1.9684	-0.09065	0.9842
		Week 24	17	4.85549	1.118513	3.2634	4.68790	7.0189	17	-0.35651	0.546402	-1.7612	-0.31080	0.2849
		Discontinuation	11	4.32765	0.999314	2.8231	4.04040	6.0347	11	-0.17424	0.495914	-0.9065	-0.18130	0.8029

表 2.7.4.7-2 血液生化学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Cholesterol/HDL-Cholesterol (mmol/L)	NPC-25	Start of Administration	107	1.59880	0.455565	0.7252	1.60580	3.2893	-	-	-	-	-	-
		Week 4	104	1.57201	0.455613	0.7770	1.56695	3.3152	104	-0.03432	0.169807	-0.8029	-0.02590	0.4403
		Week 8	100	1.56312	0.452309	0.6993	1.55400	3.2116	100	-0.04351	0.188153	-0.5180	-0.07770	0.7511
		Week 12	99	1.54181	0.454761	0.5439	1.52810	3.1080	99	-0.07163	0.204852	-0.7252	-0.07770	0.8029
		Week 16	77	1.48737	0.468256	0.6216	1.45040	3.0821	77	-0.13448	0.240232	-0.6993	-0.18130	0.8029
		Week 20	67	1.48968	0.441836	0.6993	1.45040	3.1080	67	-0.10677	0.290395	-0.6216	-0.15540	1.1655
		Week 24	57	1.48707	0.442845	0.6216	1.37270	3.1857	57	-0.11682	0.264151	-0.6993	-0.12950	0.9324
		Week 28	53	1.48172	0.415905	0.6993	1.47630	3.1080	53	-0.11567	0.226281	-0.7252	-0.10360	0.3367
		Week 32	35	1.52100	0.516052	0.7511	1.47630	3.3670	35	-0.10686	0.228691	-0.7511	-0.15540	0.3626
		Week 36	31	1.57489	0.522916	0.7770	1.55400	3.2893	31	-0.09608	0.210646	-0.6993	-0.02590	0.2072
		Week 40	30	1.59026	0.540363	0.7252	1.52810	3.0821	30	-0.08633	0.194215	-0.4921	-0.11655	0.2331
		Week 44	30	1.61184	0.580246	0.7511	1.52810	3.4447	30	-0.06475	0.183614	-0.5180	-0.05180	0.2331
		Week 48	29	1.56472	0.513565	0.7511	1.50220	3.2893	29	-0.07056	0.220628	-0.5180	-0.10360	0.4662
		Week 52	28	1.60950	0.542538	0.6993	1.59285	3.1598	28	-0.07400	0.238392	-0.4662	-0.09065	0.6993
		Discontinuation	14	1.31905	0.396828	0.6993	1.26263	2.1238	14	-0.10638	0.163183	-0.5180	-0.09583	0.1036
	NOBELZIN	Start of Administration	109	1.66406	0.408352	0.7511	1.65760	2.9267	-	-	-	-	-	-
		Week 4	108	1.61897	0.448308	0.6734	1.57990	3.0044	108	-0.04827	0.223854	-0.8547	-0.02590	0.4921
		Week 8	105	1.60198	0.442858	0.7511	1.55400	3.2375	105	-0.06899	0.217440	-0.7252	-0.07770	0.5698
		Week 12	104	1.57283	0.427431	0.7511	1.52810	3.1080	104	-0.09478	0.228419	-0.8029	-0.09065	0.4403
		Week 16	62	1.52451	0.447383	0.7252	1.45040	3.0303	62	-0.16576	0.226388	-0.7459	-0.14245	0.4040
		Week 20	30	1.61668	0.475239	0.7252	1.57990	2.8490	30	-0.15264	0.297132	-1.2691	-0.10360	0.2590
		Week 24	17	1.75907	0.547275	0.8806	1.73530	3.1080	17	-0.10421	0.304266	-0.8547	-0.05180	0.3626
		Discontinuation	11	1.31619	0.429006	0.7252	1.42450	2.0202	11	-0.27548	0.423886	-1.2691	-0.23310	0.3626

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Triglycerides (mmol/L)	NPC-25	Start of Administration	107	1.45707	1.219171	0.3164	1.19780	9.9101	-	-	-	-	-	-
		Week 4	104	1.43869	0.926028	0.3616	1.17520	7.2659	104	-0.02597	0.785550	-6.1246	0.02260	1.3334
		Week 8	100	1.45194	1.066229	0.3503	1.10740	6.6670	100	-0.02961	0.670455	-3.2431	0.00000	2.5877
		Week 12	99	1.46832	1.082732	0.3616	1.19780	8.0908	99	0.00742	0.974462	-3.9098	0.02260	6.1133
		Week 16	77	1.64554	1.536732	0.4294	1.14130	11.6390	77	0.20604	0.708789	-1.5255	0.09040	2.6329
		Week 20	67	1.63125	1.007769	0.4294	1.32210	5.5144	67	0.12261	0.952092	-4.3957	0.04520	2.2826
		Week 24	57	1.63553	1.346848	0.4520	1.22040	9.1982	57	0.10864	0.816241	-1.4803	0.09040	2.6781
		Week 28	53	1.43105	0.805910	0.5085	1.29950	4.4409	53	-0.13198	0.984158	-5.4692	-0.03390	1.8419
		Week 32	35	1.38280	0.642624	0.4746	1.26560	3.5934	35	-0.27185	1.223393	-6.3167	-0.13560	1.7289
		Week 36	31	1.46718	0.910461	0.5424	1.10740	4.4748	31	-0.19465	1.180244	-5.4353	-0.04520	1.6159
		Week 40	30	1.53680	0.893521	0.5537	1.37860	4.2714	30	-0.16347	1.800184	-8.1134	-0.11865	2.9945
		Week 44	30	1.52776	0.828957	0.4972	1.38425	3.8194	30	-0.17251	1.521417	-7.1868	-0.16950	2.3617
		Week 48	29	1.45731	0.586330	0.6554	1.25430	2.7120	29	-0.27666	1.559378	-7.8535	-0.07910	1.0170
		Week 52	28	1.44640	0.666633	0.5989	1.32775	3.1301	28	-0.22883	1.509143	-7.0625	0.05085	1.8532
		Discontinuation	14	1.47626	0.859596	0.5650	1.23735	4.0228	14	0.08717	0.916297	-1.4012	-0.09040	2.7459
	NOBELZIN	Start of Administration	109	1.26498	0.684026	0.3955	1.03960	4.3053	-	-	-	-	-	-
		Week 4	108	1.28464	0.815273	0.3390	1.10740	6.2037	108	0.01559	0.733718	-1.8306	-0.01130	4.7121
		Week 8	105	1.29380	0.739123	0.2938	1.08480	3.9663	105	0.01550	0.667968	-1.7967	0.00000	2.4747
		Week 12	104	1.35817	0.815258	0.3729	1.27690	5.9664	104	0.07693	0.806580	-2.2713	0.00000	4.5878
		Week 16	62	1.32228	0.731696	0.5198	1.09045	3.6386	62	0.11883	0.674914	-1.7628	0.06215	2.6216
		Week 20	30	1.33453	0.876965	0.2486	1.00570	3.0284	30	0.20792	0.751280	-1.0396	-0.05085	2.0453
		Week 24	17	1.24234	0.844448	0.3277	0.96050	3.4804	17	0.10968	0.472439	-0.5537	0.00000	0.9944
		Discontinuation	11	1.52961	0.729166	0.6667	1.59330	2.7233	11	0.37906	0.730340	-0.9040	0.38420	2.0453

表 2.7.4.7-2 血液生化学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Urea Nitrogen (mmol/L)	NPC-25	Start of Administration	107	6.09135	2.636135	2.4990	5.53350	19.5993	-	-	-	-	-	-
		Week 4	104	6.03364	2.852838	1.8921	5.44425	20.5275	104	-0.07037	1.173828	-3.2130	-0.12495	3.2130
		Week 8	100	5.95298	2.403052	2.1420	5.58705	17.5644	100	0.00286	1.322197	-3.9984	0.12495	3.5700
		Week 12	99	6.06648	2.502319	1.3566	5.42640	17.0646	99	0.12874	1.287534	-3.0702	0.00000	5.6763
		Week 16	77	5.96654	2.298516	2.2848	5.71200	17.3502	77	0.10525	1.490661	-3.9627	-0.10710	5.9619
		Week 20	67	5.86173	1.822886	2.2848	5.46210	10.7100	67	-0.04849	1.389464	-4.2840	-0.17850	2.8560
		Week 24	57	6.22370	1.854834	2.4990	6.31890	9.9960	57	0.26368	1.523563	-4.3197	0.14280	5.2479
		Week 28	53	5.59345	1.938144	2.8560	5.35500	13.3518	53	-0.26000	1.676196	-3.9627	-0.35700	5.4621
		Week 32	35	5.48964	1.461344	2.5704	5.17650	7.9968	35	-0.27540	1.264635	-4.1055	-0.17850	2.4990
		Week 36	31	5.43907	1.522416	3.2130	5.39070	9.4248	31	-0.29366	1.432773	-4.0698	-0.28560	3.6771
		Week 40	30	5.54421	2.126704	2.4633	5.12295	11.3526	30	-0.22372	1.556662	-2.6775	-0.39270	5.6049
		Week 44	30	5.44544	1.422905	3.2844	4.98015	7.8540	30	-0.32249	1.152568	-2.7489	-0.64260	2.0706
		Week 48	29	5.54335	1.445327	3.1059	5.46210	8.2110	29	-0.27329	1.312197	-3.8199	-0.10710	1.7850
		Week 52	28	5.48123	1.516849	2.8917	5.53350	8.2467	28	-0.30345	1.365945	-4.0341	-0.26775	1.8921
		Discontinuation	14	5.99250	3.777558	2.2848	5.44425	17.0646	14	-0.12240	1.194973	-1.4280	-0.35700	2.9988
	NOBELZIN	Start of Administration	109	5.76604	2.182077	2.1420	5.35500	13.1019	-	-	-	-	-	-
		Week 4	108	5.83530	2.344033	2.3562	5.14080	14.6013	108	0.04661	1.095993	-2.1420	0.00000	3.2130
		Week 8	105	5.70554	2.335916	2.4990	5.35500	17.8500	105	-0.02448	1.352269	-2.9631	-0.10710	7.4970
		Week 12	104	5.60318	2.243784	2.4990	5.01585	14.2800	104	-0.12014	1.248564	-3.5700	0.00000	4.7124
		Week 16	62	5.91699	2.260095	2.2491	5.64060	15.5295	62	-0.08580	1.222401	-3.2844	-0.08925	2.9631
		Week 20	30	5.37761	1.600882	3.3558	4.73025	9.6390	30	0.07735	0.926356	-1.7493	-0.05355	2.7846
		Week 24	17	5.16390	1.322945	3.8199	4.92660	8.9250	17	-0.34020	0.939809	-1.8921	-0.53550	1.8921
		Discontinuation	11	6.36434	3.499587	2.3562	5.35500	13.5660	11	0.58418	1.903468	-1.4994	0.32130	4.9980

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Creatinine (umol/L)	NPC-25	Start of Administration	107	72.5210	36.48059	34.476	63.6480	271.388	-	-	-	-	-	-
		Week 4	104	72.7855	38.05192	39.780	63.6480	289.068	104	0.0935	6.64605	-16.796	0.0000	17.680
		Week 8	100	69.8360	29.07836	36.244	64.0900	236.028	100	-0.0265	8.13840	-35.360	0.0000	22.984
		Week 12	99	72.0505	36.88632	39.780	64.5320	334.152	99	2.5448	9.31375	-17.680	1.7680	62.764
		Week 16	77	68.1139	26.87889	41.548	61.8800	227.188	77	1.2169	8.87835	-18.564	0.8840	31.824
		Week 20	67	67.6326	20.96696	38.012	64.5320	144.976	67	1.1347	8.70068	-15.912	0.8840	26.520
		Week 24	57	65.6021	17.70740	42.432	61.8800	115.804	57	-0.4498	7.81821	-21.216	0.0000	29.172
		Week 28	53	65.3493	18.42003	40.664	61.8800	119.340	53	-0.4337	8.48899	-17.680	0.0000	27.404
		Week 32	35	61.7032	15.55379	40.664	59.2280	94.588	35	-0.8082	5.99317	-12.376	0.0000	7.956
		Week 36	31	59.9979	13.87578	44.200	53.0400	90.168	31	-1.0836	6.23710	-16.796	-1.7680	12.376
		Week 40	30	59.5816	13.07191	39.780	57.0180	85.748	30	-1.5617	6.67883	-15.912	-0.8840	10.608
		Week 44	30	58.2261	13.56187	37.128	54.8080	88.400	30	-2.9172	6.12079	-14.144	-3.5360	7.072
		Week 48	29	60.5388	14.17676	39.780	56.5760	86.632	29	-1.0059	7.82771	-15.028	-2.6520	16.796
		Week 52	28	59.8594	13.23456	39.780	57.0180	89.284	28	-1.7049	8.17995	-17.680	-0.4420	11.492
		Discontinuation	14	76.7817	41.40068	34.476	59.6700	197.132	14	-0.6946	7.64528	-15.912	0.4420	14.144
	NOBELZIN	Start of Administration	109	66.4865	23.03842	38.012	60.1120	190.060	-	-	-	-	-	-
		Week 4	108	67.0530	24.80441	31.824	59.2280	196.248	108	0.3601	6.32058	-16.796	0.0000	26.520
		Week 8	105	67.1840	25.73663	31.824	60.1120	219.232	105	0.9429	7.69508	-8.840	0.0000	36.244
		Week 12	104	67.9575	25.87847	32.708	60.9960	205.972	104	1.8360	9.52471	-15.028	0.8840	60.996
		Week 16	62	71.1905	23.80793	38.012	64.0900	163.540	62	2.5950	8.86152	-13.260	1.3260	36.244
		Week 20	30	61.5559	14.75655	42.432	57.9020	99.892	30	0.7367	4.19853	-7.072	0.0000	9.724
		Week 24	17	57.8760	13.51580	37.128	58.3440	86.632	17	-0.0520	4.96607	-5.304	-1.7680	14.144
		Discontinuation	11	74.8185	32.94907	37.128	67.1840	160.004	11	7.8756	14.92602	-7.072	3.5360	45.968

表 2.7.4.7-2 血液生化学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Iron (umol/L)	NPC-25	Start of Administration	107	14.8520	7.03738	2.864	13.9620	39.738	-	-	-	-	-	-
		Week 4	104	14.7365	6.63041	2.327	14.5885	38.843	104	0.0499	6.07195	-23.986	0.0000	17.184
		Week 8	100	14.8409	6.84985	3.043	13.6040	44.213	100	0.0913	6.25931	-22.196	0.9845	14.320
		Week 12	99	14.8335	5.76621	2.864	14.1410	29.893	99	0.0452	6.86831	-19.332	-0.3580	22.733
		Week 16	77	14.1015	5.52590	3.401	13.4250	29.893	77	-0.7904	6.59284	-18.437	-0.5370	15.573
		Week 20	67	14.6379	6.68885	3.580	13.4250	39.380	67	-0.3847	7.21062	-12.530	-0.8950	29.893
		Week 24	57	13.9903	5.09564	4.296	14.3200	26.313	57	-1.4508	5.21889	-15.573	-0.7160	8.771
		Week 28	53	14.6273	5.42791	3.938	13.7830	29.177	53	-0.6012	6.04904	-13.067	0.1790	11.993
		Week 32	35	13.8751	5.21859	3.759	13.6040	27.029	35	-1.9332	5.75210	-15.036	-1.6110	10.024
		Week 36	31	13.7137	5.11695	3.759	12.1720	25.597	31	-2.0672	8.29433	-22.554	-0.1790	16.826
		Week 40	30	12.6195	4.74260	3.043	12.5300	25.597	30	-3.2339	7.63610	-23.807	-3.3115	8.592
		Week 44	30	13.4906	6.36802	2.327	12.6195	28.998	30	-2.3628	6.97940	-17.184	-2.4165	17.542
		Week 48	29	12.7275	4.90896	4.654	12.7090	21.659	29	-3.4442	7.81630	-23.270	-1.9690	10.561
		Week 52	28	13.7894	5.75765	3.043	13.3355	33.473	28	-2.1928	7.51099	-19.332	-0.5370	10.561
		Discontinuation	14	16.5831	10.57665	2.864	14.1410	39.380	14	1.8284	9.22586	-7.160	1.1635	29.893
	NOBELZIN	Start of Administration	109	15.5172	7.44670	1.790	15.0360	42.960	-	-	-	-	-	-
		Week 4	108	15.4255	8.85237	2.864	14.3200	63.545	108	-0.1077	8.23294	-23.807	-0.9845	56.922
		Week 8	105	15.6565	7.16994	2.148	14.4990	41.349	105	0.0358	6.67076	-15.573	-0.1790	19.511
		Week 12	104	16.1169	6.94797	2.327	15.1255	42.781	104	0.4475	7.07235	-21.659	0.0895	17.721
		Week 16	62	15.7433	7.42898	3.043	13.8725	39.380	62	-0.1588	7.05886	-13.783	-0.7160	29.356
		Week 20	30	17.2258	8.06887	4.475	17.3630	35.263	30	0.3759	8.29141	-21.838	1.8795	13.962
		Week 24	17	16.2258	8.84510	3.938	15.3940	29.893	17	-2.5797	9.15245	-24.523	-0.7160	10.740
		Discontinuation	11	12.8880	7.91860	6.265	10.0240	35.263	11	-1.0740	6.03896	-9.845	-1.6110	13.425

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Sodium (mmol/L)	NPC-25	Start of Administration	107	140.33	2.476	129.0	141.00	145.0	-	-	-	-	-	-
		Week 4	104	140.05	3.013	128.0	140.15	145.0	104	-0.32	2.333	-9.0	0.00	5.0
		Week 8	100	140.21	2.693	130.0	140.85	145.0	100	-0.16	2.275	-6.5	0.00	5.0
		Week 12	99	140.12	2.576	127.0	140.00	146.0	99	-0.26	2.018	-6.3	0.00	5.0
		Week 16	77	140.05	3.030	128.0	141.00	144.0	77	-0.31	2.177	-5.4	0.00	5.6
		Week 20	67	140.52	2.832	129.0	141.00	146.0	67	0.23	2.531	-10.0	0.10	7.0
		Week 24	57	140.38	2.826	125.0	140.50	145.0	57	-0.01	2.047	-5.7	0.00	6.0
		Week 28	53	140.91	2.174	131.0	141.00	145.0	53	0.41	2.167	-4.0	0.00	6.6
		Week 32	35	140.42	2.610	130.0	140.00	144.0	35	0.03	2.276	-4.0	0.00	7.0
		Week 36	31	141.03	2.716	132.0	142.00	145.0	31	0.88	1.682	-2.3	1.00	4.0
		Week 40	30	140.94	2.530	131.0	141.00	144.7	30	0.82	1.937	-3.0	1.00	5.0
		Week 44	30	141.20	3.073	131.0	142.00	146.0	30	1.08	1.893	-2.6	1.00	6.0
		Week 48	29	140.83	2.632	131.0	141.00	145.0	29	0.64	2.170	-3.0	1.00	5.0
		Week 52	28	140.60	3.349	128.0	141.00	145.0	28	0.51	1.985	-3.0	0.80	5.0
		Discontinuation	14	139.29	1.867	135.9	139.60	142.0	14	-0.91	1.849	-4.0	-0.60	2.0
	NOBELZIN	Start of Administration	109	140.21	2.566	126.0	140.00	146.6	-	-	-	-	-	-
		Week 4	108	140.16	2.847	122.0	140.00	146.0	108	-0.06	1.976	-6.0	0.00	5.0
		Week 8	105	139.93	2.985	123.0	140.00	146.0	105	-0.23	1.871	-5.0	0.00	4.0
		Week 12	104	140.11	2.926	123.0	140.00	147.0	104	-0.07	2.093	-5.0	0.00	4.0
		Week 16	62	140.22	2.855	125.0	140.10	145.0	62	0.21	1.765	-6.0	0.00	4.0
		Week 20	30	139.53	2.867	128.0	140.00	144.5	30	0.42	1.729	-3.0	0.90	3.0
		Week 24	17	138.43	3.669	125.0	140.00	141.0	17	-0.13	1.495	-3.0	0.00	2.0
		Discontinuation	11	140.53	2.300	137.0	141.00	144.5	11	0.04	2.039	-4.0	1.00	3.0

表 2.7.4.7-2 血液生化学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Potassium (mmol/L)	NPC-25	Start of Administration	107	4.18	0.442	3.4	4.10	5.6	-	-	-	-	-	-
		Week 4	104	4.17	0.407	2.6	4.20	5.4	104	-0.02	0.389	-1.2	0.00	1.0
		Week 8	100	4.16	0.461	3.0	4.10	5.9	100	-0.03	0.478	-1.3	0.00	1.3
		Week 12	99	4.12	0.367	3.1	4.10	5.4	99	-0.06	0.467	-1.3	-0.10	1.2
		Week 16	77	4.14	0.403	3.2	4.10	5.3	77	-0.05	0.531	-1.4	0.00	1.7
		Week 20	67	4.14	0.414	3.0	4.10	5.2	67	-0.07	0.434	-1.4	0.00	1.0
		Week 24	57	4.11	0.427	3.2	4.10	5.8	57	-0.18	0.485	-1.6	-0.10	1.0
		Week 28	53	4.16	0.391	3.4	4.10	5.4	53	-0.12	0.482	-1.5	0.00	1.2
		Week 32	35	4.07	0.374	3.5	4.00	4.8	35	-0.23	0.487	-1.8	-0.10	0.4
		Week 36	31	4.20	0.358	3.7	4.20	5.0	31	-0.10	0.494	-1.4	-0.10	1.2
		Week 40	30	4.20	0.353	3.6	4.10	5.2	30	-0.09	0.429	-1.4	0.00	0.6
		Week 44	30	4.10	0.474	3.4	4.00	5.3	30	-0.20	0.419	-1.3	-0.20	0.9
		Week 48	29	4.09	0.359	3.5	4.00	5.1	29	-0.19	0.396	-1.4	-0.20	0.8
		Week 52	28	4.13	0.391	3.3	4.10	5.2	28	-0.16	0.456	-1.4	-0.05	0.4
		Discontinuation	14	4.06	0.429	3.5	4.02	5.3	14	-0.08	0.360	-0.6	-0.10	0.7
	NOBELZIN	Start of Administration	109	4.16	0.417	3.1	4.20	5.1	-	-	-	-	-	-
		Week 4	108	4.18	0.422	3.0	4.20	5.8	108	0.02	0.366	-1.0	0.00	1.3
		Week 8	105	4.21	0.459	3.2	4.20	6.3	105	0.05	0.423	-1.1	0.10	1.8
		Week 12	104	4.16	0.433	3.1	4.10	5.7	104	0.00	0.398	-1.4	0.00	1.1
		Week 16	62	4.12	0.428	3.2	4.10	5.6	62	-0.01	0.320	-1.2	0.00	0.8
		Week 20	30	4.06	0.463	3.4	4.00	6.0	30	0.02	0.400	-0.7	0.00	1.2
		Week 24	17	4.05	0.490	3.3	4.00	5.5	17	-0.08	0.335	-0.6	-0.10	0.7
		Discontinuation	11	4.13	0.352	3.7	4.00	4.8	11	0.04	0.254	-0.3	0.00	0.6

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Chloride (mmol/L)	NPC-25	Start of Administration	107	104.07	2.765	96.0	104.00	110.0	-	-	-	-	-	-
		Week 4	104	104.15	3.257	92.0	104.60	110.3	104	0.06	2.313	-9.0	0.00	6.0
		Week 8	100	104.31	2.952	94.0	104.00	110.8	100	0.31	2.093	-7.4	0.00	6.0
		Week 12	99	104.39	2.958	95.1	104.40	112.0	99	0.40	2.252	-4.0	0.00	7.6
		Week 16	77	104.40	2.904	93.0	104.60	112.0	77	0.40	1.860	-3.0	0.00	6.0
		Week 20	67	104.02	3.103	96.0	104.10	111.0	67	0.17	2.629	-8.0	0.00	7.0
		Week 24	57	104.49	2.768	93.0	104.10	109.0	57	0.41	2.161	-6.0	0.00	7.0
		Week 28	53	104.45	2.243	99.0	104.00	108.3	53	0.29	2.047	-3.0	0.00	7.5
		Week 32	35	104.37	2.090	97.0	104.00	108.2	35	0.30	2.166	-4.0	0.00	7.0
		Week 36	31	104.23	2.485	99.0	104.00	110.0	31	0.42	1.810	-3.0	0.00	4.0
		Week 40	30	103.85	1.982	99.0	104.00	109.1	30	0.00	1.922	-5.0	0.00	4.0
		Week 44	30	104.52	2.780	98.0	105.00	109.7	30	0.68	2.032	-2.9	0.65	5.0
		Week 48	29	104.12	2.520	99.0	104.00	110.0	29	0.25	1.759	-3.0	0.00	4.0
		Week 52	28	104.52	2.715	97.0	105.00	110.0	28	0.76	2.513	-3.0	1.00	8.0
		Discontinuation	14	105.34	2.033	102.0	105.00	108.4	14	0.44	1.615	-2.0	1.00	3.7
	NOBELZIN	Start of Administration	109	104.37	2.740	93.0	105.00	112.0	-	-	-	-	-	-
		Week 4	108	104.29	2.833	92.0	104.65	111.0	108	-0.07	2.032	-6.3	0.00	5.0
		Week 8	105	104.40	2.911	93.0	105.00	112.0	105	0.04	2.191	-6.0	0.00	5.0
		Week 12	104	104.40	2.622	95.0	104.00	112.0	104	-0.01	2.104	-6.0	0.00	5.0
		Week 16	62	104.45	2.572	96.0	104.30	110.0	62	0.26	2.301	-7.0	0.00	6.0
		Week 20	30	104.26	2.704	98.0	104.00	110.0	30	0.38	2.283	-3.0	-0.15	6.0
		Week 24	17	103.64	3.512	94.0	104.00	107.0	17	0.12	2.258	-3.0	-0.90	4.0
		Discontinuation	11	104.49	1.765	101.8	105.00	107.6	11	0.48	2.076	-2.0	0.00	5.0

表 2.7.4.7-2 血液生化学的検査の要約統計量（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	Observed Value						Change From Baseline					
			n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Copper (ug/dL)	NPC-25	Start of Administration	107	113.5	21.30	77	110.0	189	-	-	-	-	-	-
		Week 4	104	109.1	22.88	58	104.0	186	104	-3.8	12.17	-36	-4.0	45
		Week 8	100	104.8	24.29	26	103.0	201	100	-7.2	16.36	-64	-7.0	60
		Week 12	99	102.6	22.86	28	101.0	169	99	-9.3	14.99	-62	-8.0	29
		Week 16	77	100.8	23.83	26	102.0	184	77	-11.6	17.20	-69	-9.0	31
		Week 20	67	100.7	24.40	22	96.0	184	67	-11.7	18.35	-83	-9.0	31
		Week 24	57	98.8	23.83	20	98.0	159	57	-12.3	19.18	-92	-11.0	20
		Week 28	53	101.6	23.34	40	99.0	173	53	-11.0	20.16	-96	-9.0	31
		Week 32	35	103.2	21.17	68	99.0	156	35	-9.6	15.16	-44	-7.0	13
		Week 36	31	105.5	16.44	82	103.0	132	31	-6.1	14.95	-38	-11.0	19
		Week 40	30	108.6	22.09	75	105.5	175	30	-3.5	17.67	-32	-4.0	37
		Week 44	30	110.9	22.06	69	110.0	180	30	-1.2	15.84	-32	0.0	27
		Week 48	29	108.4	21.62	65	106.0	162	29	-3.9	13.72	-32	-4.0	23
		Week 52	28	103.9	18.33	71	101.5	147	28	-8.6	10.59	-32	-7.5	11
		Discontinuation	14	111.8	39.43	22	119.0	176	14	-10.0	22.26	-68	-13.0	24
	NOBELZIN	Start of Administration	109	115.1	26.19	73	112.0	231	-	-	-	-	-	-
		Week 4	108	111.1	25.51	72	105.0	235	108	-4.0	13.98	-87	-2.0	30
		Week 8	105	109.2	25.65	65	107.0	213	105	-5.9	18.62	-106	-5.0	63
		Week 12	104	105.1	27.47	36	103.0	208	104	-9.9	22.20	-135	-7.0	87
		Week 16	62	102.9	22.20	45	101.0	170	62	-8.8	14.73	-47	-6.0	18
		Week 20	30	101.2	21.40	58	96.5	146	30	-10.9	20.96	-66	-7.5	23
		Week 24	17	100.9	28.75	39	95.0	151	17	-17.2	31.33	-85	-10.0	31
		Discontinuation	11	110.7	27.59	65	104.0	167	11	-2.3	20.24	-27	-1.0	32

Change From Baseline : Each visit - Start of Administration

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
Urine Protein	NPC-25	Week 4	104	(-)	72	9	1	0	0	0
				(+-)	5	2	1	1	0	0
				(1+)	1	1	3	1	0	0
				(2+)	0	0	1	2	3	0
				(3+)	0	0	0	1	0	0
				(4+)	0	0	0	0	0	0
		Week 8	100	(-)	69	9	2	1	0	0
				(+-)	4	1	1	0	0	0
				(1+)	3	2	3	2	2	0
				(2+)	0	0	0	1	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 12	99	(-)	71	7	3	0	0	0
				(+-)	4	3	2	1	0	0
				(1+)	1	2	1	0	1	0
				(2+)	0	0	0	3	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 16	77	(-)	49	5	1	0	0	0
				(+-)	10	1	2	0	0	0
				(1+)	1	2	2	0	0	0
				(2+)	1	0	0	2	1	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 20	67	(-)	45	5	0	0	0	0
				(+-)	6	0	2	0	0	0
				(1+)	3	1	3	0	0	0
				(2+)	0	0	0	1	1	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 24	57	(-)	40	4	0	0	0	0
				(+-)	5	0	1	0	0	0
				(1+)	2	0	3	0	1	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	1	0	0	0	0
		Week 28	53	(-)	36	3	1	0	0	0
				(+-)	7	0	1	0	0	0
				(1+)	1	1	2	0	0	0
				(2+)	0	0	0	0	1	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 32	35	(-)	29	1	1	0	0	0
				(+-)	2	0	0	0	0	0
				(1+)	0	1	0	0	1	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
		Week 36	31	(-)	25	1	1	0	0	0
				(+-)	2	0	0	0	0	0
				(1+)	1	1	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 40	30	(-)	23	2	1	0	0	0
				(+-)	3	0	0	0	0	0
				(1+)	1	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 44	30	(-)	23	2	0	0	0	0
				(+-)	3	0	0	0	0	0
				(1+)	1	0	1	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 48	29	(-)	23	1	1	0	0	0
				(+-)	4	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 52	28	(-)	23	2	1	0	0	0
				(+-)	1	0	0	0	0	0
				(1+)	1	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Discontinuation	14	(-)	10	0	0	0	0	0
				(+-)	1	0	0	0	0	0
				(1+)	0	0	0	1	2	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
	NOBELZIN	Week 4	108	(-)	76	8	3	0	0	0
				(+-)	9	3	0	1	0	0
				(1+)	2	1	2	0	0	0
				(2+)	1	0	0	2	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 8	105	(-)	81	8	3	0	0	0
				(+-)	6	2	1	0	0	0
				(1+)	0	0	1	1	0	0
				(2+)	0	1	0	1	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 12	104	(-)	76	5	3	0	0	0
				(+-)	7	6	1	1	0	0
				(1+)	3	0	1	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	1	0	0
				(4+)	0	0	0	0	0	0
		Week 16	62	(-)	46	4	0	0	0	0
				(+-)	5	1	1	0	0	0
				(1+)	1	2	0	1	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	1	0	0
				(4+)	0	0	0	0	0	0
		Week 20	30	(-)	26	0	0	0	0	0
				(+-)	3	1	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 24	17	(-)	16	0	0	0	0	0
				(+-)	1	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Discontinuation	11	(-)	6	2	0	0	0	0
				(+-)	2	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	1	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
Urine Glucose	NPC-25	Week 4	104	(-)	89	2	0	1	0	0
				(+-)	2	0	0	0	0	0
				(1+)	1	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	1
				(4+)	1	0	0	1	0	6
		Week 8	100	(-)	86	2	0	1	0	2
				(+-)	1	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	1	0	0
				(4+)	2	0	0	0	0	5
		Week 12	99	(-)	84	2	0	1	0	1
				(+-)	1	0	0	0	0	0
				(1+)	3	0	0	0	0	0
				(2+)	1	0	0	0	0	0
				(3+)	0	0	0	1	0	0
				(4+)	0	0	0	0	0	5
		Week 16	77	(-)	66	0	0	1	0	0
				(+-)	1	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	1	0	0	0	0	0
				(4+)	2	0	0	0	0	6
		Week 20	67	(-)	56	0	0	0	0	1
				(+-)	1	0	0	0	0	0
				(1+)	1	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	1	0	0	1	0	0
				(4+)	2	0	0	0	0	4
		Week 24	57	(-)	48	0	0	0	0	0
				(+-)	2	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	1	0	0	1	0	1
				(4+)	1	0	0	0	0	3
		Week 28	53	(-)	46	0	0	0	0	1
				(+-)	0	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	1	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	2	0	0	0	0	3
		Week 32	35	(-)	30	0	0	0	0	1
				(+-)	0	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	3	0	0	0	0	1

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
		Week 36	31	(-)	26	0	0	0	0	1
				(+-)	1	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	1	0	0	0	0	0
				(4+)	1	0	0	0	0	1
		Week 40	30	(-)	27	0	0	0	0	0
				(+-)	0	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	1	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	1	0	0	0	0	1
		Week 44	30	(-)	27	0	0	0	0	0
				(+-)	0	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	2	0	0	0	0	1
		Week 48	29	(-)	27	0	0	0	0	0
				(+-)	0	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	1	0	0	0	0	1
		Week 52	28	(-)	25	0	0	0	0	0
				(+-)	0	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	2	0	0	0	0	1
		Discontinuation	14	(-)	10	0	0	0	0	1
				(+-)	0	0	0	0	0	0
				(1+)	1	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	2	0	0	0	0	0

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
	NOBELZIN	Week 4	108	(-)	94	2	1	2	0	0
				(+-)	0	0	0	0	0	0
				(1+)	2	0	0	0	0	0
				(2+)	1	0	0	0	0	0
				(3+)	0	1	0	0	0	0
				(4+)	0	0	1	0	1	3
		Week 8	105	(-)	94	2	1	1	0	0
				(+-)	0	0	0	0	0	0
				(1+)	0	1	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	1	0	1	0	1	3
		Week 12	104	(-)	94	3	1	1	0	0
				(+-)	0	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	1	0	1	3
		Week 16	62	(-)	56	0	0	1	0	0
				(+-)	0	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	1	0
				(4+)	0	0	1	0	0	3
		Week 20	30	(-)	25	0	0	1	0	0
				(+-)	0	0	0	0	0	0
				(1+)	1	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	1	2
		Week 24	17	(-)	16	0	0	0	0	0
				(+-)	0	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	1	0
		Discontinuation	11	(-)	10	0	0	1	0	0
				(+-)	0	0	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
Urobilinogen	NPC-25	Week 4	104	(-)	8	0	0	0	0	0
				(+-)	4	83	4	1	0	0
				(1+)	0	1	1	0	0	0
				(2+)	0	0	0	1	0	1
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 8	100	(-)	4	0	0	0	0	0
				(+-)	7	76	4	1	0	1
				(1+)	0	4	1	0	0	0
				(2+)	1	0	0	1	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 12	99	(-)	5	0	0	0	0	0
				(+-)	7	77	5	1	0	0
				(1+)	0	2	0	0	0	0
				(2+)	0	0	0	1	0	1
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 16	77	(-)	3	0	0	0	0	0
				(+-)	3	62	3	0	0	0
				(1+)	0	3	2	0	0	0
				(2+)	0	0	0	1	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 20	67	(-)	3	0	1	0	0	0
				(+-)	3	54	4	0	0	0
				(1+)	0	0	0	0	0	1
				(2+)	0	0	0	1	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 24	57	(-)	2	0	0	0	0	0
				(+-)	3	46	3	0	0	0
				(1+)	0	2	0	0	0	0
				(2+)	0	0	0	0	0	1
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 28	53	(-)	2	0	0	0	0	0
				(+-)	3	43	3	0	0	0
				(1+)	0	2	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 32	35	(-)	2	0	0	0	0	0
				(+-)	3	28	2	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
		Week 36	31	(-)	1	0	0	0	0	0
				(+-)	2	27	1	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 40	30	(-)	1	0	0	0	0	0
				(+-)	2	26	1	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 44	30	(-)	1	0	0	0	0	0
				(+-)	2	26	1	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 48	29	(-)	0	0	0	0	0	0
				(+-)	2	25	1	0	0	0
				(1+)	1	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 52	28	(-)	1	0	0	0	0	0
				(+-)	2	24	1	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Discontinuation	14	(-)	0	0	0	0	0	0
				(+-)	1	11	2	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
	NOBELZIN	Week 4	108	(-)	9	0	0	0	0	0
				(+-)	6	79	7	0	0	0
				(1+)	1	1	1	0	1	0
				(2+)	0	0	0	1	1	0
				(3+)	0	1	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 8	105	(-)	7	0	0	1	0	0
				(+-)	6	76	8	0	0	0
				(1+)	1	3	0	0	0	0
				(2+)	1	0	0	0	2	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 12	104	(-)	6	0	0	0	0	0
				(+-)	7	75	6	0	0	0
				(1+)	1	3	2	1	1	0
				(2+)	1	0	0	0	1	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 16	62	(-)	3	0	0	0	0	0
				(+-)	6	43	4	0	0	0
				(1+)	0	3	0	0	1	0
				(2+)	0	0	1	1	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 20	30	(-)	1	0	0	0	0	0
				(+-)	2	24	2	0	0	0
				(1+)	0	1	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 24	17	(-)	1	0	0	0	0	0
				(+-)	0	13	1	0	0	0
				(1+)	1	0	1	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Discontinuation	11	(-)	1	0	0	0	0	0
				(+-)	1	9	0	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
Occult Blood	NPC-25	Week 4	104	(-)	64	2	4	0	1	0
				(+-)	7	3	5	1	0	0
				(1+)	2	1	4	1	0	0
				(2+)	1	1	1	2	0	0
				(3+)	1	0	2	0	1	0
				(4+)	0	0	0	0	0	0
		Week 8	100	(-)	58	1	3	0	1	0
				(+-)	8	3	4	1	0	0
				(1+)	4	2	7	3	0	0
				(2+)	2	1	2	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 12	99	(-)	61	2	2	0	1	0
				(+-)	6	3	9	1	0	0
				(1+)	3	1	2	1	0	0
				(2+)	2	1	2	2	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 16	77	(-)	46	2	1	0	0	0
				(+-)	3	3	7	0	0	0
				(1+)	4	0	2	0	0	0
				(2+)	1	1	1	2	0	0
				(3+)	1	0	3	0	0	0
				(4+)	0	0	0	0	0	0
		Week 20	67	(-)	37	4	4	0	0	0
				(+-)	6	0	5	0	0	0
				(1+)	3	0	2	2	0	0
				(2+)	1	2	0	0	0	0
				(3+)	1	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 24	57	(-)	35	2	0	0	0	0
				(+-)	2	1	7	0	0	0
				(1+)	3	1	2	1	0	0
				(2+)	1	0	1	0	0	0
				(3+)	1	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 28	53	(-)	33	2	3	0	0	0
				(+-)	4	1	4	0	0	0
				(1+)	1	0	2	0	0	0
				(2+)	1	1	0	0	0	0
				(3+)	1	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 32	35	(-)	22	1	0	0	0	0
				(+-)	4	0	4	0	0	0
				(1+)	3	0	1	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
		Week 36	31	(-)	21	0	2	0	0	0
				(+-)	2	0	2	0	0	0
				(1+)	0	1	0	0	0	0
				(2+)	1	0	0	0	0	0
				(3+)	2	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 40	30	(-)	21	1	1	0	0	0
				(+-)	1	0	2	0	0	0
				(1+)	1	0	0	0	0	0
				(2+)	1	0	1	0	0	0
				(3+)	1	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 44	30	(-)	22	0	1	0	0	0
				(+-)	2	0	3	0	0	0
				(1+)	0	0	0	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	1	1	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 48	29	(-)	19	0	0	0	0	0
				(+-)	3	0	3	0	0	0
				(1+)	0	1	1	0	0	0
				(2+)	1	0	0	0	0	0
				(3+)	1	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 52	28	(-)	22	0	1	0	0	0
				(+-)	0	0	2	0	0	0
				(1+)	0	1	0	0	0	0
				(2+)	0	0	1	0	0	0
				(3+)	1	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Discontinuation	14	(-)	6	0	0	0	0	0
				(+-)	2	0	1	0	0	0
				(1+)	1	0	2	0	0	0
				(2+)	0	0	0	0	0	0
				(3+)	1	0	0	0	1	0
				(4+)	0	0	0	0	0	0

表 2.7.4.7-3 尿検査値の推移（シフトテーブル）（SP）（NPC-25-3 試験）（続き）

Parameter	Group	Visit	n		Start of Administration					
					(-)	(+-)	(1+)	(2+)	(3+)	(4+)
	NOBELZIN	Week 4	108	(-)	67	9	2	0	0	0
				(+-)	4	3	2	0	0	0
				(1+)	4	1	3	2	0	0
				(2+)	1	0	2	4	1	0
				(3+)	2	0	0	1	0	0
				(4+)	0	0	0	0	0	0
		Week 8	105	(-)	69	7	4	0	0	0
				(+-)	5	3	2	0	0	0
				(1+)	1	2	1	3	1	0
				(2+)	2	0	1	4	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 12	104	(-)	66	7	3	1	0	0
				(+-)	5	1	1	2	0	0
				(1+)	2	3	3	2	0	0
				(2+)	1	0	0	2	0	0
				(3+)	3	1	0	0	1	0
				(4+)	0	0	0	0	0	0
		Week 16	62	(-)	41	4	3	1	0	0
				(+-)	3	1	2	0	0	0
				(1+)	0	0	0	1	0	0
				(2+)	1	0	1	3	0	0
				(3+)	0	0	0	0	1	0
				(4+)	0	0	0	0	0	0
		Week 20	30	(-)	21	1	1	1	0	0
				(+-)	2	0	0	0	0	0
				(1+)	0	0	2	0	0	0
				(2+)	0	0	0	2	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0
		Week 24	17	(-)	14	0	0	0	0	0
				(+-)	0	0	0	0	0	0
				(1+)	0	0	1	0	0	0
				(2+)	0	0	0	1	0	0
				(3+)	0	0	0	1	0	0
				(4+)	0	0	0	0	0	0
		Discontinuation	11	(-)	5	0	2	0	0	0
				(+-)	0	1	0	1	0	0
				(1+)	0	0	0	1	0	0
				(2+)	0	0	0	1	0	0
				(3+)	0	0	0	0	0	0
				(4+)	0	0	0	0	0	0

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2.7.5 参考文献

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	2	平成 17 年 7 月 1 日食安新発第 0701002 号「日本人の食事摂取基準（2005 年版）」の策定に伴う「保健機能食品制度の創設等に伴う取扱い及び改正等について」等の改正について	5.4.1-2
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	9	Spencer H, et al. Metabolic balances of cadmium, copper, manganese, and zinc in man. Am J Clin Nutr, 1979; 32 : 1867-75	5.4.1-9
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	13	Lykken GI, et al. Effect of browned and unbrowned corn products intrinsically labeled with ^{65}Zn on absorption of ^{65}Zn in humans. J Nutr, 1986; 116 : 795-801	5.4.1-13
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	16	Plum LM, et al. The Essential Toxin: Impact of Zinc on Human Health. Int J Environ Res Public Health 2010; 7:1342-65.	5.4.1-16

項番号	No.	文献／書籍名	添付資料番号
	17	Cohen NL, et al. The effect of copper supplementation on the teratogenic effects of triethylenetetramine in rats. Drug Nutr Interact. 1983; 2(3):203-10.	5.4.1-17
	18	Keen CL, et al. Teratogenic effects of D-penicillamine in rats: relation to copper deficiency. Drug Nutr Interact 1983; 2(1):17-34.	5.4.1-18
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2.7.2	1	社内資料：「NPC-02(酢酸亜鉛)の健康成人男性を対象とした食事の影響検討試験 (治験実施計画書番号:NPC-02-8)」	5.4.3-1
	2	一般社団法人 日本臨床栄養学会編. 亜鉛欠乏症の診療指針 2018.	5.4.1-1
	3	Pécoud A, et al. Effect of foodstuffs on the absorption of zinc sulfate. Clin Pharmacol Ther, 1975; 17 : 469-74	5.4.1-7
	4	Walravens PA, et al. Growth of infants fed a zinc supplemented formula. Am J Clin Nutr, 1976; 29 : 1114-21	5.4.1-8
	5	Spencer H, et al. Metabolic balances of cadmium, copper, manganese, and zinc in man. Am J Clin Nutr, 1979; 32 : 1867-75	5.4.1-9
	6	Spencer H, et al. Further studies of the effect of zinc on intestinal absorption of calcium in man. J Am Coll Nutr, 1992; 11 : 561-6	5.4.1-10
	7	Harzer G, et al. Binding of zinc to casein. Am J Clin Nutr, 1982; 35 : 981-7	5.4.1-11
	8	Flanagan PR, et al. Dual-isotope method for determination of human zinc absorption : the use of a test meal of turkey meat. J Nutr, 1985; 115 : 111-22	5.4.1-12
	9	Lykken GI, et al. Effect of browned and unbrowned corn products intrinsically labeled with ^{65}Zn on absorption of ^{65}Zn in humans. J Nutr, 1986; 116 : 795-801	5.4.1-13
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	3	一般社団法人 日本臨床栄養学会編. 亜鉛欠乏症の診療指針 2018.	5.4.1-1

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略語・略号一覧

略語･略号	内容
AUC_t	Area under the blood concentration time curve from 0 to t hours：0から投与t時間後までの血清中薬物濃度－時間曲線下面積
AUC_{0-24}	Area under the blood concentration time curve from 0 to 24 hours：0から投与24時間後までの血清中薬物濃度－時間曲線下面積
AUC_∞	Area under the blood concentration time curve from 0 to infinity：無限大時間までの血清中薬物濃度－時間曲線下面積
C_{max}	Maximum drug concentration：最高血中濃度
C_{trough}	Trough concentration：投与直前の血中濃度(投与1日目のC_{trough}は投与2日目投与直前の濃度、投与14日目のC_{trough}は投与15日目(投与14日目投与後 24時間)の濃度)
FAS	Full analysis set：最大解析対象集団
k_{el}	Elimination rate constant：消失速度定数
MedDRA	Medical Dictionary for Regulatory Activities：ICH国際医薬用語集
MedDRA/J	Medical Dictionary for Regulatory Activities /Japanese version：ICH国際医薬用語集日本語版
MRT_t	Mean residence time from 0 to t hours：0から投与t時間後までの血清濃度を用いた平均滞留時間
MRT_∞	Mean residence time from 0 to infinity：無限大時間までの平均滞留時間
PPS	Per protocol set：実施計画書適合解析対象集団
PT	Preferred Terms：MedDRA又はMedDRA/Jにおける基本語
SD	Standard deviation：標準偏差
SOC	System Organ Class：MedDRA又はMedDRA/Jにおける器官別大分類
SP	Safety Population：安全性解析対象集団
$t_{1/2}$	Elimination half life：生物学的半減期
t_{max}	Time to maximum drug concentration：最高血中濃度到達時間

2.7.6 個々の試験のまとめ

治験実施計画書番号	試験の種類（評価/参考）	試験の主な目的	対象	試験デザイン	治験薬、投与方法、投与経路	投与期間	登録被験者数（例）	試験の進行状況添付資料番号
NPC-25-1	臨床薬理試験（評価）	NPC-24 及び NPC-25 の単回投与時の薬物動態及び安全性の確認	健康成人男性	Step 1： 非盲検　無作為化 3 剤 3 期のクロスオーバー法 Step 2： 非盲検　無作為化 絶食・食後の 2 期クロスオーバー法 Step 3： 非盲検　食後の漸増投与	Step 1： NPC-24 カプセル、NPC-25 カプセル、ノベルジン錠 いずれも 25 mg/日、1 日 1 回、空腹時、経口投与 Step 2： NPC-24 カプセル、NPC-25 カプセル いずれも 25 mg/日、1 日 1 回、空腹時又は食後（高カロリー高脂肪食）、経口投与 Step 3： NPC-24 カプセル、NPC-25 カプセル いずれも 50 mg/日、100 mg/日、150 mg/日、1 日 1 回、食後（高カロリー高脂肪食）、経口投与	単回投与	計 57 Step1:9 Step2:24（各製剤:12） Step3:24（各製剤:12）	完了 ＜5.3.3.1-1＞
NPC-25-2	臨床薬理試験（評価）	NPC-25 の反復投与時の薬物動態及び安全性の確認	健康成人男性	無作為化、非盲検試験	NPC-25 カプセル ・50 mg/日、1 日 1 回　・100 mg/日、1 日 1 回 ・50 mg/日、1 日 2 回　・100 mg/日、1 日 2 回 ノベルジン錠 ・50 mg/日、1 日 2 回　・100 mg/日、1 日 2 回 いずれも食後、経口投与	14 日間	計 48 （各群:8）	完了 ＜5.3.3.1-2＞
NPC-25-3	第Ⅲ相試験（評価）	NPC-25 の有効性の非劣性の検証及び安全性の検討、長期投与時の安全性及び有効性の確認	低亜鉛血症患者	非盲検、無作為化、実薬対照試験	NPC-25 錠 開始時用量：50 mg/日又は 100 mg/日 その後の用量：目標血清亜鉛濃度到達まで増量又は減量する。最大投与量は 150 mg/日。 1 日 1 回、食後、経口投与 ノベルジン錠 開始時用量：50 mg/日又は 100 mg/日 その後の用量：目標血清亜鉛濃度到達まで増量又は減量する。最大投与量は 150 mg/日。 1 日 1～3 回、食後、経口投与	12 週間から最大 52 週間	計 216 NPC-25 107 ノベルジン 109	完了 ＜5.3.5.1-2＞
NPC-25-4	生物学的同等性試験（評価）	NPC-25 錠と NPC-25 カプセルの生物学的同等性の検討	健康成人男性	非盲検、無作為化、2 剤 2 期クロスオーバー	NPC-25 錠 50 mg/日、1 日 1 回 、空腹時、経口投与 NPC-25 カプセル 50 mg/日、1 日 1 回 、空腹時、経口投与	単回投与	36	完了 ＜5.3.1.2-1＞

※治験薬の投与量は亜鉛量で表記した。