略語・略号一覧

略語･略号	内容
Al-P	Alkaline phosphatase：アルカリホスファターゼ
ALT	Alanine aminotransferase：アラニンアミノトランスフェラーゼ
AST	Aspartate aminotransferase：アスパラギン酸アミノトランスフェラーゼ
BUN	Blood urea nitrogen：血中尿素窒素
Cl	Chlorine：塩素
Cu	Copper：銅
Fe	Ferrum(iron)：鉄
γ-GTP	Gamma glutamyl transpeptidase：γ-グルタミルトランスペプチダーゼ
Hb	Hemoglobin：ヘモグロビン
Ht	Hematocrit：ヘマトクリット
HDL	High density lipoprotein：高密度リポ蛋白質
K	Potassium：カリウム
Na	Sodium：ナトリウム
MCHC	Mean corpuscular hemoglobin concentration：平均赤血球ヘモグロビン濃度
MCV	Mean corpuscular volume：平均赤血球容積
MedDRA	Medical Dictionary for Regulatory Activities：ICH 国際医薬用語集
Plt	Platelet count：血小板数
PT	Preferred Terms：MedDRA における基本語
RBC	Red blood cell：赤血球
SOC	System Organ Class：MedDRA における器官別大分類
SP	Safety Population：安全性解析対象集団
WBC	White blood cell：白血球

2.7.4 臨床的安全性

2.7.4.1 医薬品への曝露

2.7.4.1.1 総括的安全性評価計画及び安全性試験の記述

低亜鉛血症に対する NPC-25 錠（以下、「本剤」）の安全性を評価した試験は、NPC-25-3 試験（非劣性試験）の 1 試験である（表 2.7.4.1-1）。NPC-25-3 試験に組み入れた全 216 例（NPC-25 群 107 例、ノベルジン錠群 109 例）を安全性解析対象集団（SP）とした。本項では、治験薬の投与量は亜鉛量で表記した。

表 2.7.4.1-1 安全性を評価した臨床試験の一覧

治験実施計画書番号（開発の相）	実施時期	対象	デザイン／投与期間／投与量	症例数	主な安全性評価項目	添付資料番号
NPC-25-3（第Ⅲ相）	2022/1～2023/4	低亜鉛血症	非盲検・無作為化・実薬対照試験／12 週間から最大 52 週間／開始用量：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	216	・有害事象及び副作用 ・臨床検査 ・バイタルサイン	評価資料 ＜5.3.5.1-2＞

なお、上記以外の健康成人男性を対象とした臨床試験における安全性データは、「2.7.6　個々の試験のまとめ」に記載した。

2.7.4.1.1.1 有害事象の定義

有害事象とは、治験薬投与開始から治験薬投与終了時までに生じた、あらゆる好ましくない、あるいは意図しない医療上の徴候（臨床検査値の異常変動を含む）、症状又は疾患とし、当該治験薬との因果関係の有無は問わないとした。

a) 自覚症状、他覚所見の発現又は悪化

ⅰ）治験薬投与開始前に認められず、新たに出現した症状、所見、疾患等

ⅱ）治験薬投与開始前から認められたが、悪化した症状、所見、疾患等

b) 一般臨床検査値における異常変動

治験実施計画書で規定した一般臨床検査項目一覧を表 2.7.4.1-2 に示した。

基準値を外れた場合を異常値とし、異常変動の定義を以下のとおりとした。

ⅰ）治験薬投与前に基準値内であったが、投与開始後、基準値から逸脱となった場合

ⅱ）治験薬投与開始直前値に比べ基準値逸脱が悪化した場合

上記の定義にあてはまるもののうち、臨床上意義のないものを除き異常変動として取り扱い、有害事象とした。ただし、変動が基準値内であっても、治験責任（分担）医師が異常変動と判定したものについては有害事象とした。

c) 体重、体温、血圧及び脈拍における異常変動

治験薬投与前の値との推移から治験責任（分担）医師が異常変動の有無の判定を行い、異常変動と判定した場合は有害事象とした。

表 2.7.4.1-2 一般臨床検査

血液学的検査	WBC、RBC、Hb、Plt、Ht、MCV、MCHC、網状赤血球数
血液生化学的検査	AST、ALT、Al-P、γ-GTP、総蛋白、アルブミン、総ビリルビン、リパーゼ、アミラーゼ、総コレステロール、HDL-コレステロール、トリグリセリド、BUN、クレアチニン、Fe、Na、K、Cl、Cu
尿定性検査	蛋白、糖、ウロビリノーゲン、潜血

2.7.4.1.1.2 有害事象の重症度

重症度の判定は、「医薬品等の副作用の重篤度分類基準について」（平成 4 年 6 月 29 日薬安第 80 号厚生省薬務局安全課長通知）を参考として判定した。

なお、本通知で規定する「グレード 1」は「軽度」、「グレード 2」は「中等度」、「グレード 3」は「重度」の目安とした。当該通知より重症度を判定することが困難な場合は、以下の基準を参考として判定した。

軽　度：症状が軽く容易に治癒する程度
中等度：重度ではないが、軽度ではないもの
重　度：日常生活に重度の支障をきたす程度

2.7.4.1.1.3 重篤な有害事象の定義

治験薬投与開始後に認められた有害事象のうち、以下を重篤な有害事象とした。

ⅰ）　死亡
ⅱ）　死亡につながるおそれのある事象
ⅲ）　治療のために病院又は診療所への入院又は入院期間の延長が必要とされる事象
ⅳ）　障害
ⅴ）　障害につながるおそれのある事象
ⅵ）　i）から v）までに掲げる症例に準じて重篤である事象
ⅶ）　後世代における先天性の疾病又は異常

2.7.4.1.1.4 治験薬との因果関係

因果関係は以下の基準を参考として判定し、『関連あり』の有害事象を『副作用』とした。

関連なし：治験薬投与後、発現した事象と関連づけられる時間経過がない、あるいは発現時の疾病、他の医薬品もしくは環境因子等に起因していると考えられるもの
関連あり：『関連なし』以外の事象

2.7.4.1.2 全般的な曝露状況

NPC-25-3 試験は、体重 30 kg 以上の低亜鉛血症患者を対象とし、非盲検、無作為化、実薬対照試験として実施した。用法・用量の概略を表 2.7.4.1-3 に示した。本剤及びノベルジン錠群はいずれも食後投与とし、本剤群は 1 日 1 回投与、ノベルジン錠群は承認されている用法に基づき開始用法を 1 日 2 回投与とした。開始用量及び最大投与量については、本剤及びノベルジン錠群の 1 日あたりの亜鉛としての投与量は同量とした。

表 2.7.4.1-3 用法・用量の概略（NPC-25-3 試験）

NPC-25 群	ノベルジン錠群
食後に服薬する。 [開始用量] 血清亜鉛濃度に応じて以下のとおりとする。 ・50 μg/dL 以上 70 μg/dL 未満：50 mg/日 ・50 μg/dL 未満：100 mg/日 （いずれも 1 日 1 回） [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）	食後に服薬する。 [開始用量] 血清亜鉛濃度に応じて以下のとおりとする。 ・50 μg/dL 以上 70 μg/dL 未満：50 mg/日 ・50 μg/dL 未満：100 mg/日 （いずれも 1 日 2 回） [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 3 回）

投与期間は、投与量の変更なく目標血清亜鉛濃度（80 μg/dL 以上 200 μg/dL 未満）に 8 週間維持されるまでの期間とし、最大 24 週間までとした。ただし、本剤群で継続投与が必要な患者には最大 52 週間まで投与できることとした。このため、本剤群とノベルジン錠群の比較についてはノベルジン錠群と同様の期間で比較することとした。すなわち、被験者ごとに治験薬投与開始後から主要評価項目達成時点（同一投与量で目標血清亜鉛濃度を 8 週間維持できた時点）又は主要評価項目未達例では最大 24 週時点までを「有効性評価期」と定義して、全期間ではなく有効性評価期における有害事象及び副作用を 2.7.4.2.1.1.5 項で本剤群とノベルジン錠群で比較をした。その他の項では、特に記載がない限りは、全期間における有害事象及び副作用について記載した。投与量及び投与期間の詳細は、＜2.7.6.3＞に記述した。

観察時点ごとの服薬率を表 2.7.4.1-4 に、観察時点ごとの投与量別被験者の割合を表 2.7.4.1-5 に示した。治験薬が投与された被験者数は、本剤群 107 例、ノベルジン錠群 109 例であった。本剤群の平均服薬日数は 194.2 日であった。また有効性評価期での平均服薬日数は本剤群 102.3 日、ノベルジン錠群 112.4 日であった。ノベルジン錠群に比べて本剤群の平均服用日数は少ない傾向があったが、本剤群でより早期に主要評価項目を達成する傾向が認められた（2.7.3.2.2.2.5 項）ためと考えられた。全期間での平均服薬率は、本剤群 97.87%、ノベルジン錠群 97.30%であった。観察時点別の平均服薬率は、いずれの投与群においても特別に低い時点はなかった。服薬コンプライアンスはいずれの投与群でも良好であった。

表 2.7.4.1-4 観察時点ごとの服薬率(SP)（NPC-25-3 試験）

Visit	Compliance (%)	NPC-25 N = 107	NOBELZIN N = 109
Overall	n	107	109
	Means	97.87	97.30
	SD	5.751	4.477
	Min	50.0	75.0
	Median	99.80	99.10
	Max	100.0	100.0
Start of Administration to Week 4	n	107	109
	Means	98.29	96.83
	SD	4.277	7.836
	Min	73.5	48.0
	Median	100.00	100.00
	Max	100.0	100.0
Week 4 to Week 8	n	101	106
	Means	97.66	98.45
	SD	10.699	4.056
	Min	0.0	76.5
	Median	100.00	100.00
	Max	100.0	100.0
Week 8 to Week 12	n	99	104
	Means	98.60	97.07
	SD	2.920	6.236
	Min	85.7	51.1
	Median	100.00	98.20
	Max	100.0	100.0
Week 12 to Week 16	n	78	62
	Means	98.58	97.13
	SD	3.360	5.459
	Min	85.7	69.0
	Median	100.00	98.20
	Max	100.0	100.0
Week 16 to Week 20	n	67	32
	Means	97.46	96.74
	SD	8.127	5.510
	Min	42.9	72.6
	Median	100.00	98.15
	Max	100.0	100.0
Week 20 to Week 24	n	57	17
	Means	99.25	94.64
	SD	1.783	8.088
	Min	92.9	67.9
	Median	100.00	97.60
	Max	100.0	100.0

表 2.7.4.1-4 観察時点ごとの服薬率(SP)（NPC-25-3 試験）（続き）

Visit	Compliance (%)	NPC-25 N = 107	NOBELZIN N = 109
Week 24 to Week 28	n	53	-
	Means	98.54	-
	SD	2.675	-
	Min	87.5	-
	Median	100.00	-
	Max	100.0	-
Week 28 to Week 32	n	35	-
	Means	98.78	-
	SD	3.460	-
	Min	85.7	-
	Median	100.00	-
	Max	100.0	-
Week 32 to Week 36	n	31	-
	Means	97.59	-
	SD	4.231	-
	Min	81.0	-
	Median	100.00	-
	Max	100.0	-
Week 36 to Week 40	n	30	-
	Means	97.69	-
	SD	6.972	-
	Min	62.9	-
	Median	100.00	-
	Max	100.0	-
Week 40 to Week 44	n	30	-
	Means	96.71	-
	SD	12.606	-
	Min	31.3	-
	Median	100.00	-
	Max	100.0	-
Week 44 to Week 48	n	30	-
	Means	98.56	-
	SD	5.203	-
	Min	72.5	-
	Median	100.00	-
	Max	100.0	-
Week 48 to Week 52	n	27	-
	Means	98.72	-
	SD	3.883	-
	Min	81.3	-
	Median	100.00	-
	Max	100.0	-

Compliance (%) = Actual Number of Medications Taken Tablets / Scheduled Number of Medication Tablets * 100

Scheduled Number of Medication Tablets were calculated for each visit as follows. If patients with unscheduled visits, the sum of the following calculated values during the corresponding visit were treated as the Scheduled Number of Medication Tablets:
(Last Date of Administration - Start Date of Administration) * Prescription Dose (per day) / 25.

表 2.7.4.1-5 観察時点ごとの投与量別被験者の割合(SP)（NPC-25-3 試験）

Group	Visit	N	Dose					
			25 mg/day	50 mg/day	75 mg/day	100 mg/day	125 mg/day	150 mg/day
			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
NPC-25	Start of Administration to Week 4	107	1(0.9)	102(95.3)	1(0.9)	3(2.8)	0(0.0)	0(0.0)
	Week 4 to Week 8	101	2(2.0)	60(59.4)	1(1.0)	36(35.6)	0(0.0)	2(2.0)
	Week 8 to Week 12	99	1(1.0)	51(51.5)	4(4.0)	36(36.4)	1(1.0)	6(6.1)
	Week 12 to Week 16	78	0(0.0)	29(37.2)	4(5.1)	37(47.4)	0(0.0)	8(10.3)
	Week 16 to Week 20	67	0(0.0)	25(37.3)	5(7.5)	28(41.8)	0(0.0)	9(13.4)
	Week 20 to Week 24	57	0(0.0)	23(40.4)	3(5.3)	22(38.6)	0(0.0)	9(15.8)
	Week 24 to Week 28	53	0(0.0)	21(39.6)	3(5.7)	22(41.5)	1(1.9)	6(11.3)
	Week 28 to Week 32	35	0(0.0)	16(45.7)	1(2.9)	13(37.1)	0(0.0)	5(14.3)
	Week 32 to Week 36	31	0(0.0)	12(38.7)	1(3.2)	13(41.9)	1(3.2)	4(12.9)
	Week 36 to Week 40	30	0(0.0)	12(40.0)	1(3.3)	12(40.0)	1(3.3)	4(13.3)
	Week 40 to Week 44	30	0(0.0)	12(40.0)	1(3.3)	13(43.3)	0(0.0)	4(13.3)
	Week 44 to Week 48	30	0(0.0)	12(40.0)	1(3.3)	12(40.0)	0(0.0)	5(16.7)
	Week 48 to Week 52	27	0(0.0)	12(44.4)	1(3.7)	10(37.0)	0(0.0)	4(14.8)
NOBELZIN	Start of Administration to Week 4	109	2(1.8)	101(92.7)	0(0.0)	6(5.5)	0(0.0)	0(0.0)
	Week 4 to Week 8	106	1(0.9)	54(50.9)	2(1.9)	46(43.4)	0(0.0)	3(2.8)
	Week 8 to Week 12	104	1(1.0)	44(42.3)	4(3.8)	43(41.3)	0(0.0)	12(11.5)
	Week 12 to Week 16	62	0(0.0)	3(4.8)	3(4.8)	41(66.1)	0(0.0)	15(24.2)
	Week 16 to Week 20	31	0(0.0)	3(9.7)	1(3.2)	12(38.7)	0(0.0)	15(48.4)
	Week 20 to Week 24	17	0(0.0)	2(11.8)	0(0.0)	4(23.5)	0(0.0)	11(64.7)

2.7.4.1.3 治験対象集団の人口統計学的特性及びその他の特性

NPC-25-3 試験の人口統計学的及び他の基準値の特性を表 2.7.4.1-6 に示した。本剤群は女性が多く 57.0%であった。年齢は平均 66.8 歳で、11 歳以下の症例は 2 例、12～18 歳の症例は 2 例、19～64 歳の症例は 33 例、65 歳以上の症例は 70 例であった。体重は平均 58.65 kg であり、全例が 30 kg以上であった。年齢及び既往歴ありの症例の割合がノベルジン錠群と比較して本剤群で高い傾向があったが、それ以外の患者背景に大きな差はなかった。

表 2.7.4.1-6 人口統計学的及び他の基準値の特性（SP）（NPC-25-3 試験）

Parameter/Statistics		NPC-25 N = 107	NOBELZIN N = 109	
		n (%)	n (%)	P-value *
Sex	Male	46 (43.0)	40 (36.7)	0.405
	Female	61 (57.0)	69 (63.3)	
Age (year)	n	107	109	0.034
	Means	66.8	61.4	
	SD	18.75	18.00	
	Min	10	11	
	Median	72.0	64.0	
	Max	93	90	
	<= 11	2 (1.9)	1 (0.9)	0.085
	12 <= <= 18	2 (1.9)	2 (1.8)	
	19 <= <= 64	33 (30.8)	52 (47.7)	
	>= 65	70 (65.4)	54 (49.5)	
Height (cm)	n	107	109	0.648
	Means	158.09	158.70	
	SD	9.479	10.113	
	Min	136.7	135.4	
	Median	157.50	159.00	
	Max	177.2	181.5	
	< 100	0 (0.0)	0 (0.0)	0.427
	100 <= < 150	24 (22.4)	20 (18.3)	
	150 <= < 160	40 (37.4)	38 (34.9)	
	160 <= < 170	26 (24.3)	37 (33.9)	
	170 <= < 180	17 (15.9)	13 (11.9)	
	>= 180	0 (0.0)	1 (0.9)	
Weight (kg)	n	107	109	0.918
	Means	58.65	58.46	
	SD	13.137	13.066	
	Min	34.2	32.4	
	Median	57.10	55.30	
	Max	116.9	97.1	
	30.0 <= < 50.0	27 (25.2)	27 (24.8)	0.992
	50.0 <= < 70.0	62 (57.9)	63 (57.8)	
	>= 70.0	18 (16.8)	19 (17.4)	
BMI (kg/m^2)	n	107	109	0.622
	Means	23.323	23.058	
	SD	4.0627	3.8207	
	Min	16.35	15.47	
	Median	22.594	22.550	
	Max	38.70	34.34	
Pregnancy test	Negative	13 (21.3)	26 (37.7)	-
	Positive	0 (0.0)	0 (0.0)	
	Not Done	48 (78.7)	43 (62.3)	

表 2.7.4.1-6 人口統計学的及び他の基準値の特性（SP）（NPC-25-3 試験）（続き）

Parameter/Statistics		NPC-25 N = 107	NOBELZIN N = 109	
		n (%)	n (%)	P-value *
Zinc (ug/dL)	n	107	109	0.514
	Means	60.62	60.06	
	SD	6.144	6.431	
	Min	40.0	37.0	
	Median	62.00	60.00	
	Max	69.0	69.8	
	< 50	4 (3.7)	6 (5.5)	0.818
	50 <= <= 59	38 (35.5)	37 (33.9)	
	>= 60	65 (60.7)	66 (60.6)	
Symptom related to Zinc Deficiency	Yes	39 (36.4)	36 (33.0)	0.669
	No	68 (63.6)	73 (67.0)	
Past Medical History	Yes	24 (22.4)	13 (11.9)	0.048
	No	83 (77.6)	96 (88.1)	
Complications	Yes	103 (96.3)	105 (96.3)	1.000
	No	4 (3.7)	4 (3.7)	
Concomitant Medication	Yes	99 (92.5)	97 (89.0)	0.483
	No	8 (7.5)	12 (11.0)	

Height, Weight, BMI, Zinc and Concomitant Medication collected at Screening
Pregnancy test: Population: Female only
* Continuous quantity: Student's t-test, Categorical item: Fisher's exact test (2 x 2 table), Chi-square test (n x m table).

2.7.4.2 有害事象

2.7.4.2.1 有害事象の解析

2.7.4.2.1.1 比較的よく見られる有害事象

2.7.4.2.1.1.1 全体の有害事象及び副作用

NPC-25-3 試験で発現した本剤群の有害事象を表 2.7.4.2-1 に、副作用を表 2.7.4.2-2 に示した。

(1) 有害事象

本剤群の有害事象の発現率は、75.7%（81/107 例）であった。発現率が 2%以上であった有害事象は、発熱 8.4%（9/107 例）、ＣＯＶＩＤ－１９、上咽頭炎が各 7.5%（8/107 例）、血中銅減少、浮動性めまいが各 4.7%（5/107 例）、貧血、便秘、悪心、靭帯捻挫、アミラーゼ増加、リパーゼ増加、背部痛、頭痛、そう痒症が各 3.7%（4/107 例）、腹部不快感、下痢、末梢性浮腫、肝機能異常、足部白癬、節足動物刺傷、関節痛、湿疹が各 2.8%（3/107 例）であった。

(2) 副作用

本剤群の副作用の発現率は、24.3%（26/107 例）であった。発現率が 2%以上であった副作用は、血中銅減少 4.7%(5/107 例)、リパーゼ増加 3.7%(4/107 例)、貧血、下痢、悪心、アミラーゼ増加が各 2.8%(3/107 例)であった。

表 2.7.4.2-1 有害事象（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25 N = 107	
	n Events	n (%) Patients
Any Adverse Events	229	81 (75.7)
Blood and lymphatic system disorders	5	5 (4.7)
Anaemia	4	4 (3.7)
Iron deficiency anaemia	1	1 (0.9)
Cardiac disorders	2	2 (1.9)
Prinzmetal angina	1	1 (0.9)
Tachycardia	1	1 (0.9)
Eye disorders	7	5 (4.7)
Asthenopia	1	1 (0.9)
Blepharitis	1	1 (0.9)
Conjunctivitis allergic	1	1 (0.9)
Dry eye	2	2 (1.9)
Eye discharge	1	1 (0.9)
Vitreous floaters	1	1 (0.9)
Gastrointestinal disorders	40	25 (23.4)
Abdominal discomfort	3	3 (2.8)
Abdominal pain	1	1 (0.9)
Abdominal pain lower	1	1 (0.9)
Abdominal pain upper	1	1 (0.9)
Abnormal faeces	1	1 (0.9)
Angular cheilitis	2	2 (1.9)
Aphthous ulcer	1	1 (0.9)
Chronic gastritis	1	1 (0.9)
Constipation	4	4 (3.7)
Crohn's disease	1	1 (0.9)
Dental caries	1	1 (0.9)
Diarrhoea	3	3 (2.8)
Duodenal ulcer	1	1 (0.9)
Duodenitis	1	1 (0.9)
Enterocolitis	1	1 (0.9)
Gastric ulcer	1	1 (0.9)
Gastrooesophageal reflux disease	1	1 (0.9)
Haemorrhoids	1	1 (0.9)
Large intestine polyp	1	1 (0.9)
Melaena	1	1 (0.9)
Nausea	6	4 (3.7)
Pancreatic cyst	1	1 (0.9)
Stomatitis	2	2 (1.9)
Tooth disorder	1	1 (0.9)
Vomiting	2	2 (1.9)
General disorders and administration site conditions	14	12 (11.2)
Malaise	1	1 (0.9)
Oedema peripheral	3	3 (2.8)
Pyrexia	10	9 (8.4)
Hepatobiliary disorders	7	6 (5.6)
Cirrhosis alcoholic	1	1 (0.9)

表 2.7.4.2-1 有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107	
	n Events	n (%) Patients
Drug-induced liver injury	2	2 (1.9)
Hepatic function abnormal	3	3 (2.8)
Non-alcoholic steatohepatitis	1	1 (0.9)
Infections and infestations	38	33 (30.8)
Abscess limb	1	1 (0.9)
Bronchitis	1	1 (0.9)
COVID-19	8	8 (7.5)
Coronavirus infection	2	2 (1.9)
Cystitis	2	2 (1.9)
Dermatophytosis of nail	1	1 (0.9)
Folliculitis	1	1 (0.9)
Gastroenteritis	1	1 (0.9)
Gingivitis	2	2 (1.9)
Herpes zoster	2	2 (1.9)
Influenza	1	1 (0.9)
Nasopharyngitis	9	8 (7.5)
Paronychia	1	1 (0.9)
Tinea pedis	3	3 (2.8)
Tonsillitis	1	1 (0.9)
Upper respiratory tract infection	1	1 (0.9)
Urinary tract infection	1	1 (0.9)
Injury, poisoning and procedural complications	12	11 (10.3)
Arthropod sting	3	3 (2.8)
Contusion	2	2 (1.9)
Foot fracture	1	1 (0.9)
Ligament sprain	4	4 (3.7)
Skin abrasion	1	1 (0.9)
Spinal compression fracture	1	1 (0.9)
Investigations	27	18 (16.8)
Alanine aminotransferase increased	1	1 (0.9)
Amylase increased	4	4 (3.7)
Aspartate aminotransferase increased	2	1 (0.9)
Blood aldosterone increased	1	1 (0.9)
Blood copper decreased	6	5 (4.7)
Blood iron decreased	1	1 (0.9)
Blood potassium decreased	1	1 (0.9)
Blood pressure increased	1	1 (0.9)
Intraocular pressure increased	1	1 (0.9)
Lipase increased	5	4 (3.7)
Liver function test abnormal	2	2 (1.9)
Protein urine present	1	1 (0.9)
Weight decreased	1	1 (0.9)
Metabolism and nutrition disorders	13	9 (8.4)
Decreased appetite	2	2 (1.9)
Dehydration	1	1 (0.9)
Diabetes mellitus	1	1 (0.9)

表 2.7.4.2-1 有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107	
	n Events	n (%) Patients
Hyperammonaemia	1	1 (0.9)
Hyperglycaemia	1	1 (0.9)
Hypertriglyceridaemia	1	1 (0.9)
Hyperuricaemia	1	1 (0.9)
Hypocalcaemia	1	1 (0.9)
Hypoglycaemia	2	1 (0.9)
Type 2 diabetes mellitus	2	2 (1.9)
Musculoskeletal and connective tissue disorders	14	12 (11.2)
Arthralgia	4	3 (2.8)
Back pain	4	4 (3.7)
Osteoarthritis	1	1 (0.9)
Osteoporosis	1	1 (0.9)
Periarthritis	1	1 (0.9)
Rheumatoid arthritis	1	1 (0.9)
Tendonitis	1	1 (0.9)
Trigger finger	1	1 (0.9)
Nervous system disorders	16	12 (11.2)
Cerebellar ataxia	1	1 (0.9)
Cerebral haemorrhage	1	1 (0.9)
Cerebral infarction	2	1 (0.9)
Dizziness	5	5 (4.7)
Headache	4	4 (3.7)
Hypoaesthesia	1	1 (0.9)
Sciatica	1	1 (0.9)
Somnolence	1	1 (0.9)
Psychiatric disorders	1	1 (0.9)
Insomnia	1	1 (0.9)
Renal and urinary disorders	4	3 (2.8)
Haematuria	1	1 (0.9)
Hypertonic bladder	1	1 (0.9)
Nephrolithiasis	1	1 (0.9)
Renal impairment	1	1 (0.9)
Reproductive system and breast disorders	1	1 (0.9)
Prostatitis	1	1 (0.9)
Respiratory, thoracic and mediastinal disorders	7	5 (4.7)
Epistaxis	2	1 (0.9)
Interstitial lung disease	1	1 (0.9)
Laryngeal discomfort	1	1 (0.9)
Oropharyngeal discomfort	1	1 (0.9)
Oropharyngeal pain	1	1 (0.9)
Rhinitis allergic	1	1 (0.9)
Skin and subcutaneous tissue disorders	16	12 (11.2)
Blister	1	1 (0.9)
Dermatitis	2	1 (0.9)
Dermatitis acneiform	1	1 (0.9)
Drug eruption	2	2 (1.9)

表 2.7.4.2-1 有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107	
	n Events	n (%) Patients
Eczema	3	3 (2.8)
Eczema asteatotic	1	1 (0.9)
Haemorrhage subcutaneous	1	1 (0.9)
Pruritus	4	4 (3.7)
Rash	1	1 (0.9)
Social circumstances	1	1 (0.9)
Overwork	1	1 (0.9)
Surgical and medical procedures	1	1 (0.9)
Large intestinal polypectomy	1	1 (0.9)
Vascular disorders	3	3 (2.8)
Hypertension	2	2 (1.9)
White coat hypertension	1	1 (0.9)

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表 2.7.4.2-2 副作用（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25 N = 107	
	n Events	n (%) Patients
Any Adverse Drug Reactions	44	26 (24.3)
Blood and lymphatic system disorders	4	4 (3.7)
Anaemia	3	3 (2.8)
Iron deficiency anaemia	1	1 (0.9)
Gastrointestinal disorders	16	11 (10.3)
Abdominal discomfort	2	2 (1.9)
Abdominal pain lower	1	1 (0.9)
Abdominal pain upper	1	1 (0.9)
Constipation	1	1 (0.9)
Diarrhoea	3	3 (2.8)
Gastric ulcer	1	1 (0.9)
Gastrooesophageal reflux disease	1	1 (0.9)
Nausea	5	3 (2.8)
Vomiting	1	1 (0.9)
Hepatobiliary disorders	1	1 (0.9)
Hepatic function abnormal	1	1 (0.9)
Investigations	17	13 (12.1)
Amylase increased	3	3 (2.8)
Blood copper decreased	6	5 (4.7)
Lipase increased	5	4 (3.7)
Liver function test abnormal	2	2 (1.9)
Weight decreased	1	1 (0.9)
Metabolism and nutrition disorders	1	1 (0.9)
Decreased appetite	1	1 (0.9)
Nervous system disorders	3	2 (1.9)
Dizziness	2	2 (1.9)
Headache	1	1 (0.9)
Psychiatric disorders	1	1 (0.9)
Insomnia	1	1 (0.9)
Respiratory, thoracic and mediastinal disorders	1	1 (0.9)
Interstitial lung disease	1	1 (0.9)

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2.7.4.2.1.1.2 重症度別の有害事象及び副作用

NPC-25-3 試験で発現した重症度別の有害事象を表 2.7.4.2-3 に、重症度別の副作用を表 2.7.4.2-4 に示した。

（1）有害事象

本剤群における重症度別の有害事象の発現率は、重度 2.8%（3/107 例）、中等度 22.4%（24/107 例）、軽度 69.2%（74/107 例）であった。重度と判定された有害事象は、メレナ、脱水、脳出血が各 0.9%（1/107 例）であった。

(2) 副作用

本剤群における重症度別の副作用の発現率は、重度 0.0%（0/107 例）、中等度 3.7%（4/107 例）、軽度 21.5%（23/107 例）であった。中等度と判定された副作用は、貧血、胃潰瘍、肝機能異常、血中銅減少、体重減少が各 0.9%（1/107 例）であった。

表 2.7.4.2-3 重症度別の有害事象（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25 N = 107					
	Mild		Moderate		Severe	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Events	190	74 (69.2)	35	24 (22.4)	3	3 (2.8)
Blood and lymphatic system disorders	4	4 (3.7)	1	1 (0.9)	0	0 (0.0)
Anaemia	3	3 (2.8)	1	1 (0.9)	0	0 (0.0)
Iron deficiency anaemia	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Cardiac disorders	1	1 (0.9)	1	1 (0.9)	0	0 (0.0)
Prinzmetal angina	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Tachycardia	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Eye disorders	7	5 (4.7)	0	0 (0.0)	0	0 (0.0)
Asthenopia	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Blepharitis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Conjunctivitis allergic	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Dry eye	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Eye discharge	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Vitreous floaters	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Gastrointestinal disorders	34	21 (19.6)	5	4 (3.7)	1	1 (0.9)
Abdominal discomfort	3	3 (2.8)	0	0 (0.0)	0	0 (0.0)
Abdominal pain	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Abdominal pain lower	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Abdominal pain upper	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Abnormal faeces	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Angular cheilitis	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Aphthous ulcer	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Chronic gastritis	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Constipation	4	4 (3.7)	0	0 (0.0)	0	0 (0.0)
Crohn's disease	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Dental caries	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-3 重症度別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107					
	Mild		Moderate		Severe	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Diarrhoea	3	3 (2.8)	0	0 (0.0)	0	0 (0.0)
Duodenal ulcer	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Duodenitis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Enterocolitis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Gastric ulcer	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Gastrooesophageal reflux disease	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Haemorrhoids	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Large intestine polyp	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Melaena	0	0 (0.0)	0	0 (0.0)	1	1 (0.9)
Nausea	6	4 (3.7)	0	0 (0.0)	0	0 (0.0)
Pancreatic cyst	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Stomatitis	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Tooth disorder	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Vomiting	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
General disorders and administration site conditions	14	12 (11.2)	0	0 (0.0)	0	0 (0.0)
Malaise	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Oedema peripheral	3	3 (2.8)	0	0 (0.0)	0	0 (0.0)
Pyrexia	10	9 (8.4)	0	0 (0.0)	0	0 (0.0)
Hepatobiliary disorders	4	4 (3.7)	3	3 (2.8)	0	0 (0.0)
Cirrhosis alcoholic	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Drug-induced liver injury	1	1 (0.9)	1	1 (0.9)	0	0 (0.0)
Hepatic function abnormal	2	2 (1.9)	1	1 (0.9)	0	0 (0.0)
Non-alcoholic steatohepatitis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Infections and infestations	31	27 (25.2)	7	6 (5.6)	0	0 (0.0)
Abscess limb	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Bronchitis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
COVID-19	6	6 (5.6)	2	2 (1.9)	0	0 (0.0)

表 2.7.4.2-3 重症度別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107					
	Mild		Moderate		Severe	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Coronavirus infection	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Cystitis	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Dermatophytosis of nail	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Folliculitis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Gastroenteritis	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Gingivitis	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Herpes zoster	1	1 (0.9)	1	1 (0.9)	0	0 (0.0)
Influenza	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Nasopharyngitis	9	8 (7.5)	0	0 (0.0)	0	0 (0.0)
Paronychia	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Tinea pedis	3	3 (2.8)	0	0 (0.0)	0	0 (0.0)
Tonsillitis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Upper respiratory tract infection	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Urinary tract infection	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Injury, poisoning and procedural complications	12	11 (10.3)	0	0 (0.0)	0	0 (0.0)
Arthropod sting	3	3 (2.8)	0	0 (0.0)	0	0 (0.0)
Contusion	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Foot fracture	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Ligament sprain	4	4 (3.7)	0	0 (0.0)	0	0 (0.0)
Skin abrasion	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Spinal compression fracture	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Investigations	24	16 (15.0)	3	3 (2.8)	0	0 (0.0)
Alanine aminotransferase increased	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Amylase increased	4	4 (3.7)	0	0 (0.0)	0	0 (0.0)
Aspartate aminotransferase increased	2	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Blood aldosterone increased	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Blood copper decreased	5	4 (3.7)	1	1 (0.9)	0	0 (0.0)

表 2.7.4.2-3 重症度別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107					
	Mild		Moderate		Severe	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Blood iron decreased	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Blood potassium decreased	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Blood pressure increased	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Intraocular pressure increased	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Lipase increased	5	4 (3.7)	0	0 (0.0)	0	0 (0.0)
Liver function test abnormal	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Protein urine present	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Weight decreased	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Metabolism and nutrition disorders	8	6 (5.6)	4	3 (2.8)	1	1 (0.9)
Decreased appetite	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Dehydration	0	0 (0.0)	0	0 (0.0)	1	1 (0.9)
Diabetes mellitus	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Hyperammonaemia	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Hyperglycaemia	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Hypertriglyceridaemia	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Hyperuricaemia	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Hypocalcaemia	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Hypoglycaemia	2	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Type 2 diabetes mellitus	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Musculoskeletal and connective tissue disorders	9	8 (7.5)	5	4 (3.7)	0	0 (0.0)
Arthralgia	4	3 (2.8)	0	0 (0.0)	0	0 (0.0)
Back pain	2	2 (1.9)	2	2 (1.9)	0	0 (0.0)
Osteoarthritis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Osteoporosis	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Periarthritis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Rheumatoid arthritis	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Tendonitis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-3 重症度別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107					
	Mild		Moderate		Severe	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Trigger finger	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Nervous system disorders	13	9 (8.4)	2	2 (1.9)	1	1 (0.9)
Cerebellar ataxia	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Cerebral haemorrhage	0	0 (0.0)	0	0 (0.0)	1	1 (0.9)
Cerebral infarction	2	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Dizziness	5	5 (4.7)	0	0 (0.0)	0	0 (0.0)
Headache	4	4 (3.7)	0	0 (0.0)	0	0 (0.0)
Hypoaesthesia	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Sciatica	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Somnolence	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Psychiatric disorders	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Insomnia	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Renal and urinary disorders	3	2 (1.9)	1	1 (0.9)	0	0 (0.0)
Haematuria	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Hypertonic bladder	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Nephrolithiasis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Renal impairment	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Reproductive system and breast disorders	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Prostatitis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Respiratory, thoracic and mediastinal disorders	7	5 (4.7)	0	0 (0.0)	0	0 (0.0)
Epistaxis	2	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Interstitial lung disease	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Laryngeal discomfort	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Oropharyngeal discomfort	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Oropharyngeal pain	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Rhinitis allergic	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-3 重症度別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107					
	Mild		Moderate		Severe	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Skin and subcutaneous tissue disorders	14	11 (10.3)	1	1 (0.9)	0	0 (0.0)
Blister	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Dermatitis	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Dermatitis acneiform	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Drug eruption	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Eczema	3	3 (2.8)	0	0 (0.0)	0	0 (0.0)
Eczema asteatotic	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Haemorrhage subcutaneous	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Pruritus	4	4 (3.7)	0	0 (0.0)	0	0 (0.0)
Rash	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Social circumstances	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Overwork	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Surgical and medical procedures	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Large intestinal polypectomy	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Vascular disorders	2	2 (1.9)	1	1 (0.9)	0	0 (0.0)
Hypertension	1	1 (0.9)	1	1 (0.9)	0	0 (0.0)
White coat hypertension	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)

MedDRA: Version 24.1
If a patient experiences the same PT multiple times, then the event was counted only once and by greatest severity.

表 2.7.4.2-4 重症度別の副作用（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25 N = 107					
	Mild		Moderate		Severe	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Drug Reactions	39	23 (21.5)	5	4 (3.7)	0	0 (0.0)
Blood and lymphatic system disorders	3	3 (2.8)	1	1 (0.9)	0	0 (0.0)
Anaemia	2	2 (1.9)	1	1 (0.9)	0	0 (0.0)
Iron deficiency anaemia	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Gastrointestinal disorders	15	10 (9.3)	1	1 (0.9)	0	0 (0.0)
Abdominal discomfort	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Abdominal pain lower	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Abdominal pain upper	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Constipation	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Diarrhoea	3	3 (2.8)	0	0 (0.0)	0	0 (0.0)
Gastric ulcer	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Gastrooesophageal reflux disease	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Nausea	5	3 (2.8)	0	0 (0.0)	0	0 (0.0)
Vomiting	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Hepatobiliary disorders	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Hepatic function abnormal	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Investigations	15	11 (10.3)	2	2 (1.9)	0	0 (0.0)
Amylase increased	3	3 (2.8)	0	0 (0.0)	0	0 (0.0)
Blood copper decreased	5	4 (3.7)	1	1 (0.9)	0	0 (0.0)
Lipase increased	5	4 (3.7)	0	0 (0.0)	0	0 (0.0)
Liver function test abnormal	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Weight decreased	0	0 (0.0)	1	1 (0.9)	0	0 (0.0)
Metabolism and nutrition disorders	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Decreased appetite	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Nervous system disorders	3	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Dizziness	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)
Headache	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-4 重症度別の副作用（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107					
	Mild		Moderate		Severe	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Psychiatric disorders	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Insomnia	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Respiratory, thoracic and mediastinal disorders	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)
Interstitial lung disease	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)

MedDRA: Version 24.1
If a patient experiences the same PT multiple times, then the event was counted only once and by greatest severity.

2.7.4.2.1.1.3 発現時投与量別の有害事象及び副作用

NPC-25-3 試験で発現した発現時投与量別の有害事象及び副作用を、それぞれ表 2.7.4.2-5 及び表 2.7.4.2-6 に示した。

(1) 有害事象

本剤群における発現時投与量別の有害事象の発現率は、25 mg/日が 66.7%（2/3 例）、50 mg/日が 49.5%（51/103 例）、75 mg/日が 50.0%（3/6 例）、100 mg/日が 60.0%（33/55 例）、125 mg/日が 33.3%（1/3 例）、150 mg/日が 83.3%（10/12 例）であり、25～125 mg/日では発現率に大きな差はなく、150 mg/日では発現率が高かった。2.7.4.2.1.1.1 の項で示した発現率が 2%以上の有害事象であった発熱、ＣＯＶＩＤ－１９、上咽頭炎、血中銅減少、浮動性めまい、貧血、便秘、悪心、靭帯捻挫、アミラーゼ増加、リパーゼ増加、背部痛、頭痛、そう痒症、腹部不快感、下痢、末梢性浮腫、肝機能異常、足部白癬、節足動物刺傷、関節痛、湿疹は、いずれも投与量による特筆すべき発現率の変化は認められなかった。

(2) 副作用

本剤群における発現時投与量別の副作用の発現率は、25 mg/日が 33.3%（1/3 例）、50 mg/日が 14.6%（15/103 例）、75 mg/日が 33.3%（2/6 例）、100 mg/日が 16.4%（9/55 例）、125 mg/日が 33.3%（1/3 例）、150 mg/日が 25.0%（3/12 例）であり、発現率に大きな差はなかった。また、2.7.4.2.1.1.1 の項で示した発現率が 2%以上の副作用であった血中銅減少、リパーゼ増加、貧血、下痢、悪心、アミラーゼ増加は、いずれも投与量による特筆すべき発現率の変化は認められなかった。

表 2.7.4.2-5 発現時投与量別の有害事象（SP）（NPC-25-3 試験）

System Organ Class / Preferred Term	NPC-25													
	25 mg/day N=3		50 mg/day N=103		75 mg/day N=6		100 mg/day N=55		125 mg/day N=3		150 mg/day N=12		After Treatment Period	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n Patients
Any Adverse Events	5	2 (66.7)	121	51 (49.5)	5	3 (50.0)	73	33 (60.0)	1	1 (33.3)	17	10 (83.3)	7	7
Blood and lymphatic system disorders	0	0 (0.0)	3	3 (2.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (16.7)	0	0
Anaemia	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (16.7)	0	0
Iron deficiency anaemia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Cardiac disorders	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Prinzmetal angina	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Tachycardia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Eye disorders	0	0 (0.0)	3	2 (1.9)	0	0 (0.0)	4	3 (5.5)	0	0 (0.0)	0	0 (0.0)	0	0
Asthenopia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Blepharitis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Conjunctivitis allergic	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Dry eye	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (3.6)	0	0 (0.0)	0	0 (0.0)	0	0
Eye discharge	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Vitreous floaters	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Gastrointestinal disorders	2	1 (33.3)	24	16 (15.5)	0	0 (0.0)	8	7 (12.7)	0	0 (0.0)	3	3 (25.0)	3	3
Abdominal discomfort	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	2	2 (3.6)	0	0 (0.0)	0	0 (0.0)	0	0
Abdominal pain	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Abdominal pain lower	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Abdominal pain upper	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Abnormal faeces	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Angular cheilitis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Aphthous ulcer	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Chronic gastritis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Constipation	0	0 (0.0)	4	4 (3.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Crohn's disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Dental caries	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0

表 2.7.4.2-5 発現時投与量別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25													
	25 mg/day N=3		50 mg/day N=103		75 mg/day N=6		100 mg/day N=55		125 mg/day N=3		150 mg/day N=12		After Treatment Period	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n Patients
Diarrhoea	1	1 (33.3)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1
Duodenal ulcer	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Duodenitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Enterocolitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Gastric ulcer	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Gastrooesophageal reflux disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Haemorrhoids	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Large intestine polyp	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Melaena	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1
Nausea	1	1 (33.3)	3	3 (2.9)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	1	1
Pancreatic cyst	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Stomatitis	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Tooth disorder	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Vomiting	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
General disorders and administration site conditions	0	0 (0.0)	10	9 (8.7)	0	0 (0.0)	4	3 (5.5)	0	0 (0.0)	0	0 (0.0)	0	0
Malaise	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Oedema peripheral	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Pyrexia	0	0 (0.0)	8	7 (6.8)	0	0 (0.0)	2	2 (3.6)	0	0 (0.0)	0	0 (0.0)	0	0
Hepatobiliary disorders	1	1 (33.3)	4	4 (3.9)	1	1 (16.7)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Cirrhosis alcoholic	0	0 (0.0)	0	0 (0.0)	1	1 (16.7)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Drug-induced liver injury	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Hepatic function abnormal	1	1 (33.3)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Non-alcoholic steatohepatitis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Infections and infestations	0	0 (0.0)	20	19 (18.4)	0	0 (0.0)	15	12 (21.8)	0	0 (0.0)	3	3 (25.0)	0	0
Abscess limb	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0

表 2.7.4.2-5 発現時投与量別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25													
	25 mg/day N=3		50 mg/day N=103		75 mg/day N=6		100 mg/day N=55		125 mg/day N=3		150 mg/day N=12		After Treatment Period	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n Patients
Bronchitis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
COVID-19	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	5	5 (9.1)	0	0 (0.0)	1	1 (8.3)	0	0
Coronavirus infection	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Cystitis	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Dermatophytosis of nail	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Folliculitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Gastroenteritis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Gingivitis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Herpes zoster	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Influenza	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Nasopharyngitis	0	0 (0.0)	4	4 (3.9)	0	0 (0.0)	5	4 (7.3)	0	0 (0.0)	0	0 (0.0)	0	0
Paronychia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Tinea pedis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	2	2 (3.6)	0	0 (0.0)	0	0 (0.0)	0	0
Tonsillitis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Upper respiratory tract infection	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Urinary tract infection	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Injury, poisoning and procedural complications	1	1 (33.3)	5	4 (3.9)	1	1 (16.7)	5	5 (9.1)	0	0 (0.0)	0	0 (0.0)	0	0
Arthropod sting	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Contusion	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Foot fracture	1	1 (33.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Ligament sprain	0	0 (0.0)	1	1 (1.0)	1	1 (16.7)	2	2 (3.6)	0	0 (0.0)	0	0 (0.0)	0	0
Skin abrasion	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Spinal compression fracture	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Investigations	0	0 (0.0)	14	8 (7.8)	3	2 (33.3)	7	6 (10.9)	1	1 (33.3)	1	1 (8.3)	1	1
Alanine aminotransferase increased	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0

表 2.7.4.2-5 発現時投与量別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25													
	25 mg/day N=3		50 mg/day N=103		75 mg/day N=6		100 mg/day N=55		125 mg/day N=3		150 mg/day N=12		After Treatment Period	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n Patients
Amylase increased	0	0 (0.0)	3	3 (2.9)	1	1 (16.7)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Aspartate aminotransferase increased	0	0 (0.0)	2	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Blood aldosterone increased	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Blood copper decreased	0	0 (0.0)	2	1 (1.0)	1	1 (16.7)	1	1 (1.8)	1	1 (33.3)	1	1 (8.3)	0	0
Blood iron decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Blood potassium decreased	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Blood pressure increased	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Intraocular pressure increased	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Lipase increased	0	0 (0.0)	2	1 (1.0)	1	1 (16.7)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	1	1
Liver function test abnormal	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (3.6)	0	0 (0.0)	0	0 (0.0)	0	0
Protein urine present	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Weight decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Metabolism and nutrition disorders	0	0 (0.0)	7	6 (5.8)	0	0 (0.0)	3	2 (3.6)	0	0 (0.0)	1	1 (8.3)	2	2
Decreased appetite	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Dehydration	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1
Diabetes mellitus	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Hyperammonaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Hyperglycaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Hypertriglyceridaemia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Hyperuricaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Hypocalcaemia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Hypoglycaemia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1
Type 2 diabetes mellitus	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Musculoskeletal and connective tissue disorders	1	1 (33.3)	6	6 (5.8)	0	0 (0.0)	5	4 (7.3)	0	0 (0.0)	2	2 (16.7)	0	0
Arthralgia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	2	1 (1.8)	0	0 (0.0)	1	1 (8.3)	0	0

表 2.7.4.2-5 発現時投与量別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class	NPC-25													
Preferred Term	25 mg/day N=3		50 mg/day N=103		75 mg/day N=6		100 mg/day N=55		125 mg/day N=3		150 mg/day N=12		After Treatment Period	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n Patients
Back pain	1	1 (33.3)	1	1 (1.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	1	1 (8.3)	0	0
Osteoarthritis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Osteoporosis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Periarthritis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Rheumatoid arthritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Tendonitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Trigger finger	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Nervous system disorders	0	0 (0.0)	7	4 (3.9)	0	0 (0.0)	6	6 (10.9)	0	0 (0.0)	2	1 (8.3)	1	1
Cerebellar ataxia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1
Cerebral haemorrhage	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Cerebral infarction	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	1 (8.3)	0	0
Dizziness	0	0 (0.0)	3	3 (2.9)	0	0 (0.0)	2	2 (3.6)	0	0 (0.0)	0	0 (0.0)	0	0
Headache	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	2	2 (3.6)	0	0 (0.0)	0	0 (0.0)	0	0
Hypoaesthesia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Sciatica	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Somnolence	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Psychiatric disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Insomnia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Renal and urinary disorders	0	0 (0.0)	3	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Haematuria	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Hypertonic bladder	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Nephrolithiasis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Renal impairment	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Reproductive system and breast disorders	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Prostatitis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0

表 2.7.4.2-5 発現時投与量別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25													
	25 mg/day N=3		50 mg/day N=103		75 mg/day N=6		100 mg/day N=55		125 mg/day N=3		150 mg/day N=12		After Treatment Period	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n Patients
Respiratory, thoracic and mediastinal disorders	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	5	4 (7.3)	0	0 (0.0)	0	0 (0.0)	0	0
Epistaxis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Interstitial lung disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Laryngeal discomfort	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Oropharyngeal discomfort	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Oropharyngeal pain	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Rhinitis allergic	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Skin and subcutaneous tissue disorders	0	0 (0.0)	9	7 (6.8)	0	0 (0.0)	7	6 (10.9)	0	0 (0.0)	0	0 (0.0)	0	0
Blister	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Dermatitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Dermatitis acneiform	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Drug eruption	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Eczema	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	3	3 (5.5)	0	0 (0.0)	0	0 (0.0)	0	0
Eczema asteatotic	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Haemorrhage subcutaneous	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Pruritus	0	0 (0.0)	4	4 (3.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Rash	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Social circumstances	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Overwork	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Surgical and medical procedures	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Large intestinal polypectomy	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0

表 2.7.4.2-5 発現時投与量別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25													
	25 mg/day N=3		50 mg/day N=103		75 mg/day N=6		100 mg/day N=55		125 mg/day N=3		150 mg/day N=12		After Treatment Period	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n Patients
Vascular disorders	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Hypertension	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
White coat hypertension	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0

MedDRA: Version 24.1
If a patient experiences the same PT multiple times in same dose, then the event was counted only first occurrence for number of patients.
N: Number of Patients who administered the relevant dose.

表 2.7.4.2-6 発現時投与量別の副作用（SP）（NPC-25-3 試験）

System Organ Class / Preferred Term	NPC-25													
	25 mg/day N=3		50 mg/day N=103		75 mg/day N=6		100 mg/day N=55		125 mg/day N=3		150 mg/day N=12		After Treatment Period	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n Patients
Any Adverse Drug Reactions	2	1 (33.3)	21	15 (14.6)	3	2 (33.3)	11	9 (16.4)	1	1 (33.3)	3	3 (25.0)	3	3
Blood and lymphatic system disorders	0	0 (0.0)	3	3 (2.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Anaemia	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Iron deficiency anaemia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Gastrointestinal disorders	2	1 (33.3)	7	7 (6.8)	0	0 (0.0)	4	4 (7.3)	0	0 (0.0)	1	1 (8.3)	2	2
Abdominal discomfort	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Abdominal pain lower	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Abdominal pain upper	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (8.3)	0	0
Constipation	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Diarrhoea	1	1 (33.3)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1
Gastric ulcer	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Gastrooesophageal reflux disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Nausea	1	1 (33.3)	2	2 (1.9)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	1	1
Vomiting	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Hepatobiliary disorders	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Hepatic function abnormal	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Investigations	0	0 (0.0)	6	4 (3.9)	3	2 (33.3)	5	5 (9.1)	1	1 (33.3)	1	1 (8.3)	1	1
Amylase increased	0	0 (0.0)	2	2 (1.9)	1	1 (16.7)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Blood copper decreased	0	0 (0.0)	2	1 (1.0)	1	1 (16.7)	1	1 (1.8)	1	1 (33.3)	1	1 (8.3)	0	0
Lipase increased	0	0 (0.0)	2	1 (1.0)	1	1 (16.7)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	1	1
Liver function test abnormal	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	2 (3.6)	0	0 (0.0)	0	0 (0.0)	0	0
Weight decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Metabolism and nutrition disorders	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Decreased appetite	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Nervous system disorders	0	0 (0.0)	3	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Dizziness	0	0 (0.0)	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0

表 2.7.4.2-6 発現時投与量別の副作用（SP）（NPC-25-3 試験）（続き）

System Organ Class	NPC-25													
Preferred Term	25 mg/day N=3		50 mg/day N=103		75 mg/day N=6		100 mg/day N=55		125 mg/day N=3		150 mg/day N=12		After Treatment Period	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n Patients
Headache	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0
Psychiatric disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Insomnia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Respiratory, thoracic and mediastinal disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0
Interstitial lung disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)	0	0 (0.0)	0	0 (0.0)	0	0

MedDRA: Version 24.1
If a patient experiences the same PT multiple times in same dose, then the event was counted only first occurrence for number of patients.
N: Number of Patients who administered the relevant dose.

2.7.4.2.1.1.4 発現時期別の有害事象及び副作用

NPC-25-3 試験で発現した発現時期別の有害事象及び副作用を、それぞれ表 2.7.4.2-7 及び表 2.7.4.2-8 に示した。

(1) 有害事象

本剤群における有害事象発現率の経時的推移は、投与開始後 0～4 週が 27.1%（29/107 例）、4～8 週が 21.8%（22/101 例）、8～12 週が 20.2%（20/99 例）、12～16 週が 25.6%（20/78 例）、16～20 週が 19.4%（13/67 例）、20～24 週が 24.6%（14/57 例）、24～28 週が 15.1%（8/53 例）、28～32 週が 17.1%（6/35 例）、32～36 週が 25.8%（8/31 例）、36～40 週が 23.3%（7/30 例）、40～44 週が 16.7%（5/30 例）、44～48 週が 10.0%（3/30 例）、48 週以降が 22.2%（6/27 例）であり、投与期間の延長に伴う有害事象発現率の上昇は認められなかった。また、2.7.4.2.1.1.1 の項で示した発現率が 2%以上の有害事象であった発熱、ＣＯＶＩＤ－１９、上咽頭炎、血中銅減少、浮動性めまい、貧血、便秘、悪心、靭帯捻挫、アミラーゼ増加、リパーゼ増加、背部痛、頭痛、そう痒症、腹部不快感、下痢、末梢性浮腫、肝機能異常、足部白癬、節足動物刺傷、関節痛、湿疹は、いずれも投与期間による特筆すべき発現率の変化は認められなかった。

(2) 副作用

本剤群における副作用発現率の経時的推移は、投与開始後 0～4 週が 7.5%（8/107 例）、4～8 週が 6.9%（7/101 例）、8～12 週が 6.1%（6/99 例）、12～16 週が 3.8%（3/78 例）、16～20 週が 4.5%（3/67 例）、20～24 週が 1.8%（1/57 例）、24～28 週が 3.8%（2/53 例）、28～32 週が 5.7%（2/35 例）、32～36 週が 0.0%（0/31 例）、36～40 週が 0.0%（0/30 例）、40～44 週が 0.0%（0/30 例）、44～48 週が 3.3%（1/30 例）、48 週以降が 7.4%（2/27 例）であり、投与期間の延長に伴う副作用発現率の上昇は認められなかった。また、2.7.4.2.1.1.1 の項で示した発現率が 2%以上の副作用であった血中銅減少、リパーゼ増加、貧血、下痢、悪心、アミラーゼ増加は、いずれも投与期間による特筆すべき発現率の変化は認められなかった。

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）

System Organ Class / Preferred Term	NPC-25											
	Start of Administration to Week 4 N = 107		Week 4 to Week 8 N = 101		Week 8 to Week 12 N = 99		Week 12 to Week 16 N = 78		Week 16 to Week 20 N = 67		Week 20 to Week 24 N = 57	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Events	44	29 (27.1)	30	22 (21.8)	24	20 (20.2)	27	20 (25.6)	18	13 (19.4)	20	14 (24.6)
Blood and lymphatic system disorders	0	0 (0.0)	2	2 (2.0)	1	1 (1.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Anaemia	0	0 (0.0)	2	2 (2.0)	1	1 (1.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Iron deficiency anaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Cardiac disorders	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Prinzmetal angina	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Tachycardia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Eye disorders	0	0 (0.0)	1	1 (1.0)	2	2 (2.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Asthenopia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Blepharitis	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Conjunctivitis allergic	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dry eye	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Eye discharge	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Vitreous floaters	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gastrointestinal disorders	11	10 (9.3)	8	7 (6.9)	3	3 (3.0)	2	2 (2.6)	1	1 (1.5)	3	2 (3.5)
Abdominal discomfort	2	2 (1.9)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain lower	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain upper	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abnormal faeces	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
Angular cheilitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
Aphthous ulcer	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Chronic gastritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Constipation	1	1 (0.9)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Crohn's disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dental caries	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25											
	Start of Administration to Week 4		Week 4 to Week 8		Week 8 to Week 12		Week 12 to Week 16		Week 16 to Week 20		Week 20 to Week 24	
	N = 107		N = 101		N = 99		N = 78		N = 67		N = 57	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Diarrhoea	2	2 (1.9)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Duodenal ulcer	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Duodenitis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Enterocolitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Gastric ulcer	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gastrooesophageal reflux disease	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Haemorrhoids	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Large intestine polyp	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Melaena	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Nausea	2	2 (1.9)	2	2 (2.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Pancreatic cyst	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Stomatitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	1	1 (1.8)
Tooth disorder	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Vomiting	1	1 (0.9)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
General disorders and administration site conditions	6	6 (5.6)	0	0 (0.0)	1	1 (1.0)	3	3 (3.8)	0	0 (0.0)	3	2 (3.5)
Malaise	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
Oedema peripheral	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	2	2 (2.6)	0	0 (0.0)	0	0 (0.0)
Pyrexia	5	5 (4.7)	0	0 (0.0)	1	1 (1.0)	1	1 (1.3)	0	0 (0.0)	2	2 (3.5)
Hepatobiliary disorders	2	2 (1.9)	1	1 (1.0)	1	1 (1.0)	1	1 (1.3)	1	1 (1.5)	1	1 (1.8)
Cirrhosis alcoholic	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Drug-induced liver injury	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Hepatic function abnormal	2	2 (1.9)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Non-alcoholic steatohepatitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
Infections and infestations	6	6 (5.6)	1	1 (1.0)	3	3 (3.0)	6	6 (7.7)	2	2 (3.0)	6	6 (10.5)
Abscess limb	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25											
	Start of Administration to Week 4		Week 4 to Week 8		Week 8 to Week 12		Week 12 to Week 16		Week 16 to Week 20		Week 20 to Week 24	
	N = 107		N = 101		N = 99		N = 78		N = 67		N = 57	
	n Events	n (%) Patients	n Events	n (%) Patients	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)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
COVID-19	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	3	3 (3.8)	1	1 (1.5)	1	1 (1.8)
Coronavirus infection	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Cystitis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
Dermatophytosis of nail	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Folliculitis	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gastroenteritis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gingivitis	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
Herpes zoster	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
Influenza	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Nasopharyngitis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	2	2 (2.6)	1	1 (1.5)	0	0 (0.0)
Paronychia	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Tinea pedis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	1	1 (1.8)
Tonsillitis	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Upper respiratory tract infection	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Urinary tract infection	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Injury, poisoning and procedural complications	3	3 (2.8)	0	0 (0.0)	1	1 (1.0)	1	1 (1.3)	1	1 (1.5)	3	3 (5.3)
Arthropod sting	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	1	1 (1.5)	1	1 (1.8)
Contusion	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Foot fracture	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Ligament sprain	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	2	2 (3.5)
Skin abrasion	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Spinal compression fracture	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Investigations	2	2 (1.9)	2	2 (2.0)	4	4 (4.0)	4	2 (2.6)	5	4 (6.0)	2	2 (3.5)
Alanine aminotransferase increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class	NPC-25											
Preferred Term	Start of Administration to Week 4		Week 4 to Week 8		Week 8 to Week 12		Week 12 to Week 16		Week 16 to Week 20		Week 20 to Week 24	
	N = 107		N = 101		N = 99		N = 78		N = 67		N = 57	
	n Events	n (%) Patients	n Events	n (%) Patients	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)	1	1 (1.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Aspartate aminotransferase increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Blood aldosterone increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Blood copper decreased	0	0 (0.0)	1	1 (1.0)	3	3 (3.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Blood iron decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Blood potassium decreased	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Blood pressure increased	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Intraocular pressure increased	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Lipase increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	1	1 (1.8)
Liver function test abnormal	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Protein urine present	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
Weight decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Metabolism and nutrition disorders	4	4 (3.7)	2	1 (1.0)	3	2 (2.0)	1	1 (1.3)	1	1 (1.5)	0	0 (0.0)
Decreased appetite	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Dehydration	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Diabetes mellitus	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hyperammonaemia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hyperglycaemia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hypertriglyceridaemia	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hyperuricaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Hypocalcaemia	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hypoglycaemia	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Type 2 diabetes mellitus	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Musculoskeletal and connective tissue disorders	2	2 (1.9)	5	5 (5.0)	2	2 (2.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Arthralgia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25											
	Start of Administration to Week 4 N = 107		Week 4 to Week 8 N = 101		Week 8 to Week 12 N = 99		Week 12 to Week 16 N = 78		Week 16 to Week 20 N = 67		Week 20 to Week 24 N = 57	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Back pain	0	0 (0.0)	2	2 (2.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Osteoarthritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Osteoporosis	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Periarthritis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Rheumatoid arthritis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Tendonitis	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Trigger finger	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Nervous system disorders	3	2 (1.9)	3	3 (3.0)	2	2 (2.0)	1	1 (1.3)	1	1 (1.5)	0	0 (0.0)
Cerebellar ataxia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Cerebral haemorrhage	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Cerebral infarction	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dizziness	2	2 (1.9)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Headache	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	1	1 (1.5)	0	0 (0.0)
Hypoaesthesia	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Sciatica	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Somnolence	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Psychiatric disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Insomnia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Renal and urinary disorders	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	2	1 (1.8)
Haematuria	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hypertonic bladder	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
Nephrolithiasis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.8)
Renal impairment	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Reproductive system and breast disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Prostatitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25											
	Start of Administration to Week 4		Week 4 to Week 8		Week 8 to Week 12		Week 12 to Week 16		Week 16 to Week 20		Week 20 to Week 24	
	N = 107		N = 101		N = 99		N = 78		N = 67		N = 57	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Respiratory, thoracic and mediastinal disorders	1	1 (0.9)	1	1 (1.0)	0	0 (0.0)	3	3 (3.8)	0	0 (0.0)	0	0 (0.0)
Epistaxis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Interstitial lung disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Laryngeal discomfort	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Oropharyngeal discomfort	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Oropharyngeal pain	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Rhinitis allergic	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Skin and subcutaneous tissue disorders	2	1 (0.9)	3	3 (3.0)	0	0 (0.0)	3	3 (3.8)	2	2 (3.0)	0	0 (0.0)
Blister	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Dermatitis	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dermatitis acneiform	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Drug eruption	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Eczema	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Eczema asteatotic	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Haemorrhage subcutaneous	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Pruritus	1	1 (0.9)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Rash	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Social circumstances	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Overwork	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Surgical and medical procedures	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Large intestinal polypectomy	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25											
	Start of Administration to Week 4		Week 4 to Week 8		Week 8 to Week 12		Week 12 to Week 16		Week 16 to Week 20		Week 20 to Week 24	
	N = 107		N = 101		N = 99		N = 78		N = 67		N = 57	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Vascular disorders	0	0 (0.0)	1	1 (1.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hypertension	0	0 (0.0)	1	1 (1.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
White coat hypertension	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

MedDRA: Version 24.1
If a patient experiences the same PT multiple times, then the event was counted only first occurrence.
N: Number of Patients who administered until the relevant time.

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25													
	Week 24 to Week 28 N = 53		Week 28 to Week 32 N = 35		Week 32 to Week 36 N = 31		Week 36 to Week 40 N = 30		Week 40 to Week 44 N = 30		Week 44 to Week 48 N = 30		After Week 48 N = 27	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Events	9	8 (15.1)	6	6 (17.1)	12	8 (25.8)	8	7 (23.3)	6	5 (16.7)	3	3 (10.0)	10	6 (22.2)
Blood and lymphatic system disorders	1	1 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Anaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Iron deficiency anaemia	1	1 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Cardiac disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Prinzmetal angina	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Tachycardia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Eye disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	2	1 (3.3)	1	1 (3.3)	1	1 (3.7)
Asthenopia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)
Blepharitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Conjunctivitis allergic	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Dry eye	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)
Eye discharge	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Vitreous floaters	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)
Gastrointestinal disorders	2	2 (3.8)	0	0 (0.0)	2	2 (6.5)	4	4 (13.3)	0	0 (0.0)	1	1 (3.3)	1	1 (3.7)
Abdominal discomfort	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain lower	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain upper	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Abnormal faeces	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Angular cheilitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Aphthous ulcer	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Chronic gastritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Constipation	0	0 (0.0)	0	0 (0.0)	2	2 (6.5)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Crohn's disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dental caries	1	1 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25													
	Week 24 to Week 28 N = 53		Week 28 to Week 32 N = 35		Week 32 to Week 36 N = 31		Week 36 to Week 40 N = 30		Week 40 to Week 44 N = 30		Week 44 to Week 48 N = 30		After Week 48 N = 27	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Diarrhoea	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Duodenal ulcer	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Duodenitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Enterocolitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gastric ulcer	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)
Gastrooesophageal reflux disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Haemorrhoids	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Large intestine polyp	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Melaena	1	1 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Nausea	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Pancreatic cyst	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Stomatitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Tooth disorder	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Vomiting	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
General disorders and administration site conditions	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Malaise	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Oedema peripheral	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Pyrexia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hepatobiliary disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Cirrhosis alcoholic	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Drug-induced liver injury	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hepatic function abnormal	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Non-alcoholic steatohepatitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Infections and infestations	1	1 (1.9)	2	2 (5.7)	3	3 (9.7)	2	2 (6.7)	4	4 (13.3)	1	1 (3.3)	0	0 (0.0)
Abscess limb	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25													
	Week 24 to Week 28 N = 53		Week 28 to Week 32 N = 35		Week 32 to Week 36 N = 31		Week 36 to Week 40 N = 30		Week 40 to Week 44 N = 30		Week 44 to Week 48 N = 30		After Week 48 N = 27	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	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)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
COVID-19	0	0 (0.0)	1	1 (2.9)	0	0 (0.0)	0	0 (0.0)	2	2 (6.7)	0	0 (0.0)	0	0 (0.0)
Coronavirus infection	0	0 (0.0)	1	1 (2.9)	1	1 (3.2)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Cystitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dermatophytosis of nail	1	1 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Folliculitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gastroenteritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gingivitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Herpes zoster	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Influenza	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)
Nasopharyngitis	0	0 (0.0)	0	0 (0.0)	2	2 (6.5)	0	0 (0.0)	1	1 (3.3)	1	1 (3.3)	0	0 (0.0)
Paronychia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Tinea pedis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Tonsillitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Upper respiratory tract infection	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Urinary tract infection	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Injury, poisoning and procedural complications	2	2 (3.8)	0	0 (0.0)	1	1 (3.2)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Arthropod sting	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Contusion	1	1 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Foot fracture	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Ligament sprain	0	0 (0.0)	0	0 (0.0)	1	1 (3.2)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Skin abrasion	1	1 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Spinal compression fracture	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Investigations	2	1 (1.9)	2	2 (5.7)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Alanine aminotransferase increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25													
	Week 24 to Week 28 N = 53		Week 28 to Week 32 N = 35		Week 32 to Week 36 N = 31		Week 36 to Week 40 N = 30		Week 40 to Week 44 N = 30		Week 44 to Week 48 N = 30		After Week 48 N = 27	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Amylase increased	1	1 (1.9)	1	1 (2.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Aspartate aminotransferase increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Blood aldosterone increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Blood copper decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Blood iron decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Blood potassium decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Blood pressure increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Intraocular pressure increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Lipase increased	1	1 (1.9)	1	1 (2.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Liver function test abnormal	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Protein urine present	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Weight decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Metabolism and nutrition disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Decreased appetite	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dehydration	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Diabetes mellitus	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hyperammonaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hyperglycaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hypertriglyceridaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hyperuricaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hypocalcaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hypoglycaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Type 2 diabetes mellitus	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Musculoskeletal and connective tissue disorders	0	0 (0.0)	1	1 (2.9)	1	1 (3.2)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Arthralgia	0	0 (0.0)	1	1 (2.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25													
	Week 24 to Week 28 N = 53		Week 28 to Week 32 N = 35		Week 32 to Week 36 N = 31		Week 36 to Week 40 N = 30		Week 40 to Week 44 N = 30		Week 44 to Week 48 N = 30		After Week 48 N = 27	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	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)	1	1 (3.2)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Osteoarthritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Osteoporosis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Periarthritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Rheumatoid arthritis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Tendonitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Trigger finger	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Nervous system disorders	1	1 (1.9)	0	0 (0.0)	1	1 (3.2)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	3	1 (3.7)
Cerebellar ataxia	1	1 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Cerebral haemorrhage	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Cerebral infarction	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dizziness	0	0 (0.0)	0	0 (0.0)	1	1 (3.2)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Headache	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Hypoaesthesia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Sciatica	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Somnolence	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Psychiatric disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Insomnia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Renal and urinary disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Haematuria	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hypertonic bladder	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Nephrolithiasis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Renal impairment	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Reproductive system and breast disorders	0	0 (0.0)	0	0 (0.0)	1	1 (3.2)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Prostatitis	0	0 (0.0)	0	0 (0.0)	1	1 (3.2)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25													
	Week 24 to Week 28 N = 53		Week 28 to Week 32 N = 35		Week 32 to Week 36 N = 31		Week 36 to Week 40 N = 30		Week 40 to Week 44 N = 30		Week 44 to Week 48 N = 30		After Week 48 N = 27	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Respiratory, thoracic and mediastinal disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Epistaxis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Interstitial lung disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Laryngeal discomfort	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Oropharyngeal discomfort	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Oropharyngeal pain	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Rhinitis allergic	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Skin and subcutaneous tissue disorders	0	0 (0.0)	1	1 (2.9)	3	3 (9.7)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Blister	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dermatitis	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dermatitis acneiform	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Drug eruption	0	0 (0.0)	0	0 (0.0)	1	1 (3.2)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Eczema	0	0 (0.0)	0	0 (0.0)	2	2 (6.5)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Eczema asteatotic	0	0 (0.0)	1	1 (2.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Haemorrhage subcutaneous	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Pruritus	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Rash	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Social circumstances	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Overwork	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Surgical and medical procedures	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Large intestinal polypectomy	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-7 発現時期別の有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25													
	Week 24 to Week 28 N = 53		Week 28 to Week 32 N = 35		Week 32 to Week 36 N = 31		Week 36 to Week 40 N = 30		Week 40 to Week 44 N = 30		Week 44 to Week 48 N = 30		After Week 48 N = 27	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Vascular disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hypertension	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
White coat hypertension	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

MedDRA: Version 24.1
If a patient experiences the same PT multiple times, then the event was counted only first occurrence.
N: Number of Patients who administered until the relevant time.

表 2.7.4.2-8 発現時期別の副作用（SP）（NPC-25-3 試験）

System Organ Class / Preferred Term	NPC-25											
	Start of Administration to Week 4		Week 4 to Week 8		Week 8 to Week 12		Week 12 to Week 16		Week 16 to Week 20		Week 20 to Week 24	
	N = 107		N = 101		N = 99		N = 78		N = 67		N = 57	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Drug Reactions	12	8 (7.5)	7	7 (6.9)	6	6 (6.1)	3	3 (3.8)	3	3 (4.5)	1	1 (1.8)
Blood and lymphatic system disorders	0	0 (0.0)	2	2 (2.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Anaemia	0	0 (0.0)	2	2 (2.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Iron deficiency anaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gastrointestinal disorders	7	6 (5.6)	4	4 (4.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal discomfort	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain lower	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain upper	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Constipation	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Diarrhoea	2	2 (1.9)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gastric ulcer	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gastrooesophageal reflux disease	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Nausea	2	2 (1.9)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Vomiting	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hepatobiliary disorders	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hepatic function abnormal	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Investigations	0	0 (0.0)	1	1 (1.0)	4	4 (4.0)	2	2 (2.6)	2	2 (3.0)	1	1 (1.8)
Amylase increased	0	0 (0.0)	0	0 (0.0)	1	1 (1.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Blood copper decreased	0	0 (0.0)	1	1 (1.0)	3	3 (3.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Lipase increased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	1	1 (1.8)
Liver function test abnormal	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Weight decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Metabolism and nutrition disorders	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Decreased appetite	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-8 発現時期別の副作用（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25											
	Start of Administration to Week 4		Week 4 to Week 8		Week 8 to Week 12		Week 12 to Week 16		Week 16 to Week 20		Week 20 to Week 24	
	N = 107		N = 101		N = 99		N = 78		N = 67		N = 57	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Nervous system disorders	3	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dizziness	2	2 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Headache	1	1 (0.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Psychiatric disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Insomnia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.5)	0	0 (0.0)
Respiratory, thoracic and mediastinal disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)
Interstitial lung disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (1.3)	0	0 (0.0)	0	0 (0.0)

MedDRA: Version 24.1
If a patient experiences the same PT multiple times, then the event was counted only first occurrence.
N: Number of Patients who administered until the relevant time.

表 2.7.4.2-8 発現時期別の副作用（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25													
	Week 24 to Week 28 N = 53		Week 28 to Week 32 N = 35		Week 32 to Week 36 N = 31		Week 36 to Week 40 N = 30		Week 40 to Week 44 N = 30		Week 44 to Week 48 N = 30		After Week 48 N = 27	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Drug Reactions	3	2 (3.8)	2	2 (5.7)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	2	2 (7.4)
Blood and lymphatic system disorders	1	1 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Anaemia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Iron deficiency anaemia	1	1 (1.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gastrointestinal disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	1	1 (3.7)
Abdominal discomfort	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain lower	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Abdominal pain upper	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Constipation	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Diarrhoea	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Gastric ulcer	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.3)	0	0 (0.0)
Gastrooesophageal reflux disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Nausea	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Vomiting	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hepatobiliary disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Hepatic function abnormal	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Investigations	2	1 (1.9)	2	2 (5.7)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Amylase increased	1	1 (1.9)	1	1 (2.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Blood copper decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Lipase increased	1	1 (1.9)	1	1 (2.9)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Liver function test abnormal	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1	1 (3.7)
Weight decreased	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Metabolism and nutrition disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Decreased appetite	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

表 2.7.4.2-8 発現時期別の副作用（SP）（NPC-25-3 試験）（続き）

System Organ Class / Preferred Term	NPC-25													
	Week 24 to Week 28 N = 53		Week 28 to Week 32 N = 35		Week 32 to Week 36 N = 31		Week 36 to Week 40 N = 30		Week 40 to Week 44 N = 30		Week 44 to Week 48 N = 30		After Week 48 N = 27	
	n Events	n (%) Patients	n Events	n (%) Patients	n Events	n (%) Patients	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)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Dizziness	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Headache	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Psychiatric disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Insomnia	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Respiratory, thoracic and mediastinal disorders	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Interstitial lung disease	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

MedDRA: Version 24.1
If a patient experiences the same PT multiple times, then the event was counted only first occurrence.
N: Number of Patients who administered until the relevant time.

2.7.4.2.1.1.5 ノベルジン錠群との比較検討

2.7.4.1.2 項のとおり、ノベルジン錠群と同様の期間で評価することとし、本剤群について全期間ではなく有効性評価期で比較検討した。

本剤群及びノベルジン錠群で発現した有害事象を表 2.7.4.2-9 に、副作用を表 2.7.4.2-10 に示した。

表 2.7.4.2-9 本剤群及びノベルジン錠群で発現した有害事象（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25 N = 107		NOBELZIN N = 109	
	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Events	134	66 (61.7)	115	63 (57.8)
Blood and lymphatic system disorders	4	4 (3.7)	5	5 (4.6)
Anaemia	4	4 (3.7)	2	2 (1.8)
Iron deficiency anaemia	0	0 (0.0)	1	1 (0.9)
Nephrogenic anaemia	0	0 (0.0)	1	1 (0.9)
Pancytopenia	0	0 (0.0)	1	1 (0.9)
Cardiac disorders	2	2 (1.9)	0	0 (0.0)
Prinzmetal angina	1	1 (0.9)	0	0 (0.0)
Tachycardia	1	1 (0.9)	0	0 (0.0)
Ear and labyrinth disorders	0	0 (0.0)	1	1 (0.9)
Vertigo	0	0 (0.0)	1	1 (0.9)
Eye disorders	3	2 (1.9)	2	2 (1.8)
Blepharitis	1	1 (0.9)	0	0 (0.0)
Conjunctivitis allergic	0	0 (0.0)	1	1 (0.9)
Dry eye	1	1 (0.9)	0	0 (0.0)
Eye discharge	1	1 (0.9)	0	0 (0.0)
Normal tension glaucoma	0	0 (0.0)	1	1 (0.9)
Gastrointestinal disorders	24	20 (18.7)	36	28 (25.7)
Abdominal discomfort	3	3 (2.8)	3	3 (2.8)
Abdominal pain	1	1 (0.9)	1	1 (0.9)
Abdominal pain lower	1	1 (0.9)	0	0 (0.0)
Anal haemorrhage	0	0 (0.0)	1	1 (0.9)
Angular cheilitis	0	0 (0.0)	1	1 (0.9)
Aphthous ulcer	1	1 (0.9)	0	0 (0.0)
Ascites	0	0 (0.0)	1	1 (0.9)
Chronic gastritis	0	0 (0.0)	1	1 (0.9)
Colitis ulcerative	0	0 (0.0)	1	1 (0.9)
Constipation	2	2 (1.9)	0	0 (0.0)
Dental caries	0	0 (0.0)	1	1 (0.9)
Diarrhoea	3	3 (2.8)	3	3 (2.8)
Duodenal ulcer	1	1 (0.9)	0	0 (0.0)
Duodenitis	1	1 (0.9)	0	0 (0.0)
Gastric ulcer	0	0 (0.0)	1	1 (0.9)
Gastric ulcer haemorrhage	0	0 (0.0)	1	1 (0.9)
Gastritis	0	0 (0.0)	1	1 (0.9)
Gastrooesophageal reflux disease	1	1 (0.9)	0	0 (0.0)
Haemorrhoids	1	1 (0.9)	0	0 (0.0)
Nausea	5	4 (3.7)	8	7 (6.4)
Oesophageal varices haemorrhage	0	0 (0.0)	1	1 (0.9)
Pancreatic cyst	1	1 (0.9)	0	0 (0.0)
Stomatitis	0	0 (0.0)	3	3 (2.8)

表 2.7.4.2-9 本剤群及びノベルジン錠群で発現した有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107		NOBELZIN N = 109	
	n Events	n (%) Patients	n Events	n (%) Patients
Tooth disorder	1	1 (0.9)	0	0 (0.0)
Upper gastrointestinal haemorrhage	0	0 (0.0)	1	1 (0.9)
Varices oesophageal	0	0 (0.0)	2	2 (1.8)
Vomiting	2	2 (1.9)	5	4 (3.7)
General disorders and administration site conditions	8	8 (7.5)	4	4 (3.7)
Chest pain	0	0 (0.0)	1	1 (0.9)
Oedema peripheral	2	2 (1.9)	1	1 (0.9)
Pyrexia	6	6 (5.6)	1	1 (0.9)
Thirst	0	0 (0.0)	1	1 (0.9)
Hepatobiliary disorders	6	5 (4.7)	1	1 (0.9)
Cirrhosis alcoholic	1	1 (0.9)	0	0 (0.0)
Drug-induced liver injury	2	2 (1.9)	0	0 (0.0)
Hepatic function abnormal	3	3 (2.8)	0	0 (0.0)
Portal vein thrombosis	0	0 (0.0)	1	1 (0.9)
Infections and infestations	15	15 (14.0)	25	19 (17.4)
COVID-19	2	2 (1.9)	5	5 (4.6)
Cellulitis	0	0 (0.0)	1	1 (0.9)
Conjunctivitis	0	0 (0.0)	2	2 (1.8)
Coronavirus infection	0	0 (0.0)	1	1 (0.9)
Cystitis	1	1 (0.9)	1	1 (0.9)
Dermatophytosis of nail	0	0 (0.0)	1	1 (0.9)
Folliculitis	1	1 (0.9)	1	1 (0.9)
Gastroenteritis	1	1 (0.9)	1	1 (0.9)
Gingivitis	2	2 (1.9)	0	0 (0.0)
Herpes zoster	1	1 (0.9)	1	1 (0.9)
Nasopharyngitis	2	2 (1.9)	5	4 (3.7)
Oral herpes	0	0 (0.0)	1	1 (0.9)
Otitis externa	0	0 (0.0)	1	1 (0.9)
Paronychia	1	1 (0.9)	0	0 (0.0)
Sinusitis	0	0 (0.0)	3	3 (2.8)
Syphilis	0	0 (0.0)	1	1 (0.9)
Tinea pedis	1	1 (0.9)	0	0 (0.0)
Tonsillitis	1	1 (0.9)	0	0 (0.0)
Upper respiratory tract infection	1	1 (0.9)	0	0 (0.0)
Urinary tract infection	1	1 (0.9)	0	0 (0.0)
Injury, poisoning and procedural complications	5	5 (4.7)	5	5 (4.6)
Arthropod sting	1	1 (0.9)	2	2 (1.8)
Contusion	1	1 (0.9)	1	1 (0.9)
Foot fracture	1	1 (0.9)	0	0 (0.0)
Ligament sprain	1	1 (0.9)	0	0 (0.0)
Skin abrasion	0	0 (0.0)	1	1 (0.9)

表 2.7.4.2-9 本剤群及びノベルジン錠群で発現した有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107		NOBELZIN N = 109	
	n Events	n (%) Patients	n Events	n (%) Patients
Spinal compression fracture	1	1 (0.9)	0	0 (0.0)
Traumatic haematoma	0	0 (0.0)	1	1 (0.9)
Investigations	13	11 (10.3)	15	12 (11.0)
Alanine aminotransferase increased	1	1 (0.9)	0	0 (0.0)
Amylase increased	1	1 (0.9)	3	3 (2.8)
Aspartate aminotransferase increased	1	1 (0.9)	1	1 (0.9)
Blood copper decreased	5	5 (4.7)	4	4 (3.7)
Blood potassium decreased	1	1 (0.9)	0	0 (0.0)
Blood pressure decreased	0	0 (0.0)	1	1 (0.9)
Blood pressure increased	1	1 (0.9)	1	1 (0.9)
Blood triglycerides increased	0	0 (0.0)	1	1 (0.9)
Glucose urine present	0	0 (0.0)	1	1 (0.9)
Intraocular pressure increased	1	1 (0.9)	0	0 (0.0)
Lipase increased	1	1 (0.9)	2	2 (1.8)
Occult blood positive	0	0 (0.0)	1	1 (0.9)
Weight decreased	1	1 (0.9)	0	0 (0.0)
Metabolism and nutrition disorders	12	8 (7.5)	2	2 (1.8)
Decreased appetite	2	2 (1.9)	1	1 (0.9)
Diabetes mellitus	1	1 (0.9)	0	0 (0.0)
Hyperammonaemia	1	1 (0.9)	0	0 (0.0)
Hyperglycaemia	1	1 (0.9)	0	0 (0.0)
Hypertriglyceridaemia	1	1 (0.9)	0	0 (0.0)
Hyperuricaemia	1	1 (0.9)	1	1 (0.9)
Hypocalcaemia	1	1 (0.9)	0	0 (0.0)
Hypoglycaemia	2	1 (0.9)	0	0 (0.0)
Type 2 diabetes mellitus	2	2 (1.9)	0	0 (0.0)
Musculoskeletal and connective tissue disorders	10	9 (8.4)	4	4 (3.7)
Arthralgia	2	2 (1.9)	0	0 (0.0)
Back pain	3	3 (2.8)	0	0 (0.0)
Fasciitis	0	0 (0.0)	1	1 (0.9)
Muscle spasms	0	0 (0.0)	1	1 (0.9)
Osteoporosis	1	1 (0.9)	0	0 (0.0)
Pain in jaw	0	0 (0.0)	1	1 (0.9)
Periarthritis	1	1 (0.9)	0	0 (0.0)
Rheumatoid arthritis	1	1 (0.9)	0	0 (0.0)
Spinal osteoarthritis	0	0 (0.0)	1	1 (0.9)
Tendonitis	1	1 (0.9)	0	0 (0.0)
Trigger finger	1	1 (0.9)	0	0 (0.0)
Nervous system disorders	11	9 (8.4)	3	3 (2.8)
Cerebral haemorrhage	1	1 (0.9)	0	0 (0.0)
Cerebral infarction	2	1 (0.9)	0	0 (0.0)

表 2.7.4.2-9 本剤群及びノベルジン錠群で発現した有害事象（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107		NOBELZIN N = 109	
	n Events	n (%) Patients	n Events	n (%) Patients
Diabetic neuropathy	0	0 (0.0)	1	1 (0.9)
Dizziness	3	3 (2.8)	0	0 (0.0)
Dizziness postural	0	0 (0.0)	1	1 (0.9)
Headache	3	3 (2.8)	0	0 (0.0)
Hypoaesthesia	1	1 (0.9)	1	1 (0.9)
Sciatica	1	1 (0.9)	0	0 (0.0)
Pregnancy, puerperium and perinatal conditions	0	0 (0.0)	1	1 (0.9)
Ectopic pregnancy	0	0 (0.0)	1	1 (0.9)
Psychiatric disorders	1	1 (0.9)	0	0 (0.0)
Insomnia	1	1 (0.9)	0	0 (0.0)
Renal and urinary disorders	2	2 (1.9)	0	0 (0.0)
Haematuria	1	1 (0.9)	0	0 (0.0)
Renal impairment	1	1 (0.9)	0	0 (0.0)
Reproductive system and breast disorders	0	0 (0.0)	2	2 (1.8)
Cervix adenomatous polyp	0	0 (0.0)	1	1 (0.9)
Uterine prolapse	0	0 (0.0)	1	1 (0.9)
Respiratory, thoracic and mediastinal disorders	6	4 (3.7)	1	1 (0.9)
Epistaxis	2	1 (0.9)	1	1 (0.9)
Interstitial lung disease	1	1 (0.9)	0	0 (0.0)
Laryngeal discomfort	1	1 (0.9)	0	0 (0.0)
Oropharyngeal discomfort	1	1 (0.9)	0	0 (0.0)
Oropharyngeal pain	1	1 (0.9)	0	0 (0.0)
Skin and subcutaneous tissue disorders	9	7 (6.5)	5	5 (4.6)
Blister	1	1 (0.9)	0	0 (0.0)
Dermatitis	1	1 (0.9)	0	0 (0.0)
Dermatitis acneiform	1	1 (0.9)	0	0 (0.0)
Drug eruption	1	1 (0.9)	0	0 (0.0)
Eczema	1	1 (0.9)	1	1 (0.9)
Haemorrhage subcutaneous	1	1 (0.9)	0	0 (0.0)
Pruritus	2	2 (1.9)	1	1 (0.9)
Rash	1	1 (0.9)	2	2 (1.8)
Solar dermatitis	0	0 (0.0)	1	1 (0.9)
Surgical and medical procedures	1	1 (0.9)	1	1 (0.9)
Large intestinal polypectomy	1	1 (0.9)	0	0 (0.0)
Rehabilitation therapy	0	0 (0.0)	1	1 (0.9)
Vascular disorders	2	2 (1.9)	2	2 (1.8)
Hypertension	2	2 (1.9)	0	0 (0.0)
Internal haemorrhage	0	0 (0.0)	2	2 (1.8)

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表 2.7.4.2-10 本剤群及びノベルジン錠群で発現した副作用（SP）（NPC-25-3 試験）

System Organ Class Preferred Term	NPC-25 N = 107		NOBELZIN N = 109	
	n Events	n (%) Patients	n Events	n (%) Patients
Any Adverse Drug Reactions	31	22 (20.6)	36	25 (22.9)
Blood and lymphatic system disorders	3	3 (2.8)	2	2 (1.8)
Anaemia	3	3 (2.8)	0	0 (0.0)
Nephrogenic anaemia	0	0 (0.0)	1	1 (0.9)
Pancytopenia	0	0 (0.0)	1	1 (0.9)
Ear and labyrinth disorders	0	0 (0.0)	1	1 (0.9)
Vertigo	0	0 (0.0)	1	1 (0.9)
Gastrointestinal disorders	13	10 (9.3)	19	13 (11.9)
Abdominal discomfort	2	2 (1.9)	2	2 (1.8)
Abdominal pain lower	1	1 (0.9)	0	0 (0.0)
Constipation	1	1 (0.9)	0	0 (0.0)
Diarrhoea	3	3 (2.8)	3	3 (2.8)
Gastric ulcer haemorrhage	0	0 (0.0)	1	1 (0.9)
Gastritis	0	0 (0.0)	1	1 (0.9)
Gastrooesophageal reflux disease	1	1 (0.9)	0	0 (0.0)
Nausea	4	3 (2.8)	8	7 (6.4)
Vomiting	1	1 (0.9)	4	3 (2.8)
Hepatobiliary disorders	1	1 (0.9)	0	0 (0.0)
Hepatic function abnormal	1	1 (0.9)	0	0 (0.0)
Infections and infestations	0	0 (0.0)	1	1 (0.9)
Gastroenteritis	0	0 (0.0)	1	1 (0.9)
Investigations	8	8 (7.5)	10	8 (7.3)
Amylase increased	1	1 (0.9)	3	3 (2.8)
Aspartate aminotransferase increased	0	0 (0.0)	1	1 (0.9)
Blood copper decreased	5	5 (4.7)	4	4 (3.7)
Blood pressure increased	0	0 (0.0)	1	1 (0.9)
Lipase increased	1	1 (0.9)	1	1 (0.9)
Weight decreased	1	1 (0.9)	0	0 (0.0)
Metabolism and nutrition disorders	1	1 (0.9)	0	0 (0.0)
Decreased appetite	1	1 (0.9)	0	0 (0.0)
Nervous system disorders	3	2 (1.9)	1	1 (0.9)
Dizziness	2	2 (1.9)	0	0 (0.0)
Headache	1	1 (0.9)	0	0 (0.0)
Hypoaesthesia	0	0 (0.0)	1	1 (0.9)
Psychiatric disorders	1	1 (0.9)	0	0 (0.0)
Insomnia	1	1 (0.9)	0	0 (0.0)
Respiratory, thoracic and mediastinal disorders	1	1 (0.9)	0	0 (0.0)
Interstitial lung disease	1	1 (0.9)	0	0 (0.0)
Skin and subcutaneous tissue disorders	0	0 (0.0)	1	1 (0.9)
Rash	0	0 (0.0)	1	1 (0.9)

表 2.7.4.2-10 本剤群及びノベルジン錠群で発現した副作用（SP）（NPC-25-3 試験）（続き）

System Organ Class Preferred Term	NPC-25 N = 107		NOBELZIN N = 109	
	n Events	n (%) Patients	n Events	n (%) Patients
Vascular disorders	0	0 (0.0)	1	1 (0.9)
Internal haemorrhage	0	0 (0.0)	1	1 (0.9)

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2.7.4.2.1.1.5.1 全体

(1) 有害事象

有害事象の発現率は、本剤群で 61.7%（66/107 例）、ノベルジン錠群で 57.8%（63/109 例）であった。ノベルジン錠群に比べ本剤群で 2%以上発現率が高い有害事象は、発熱、肝機能異常、背部痛、浮動性めまい、頭痛であった。本剤群に比べノベルジン錠群で 2%以上発現率が高い有害事象は、悪心、口内炎、ＣＯＶＩＤ－１９、副鼻腔炎であった。

(2) 副作用

副作用の発現率は、本剤群で 20.6%（22/107 例）、ノベルジン錠群で 22.9%（25/109 例）であった。ノベルジン錠群に比べ本剤群で 2%以上発現率が高い副作用は、貧血であった。本剤群に比べノベルジン錠群で 2%以上発現率が高い副作用は、悪心であった。

2.7.4.2.1.1.5.2 消化器関連症状

亜鉛製剤の代表的な副作用として悪心・嘔吐があり、これらの副作用は患者の服薬アドヒアランスを低下させる。悪心・嘔吐を含めた消化器症状関連の有害事象及び副作用についてノベルジン錠群との比較検討を行った。MedDRA/SOC: 10017947（Gastrointestinal disorders(胃腸障害)）及び MedDRA/PT：10017888（Gastroenteritis(胃腸炎)）に該当する有害事象及び副作用を消化器症状関連とした。

(1) 有害事象

当該有害事象の発現率は本剤群で 18.7%（20/107 例）、ノベルジン錠群で 26.6%（29/109 例）であった。当該有害事象の中でノベルジン錠群に比べ本剤群で 2%以上発現率が高い有害事象は認められなかった。本剤群に比べノベルジン錠群で 2%以上発現率が高い有害事象は、悪心及び口内炎であった。なお、亜鉛製剤の代表的な副作用である悪心の有害事象発現率は本剤群で 3.7%（4/107 例）、ノベルジン錠群で 6.4%（7/109 例）であり、嘔吐の有害事象発現率は本剤群で 1.9%（2/107 例）、ノベルジン錠群で 3.7%（4/109 例）であった。

(2) 副作用

当該副作用の発現率は本剤群で 9.3%（10/107 例）、ノベルジン錠群で 12.8%（14/109 例）であった。当該副作用の中でノベルジン錠群に比べ本剤群で 2%以上発現率が高い副作用は認められなかった。本剤群に比べノベルジン錠群で 2%以上発現率が高い副作用は、悪心であった。なお、亜鉛製剤の代表的な副作用である悪心の副作用発現率は本剤群で 2.8%（3/107 例）、ノベルジン錠群で 6.4%（7/109 例）であり、嘔吐の副作用発現率は本剤群で 0.9%（1/107 例）、ノベルジン錠群で 2.8%（3/109 例）であった。

2.7.4.2.1.1.5.3 血中銅減少

亜鉛製剤で注意すべき副作用として銅欠乏症が挙げられる。関連するイベントとして血中銅減少についてノベルジン錠群との比較検討を行った。なお、銅欠乏症は本剤群及びノベルジン錠群のいずれにおいても認められなかった。

(1) 有害事象

有害事象である血中銅減少の発現率は本剤群で 4.7%（5/107 例）、ノベルジン錠群で 3.7%（4/109 例）であり、同程度であった。

(2) 副作用

副作用である血中銅減少の発現率は本剤群で 4.7%（5/107 例）、ノベルジン錠群で 3.7%（4/109 例）であり、同程度であった。

2.7.4.2.1.2 死亡

NPC-25-3 試験では、本剤群及びノベルジン錠群のいずれにおいても死亡に該当する有害事象は認められなかった。本剤群において重篤な有害事象であるメレナの追跡調査中に死亡した症例が 1 例認められた（被験者番号：[redacted]）。投与開始後 191 日目に下血を認め、他院に入院し、投与開始後 205 日目に治験薬を服用していないことを聴取した。その後も、被験者は多忙にて治験実施医療機関を来院できず、治験責任医師は他院での精査結果を入手できなかった。投与開始後 343 日目に被験者家族より被験者が死亡したとの報告を受けた。被験者の死因を確認することはできなかったが、治験責任医師は、治験中止から約 3 ヵ月後（治験薬投与終了から約 4 ヵ月後）に死亡したこと、下血と治験薬には因果関係がないと考えることから、死亡と治験との間に因果関係はないと判断した。

2.7.4.2.1.3 その他の重篤な有害事象

NPC-25-3 試験で発現した重篤な有害事象の一覧を表 2.7.4.2-11 に示した。本剤群の重篤な有害事象の発現率は、9.3%（10/107 例）であった。ノベルジン錠群の発現率は 8.3%（9/109 例）であり、ノベルジン錠群と同様の評価期間である有効性評価期での本剤群の重篤な有害事象の発現率は 4.7%（5/107 例）であった。

重篤な有害事象の内訳は、本剤群で脳出血、小脳性運動失調、十二指腸潰瘍、胃腸炎、高血糖、大腸ポリープ切除、クローン病、脱水、メレナ、プリンツメタル狭心症、四肢膿瘍が各 1 件の計 11 件（10 例）、ノベルジン錠群で食道静脈瘤出血、腹水、リハビリテーション療法、嘔吐、上部消化管出血、異所性妊娠、出血性胃潰瘍、汎血球減少症、食道静脈瘤、貧血が各 1 件の計 10 件（9 例）であった。いずれも重篤性は「治療のために入院が必要なもの」であった。本剤群で因果関係ありと判定された有害事象は認められなかった。ノベルジン錠群で認められた嘔吐、出血性胃潰瘍、汎血球減少症は、因果関係ありと判定された。その他の有害事象は、治験薬との因果関係は否定された。

経時的に重篤な有害事象の発現率が上昇する傾向は認められなかった。

表 2.7.4.2-11 重篤な有害事象の一覧（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]-[redacted] 2	Cerebral hemorrhage(left thalamusCorona radiata) Nervous system disorders Cerebral haemorrhage	20[redacted] (32) 20[redacted] (91)	Drug Withdrawn N Recovered/Resolved with Sequelae	Y Requires or Prolongs Hospitalization Severe	Not Related Complications (Hypertension)
	[redacted]-[redacted] 5	cerebellar ataxia Nervous system disorders Cerebellar ataxia	20[redacted] (194) 20[redacted] (294)	Drug Withdrawn Y Not Recovered/Not Resolved	Y Requires or Prolongs Hospitalization Moderate	Not Related Other (Due to benign brain tumor)
	[redacted]-[redacted] 1	Duodenal ulcer aggravated Gastrointestinal disorders Duodenal ulcer	20[redacted] (4) 20[redacted] (13)	Dose Not Changed Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Not Related Complications (Duodenal ulcer)
	[redacted]-[redacted] 1	Acute gastroenteritis Infections and infestations Gastroenteritis	20[redacted] (10) 20[redacted] (16)	Drug Interrupted Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Not Related Other (Because it is unlikely that zinc preparations may cause gastroenteritis.)
	3	Hyperglycaemia Metabolism and nutrition disorders Hyperglycaemia	20[redacted] (44) 20[redacted] (64)	Drug Withdrawn N Recovering/Resolving	Y Requires or Prolongs Hospitalization Moderate	Not Related Other (The action mechanism of the investigational drug doesn't cause hyperglycaemia.)
	[redacted]-[redacted] 1	Large intestinal polypectomy Surgical and medical procedures Large intestinal polypectomy	20[redacted] (89) 20[redacted] (91)	Dose Not Changed N Recovered/Resolved	Y Requires or Prolongs Hospitalization Mild	Not Related Complications (Large intestine polyp)

表 2.7.4.2-11 重篤な有害事象の一覧（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
	[redacted] 2	exacerbation of crohn's disease Gastrointestinal disorders Crohn's disease	20[redacted] (277) 20[redacted] (287)	Dose Not Changed Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Not Related Complications (Crohn's disease)
	[redacted] 1	Dehydration Metabolism and nutrition disorders Dehydration	20[redacted] (345) 20[redacted] (347)	Not Applicable Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Severe	Not Related Other (As the subject claimed, it is presumed that it was caused by mental and physical fatigue due to the misfortune of her relatives.)
	[redacted] 5	Melaena Gastrointestinal disorders Melaena	20[redacted] (191) 20[redacted] (364)	Dose Not Changed N Unknown	Y Requires or Prolongs Hospitalization Severe	Not Related Complications (Haemorrhagic anaemia)
	[redacted] 2	Coronary spastic angina Cardiac disorders Prinzmetal angina	20[redacted] (10) 20[redacted] (31)	Dose Not Changed N Recovering/Resolving	Y Requires or Prolongs Hospitalization Moderate	Not Related Complications (Coronary spastic angina)
	[redacted] 1	buttock subcutaneous abscess Infections and infestations Abscess limb	20[redacted] (271) 20[redacted] (320)	Dose Not Changed Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Not Related Other (Recurrent events)

表 2.7.4.2-11 重篤な有害事象の一覧（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] 1	Oesophageal varices ruptured Gastrointestinal disorders Oesophageal varices haemorrhage	20[redacted] (6) 20[redacted] (19)	Drug Interrupted Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Not Related Complications (Gastroesophageal varices)
	[redacted] 1	Refractory ascites Gastrointestinal disorders Ascites	20[redacted] (7) 20[redacted] (113)	Dose Not Changed Y Recovering/Resolving	Y Requires or Prolongs Hospitalization Moderate	Not Related Complications (Autoimmune hepatitis)
	[redacted] 1	Rehabilitation hospitalization for Parkinson's disease Surgical and medical procedures Rehabilitation therapy	20[redacted] (115) 20[redacted] (150)	Dose Not Changed N Recovered/Resolved	Y Requires or Prolongs Hospitalization Mild	Not Related Complications (Parkinson's disease)
	[redacted] 1	Vomiting Gastrointestinal disorders Vomiting	20[redacted] (136) 20[redacted] (143)	Drug Withdrawn N Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Related
	[redacted] 2	Upper gastrointestinal hemorrhage Gastrointestinal disorders Upper gastrointestinal haemorrhage	20[redacted] (119) 20[redacted] (126)	Drug Interrupted Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Not Related Complications (hepatic cirrhosis)

表 2.7.4.2-11 重篤な有害事象の一覧（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
	[redacted] 4	Extrauterine pregnancy Pregnancy, puerperium and perinatal conditions Ectopic pregnancy	20[redacted] (61) 20[redacted] (85)	Drug Withdrawn Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Severe	Not Related Other (The doctor in charge at another hospital cannot determine the cause of this SAE. This SAE is considered to be possible accidental. Therefore, we considered this SAE is not related to IMP.)
	[redacted] 8	Gastric ulcer haemorrhage Gastrointestinal disorders Gastric ulcer haemorrhage	20[redacted] (64) 20[redacted] (170)	Drug Withdrawn Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Related
	[redacted] 1	Pancytopenia Blood and lymphatic system disorders Pancytopenia	20[redacted] (81) 20[redacted] (218)	Drug Withdrawn N Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Related
	[redacted] 1	Exacerbation of esophageal varices Gastrointestinal disorders Varices oesophageal	20[redacted] (13) 20[redacted] (22)	Drug Interrupted Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Not Related Complications (Esophageal / gastric varices)

表 2.7.4.2-11 重篤な有害事象の一覧（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
	2	Anemia Blood and lymphatic system disorders Anaemia	20[redacted] (34) 20[redacted] (190)	Dose Not Changed Y Recovering/Resolving	Y Requires or Prolongs Hospitalization Moderate	Not Related Other (Due to unexplained bleeding.2022/05/06 From blood sampling data, there is no problem with serum zinc and serum copper)

1) : Number of days from first study treatment
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2.7.4.2.1.4 その他の重要な有害事象

2.7.4.2.1.4.1 治験薬投与中止に至った有害事象

NPC-25-3 試験で発現した治験薬投与中止に至った有害事象の一覧を表 2.7.4.2-12 に示した。なお、重篤な有害事象に伴い投与中止となった症例を含めて示した。本剤群の治験薬投与中止に至った有害事象の発現率は、4.7%（5/107 例）であった。ノベルジン錠群の発現率は 7.3%（8/109 例）であり、ノベルジン錠群と同様の評価期間である有効性評価期での本剤群の治験薬投与中止に至った有害事象の発現率は 3.7%（4/107 例）であった。本剤群の治験薬投与中止に至った有害事象の内訳は脳出血、小脳性運動失調、アルコール性肝硬変、肝機能異常、高血糖が各 1 例であった。肝機能異常は、因果関係ありと判定された。その他の有害事象は、治験薬との因果関係は否定された。

表 2.7.4.2-12 治験薬投与中止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] 2	Cerebral hemorrhage(left thalamusCorona radiata) Nervous system disorders Cerebral haemorrhage	20[redacted] (32) 20[redacted] (91)	Drug Withdrawn N Recovered/Resolved with Sequelae	Y Requires or Prolongs Hospitalization Severe	Not Related Complications (Hypertension)
	[redacted] 5	cerebellar ataxia Nervous system disorders Cerebellar ataxia	20[redacted] (194) 20[redacted] (294)	Drug Withdrawn Y Not Recovered/Not Resolved	Y Requires or Prolongs Hospitalization Moderate	Not Related Other (Due to benign brain tumor)
	[redacted] 4	Worsening of cirrhosis alcoholic Hepatobiliary disorders Cirrhosis alcoholic	20[redacted] (120) 20[redacted] (148)	Drug Withdrawn N Not Recovered/Not Resolved	N - Moderate	Not Related Complications (Cirrhosis alcoholic)
	[redacted] 3	Hyperglycaemia Metabolism and nutrition disorders Hyperglycaemia	20[redacted] (44) 20[redacted] (64)	Drug Withdrawn N Recovering/Resolving	Y Requires or Prolongs Hospitalization Moderate	Not Related Other (The action mechanism of the investigational drug doesn't cause hyperglycaemia.)
	[redacted] 1	Hepatic function disorder Hepatobiliary disorders Hepatic function abnormal	20[redacted] (22) 20[redacted] (47)	Drug Withdrawn N Recovered/Resolved	N - Moderate	Related
NOBELZIN	[redacted] 1	Serum copper decreased Investigations Blood copper decreased	20[redacted] (141) 20[redacted] (176)	Drug Withdrawn N Recovered/Resolved	N - Mild	Related
	[redacted] 1	Vomiting Gastrointestinal disorders Vomiting	20[redacted] (136) 20[redacted] (143)	Drug Withdrawn N Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Related

表 2.7.4.2-12 治験薬投与中止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
	[redacted] 4	Extrauterine pregnancy Pregnancy, puerperium and perinatal conditions Ectopic pregnancy	20[redacted] (61) 20[redacted] (85)	Drug Withdrawn Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Severe	Not Related Other (The doctor in charge at another hospital cannot determine the cause of this SAE. This SAE is considered to be possible accidental. Therefore, we considered this SAE is not related to IMP.)
	[redacted] 1	Worsening of renal anemia Blood and lymphatic system disorders Nephrogenic anaemia	20[redacted] (25) 20[redacted] (246)	Drug Withdrawn N Not Recovered/Not Resolved	N - Moderate	Related
	[redacted] 8	Gastric ulcer haemorrhage Gastrointestinal disorders Gastric ulcer haemorrhage	20[redacted] (64) 20[redacted] (170)	Drug Withdrawn Y Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Related
	[redacted] 1	Pancytopenia Blood and lymphatic system disorders Pancytopenia	20[redacted] (81) 20[redacted] (218)	Drug Withdrawn N Recovered/Resolved	Y Requires or Prolongs Hospitalization Moderate	Related
	[redacted] 1	Nausea Gastrointestinal disorders Nausea	20[redacted] (2) 20[redacted] (6)	Drug Withdrawn N Recovered/Resolved	N - Mild	Related

表 2.7.4.2-12 治験薬投与中止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
	[redacted]-[redacted] 1	Acute Gastroenteritis Infections and infestations Gastroenteritis	20[redacted] (22) 20[redacted] (42)	Drug Withdrawn Y Recovered/Resolved	N - Mild	Related

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

2.7.4.2.1.4.2 治験薬の減量に至った有害事象

NPC-25-3 試験で発現した治験薬の減量に至った有害事象の一覧を表 2.7.4.2-13 に示した。本剤群の治験薬の減量に至った有害事象の発現率は、4.7%（5/107 例）であった。ノベルジン錠群の発現率は 3.7%（4/109 例）であり、ノベルジン錠群と同様の評価期間である有効性評価期での本剤群の治験薬の減量に至った有害事象の発現率は 3.7%（4/107 例）であった。本剤群の治験薬の減量に至った有害事象の内訳は悪心 2 例、血中銅減少、リパーゼ増加、アミラーゼ増加、腹部不快感、上腹部痛、下痢が各 1 例であった。いずれの有害事象も因果関係ありと判定された。