表 2.7.4-55 全治験期間のペグセタコプラン単独投与群の被験者の 2%以上で発現した TEAE の発現時期（3 ヵ月毎）（APL2-302 試験：安全性解析対象集団）

	Overall APL-2 Monotherapy (RCP+OLA)					
	Total	To Month 3	Month 4 to 6	Month 7 to 9	Month 10 to 12	Month 13 or later
Number of subjects evaluated	80	80	76	72	36	3
All AEs	78 (97.5 %)	68	55	42	20	0
Number of deaths	1 (1.3 %)	0	0	0	1	0
Number of subjects with SAEs other than Deaths	23 (28.8 %)	13	6	8	2	0
Number of subjects with AE leading to study discontinuation	11 (13.8 %)	5	2	2	2	0
Haemolysis	19 (23.8 %)	9	9	3	1	0
Diarrhoea	17 (21.3 %)	13	4	3	1	0
Nasopharyngitis	14 (17.5 %)	7	4	5	0	0
Injection site erythema	13 (16.3 %)	11	6	4	2	0
Cough	10 (12.5 %)	4	2	3	1	0
Fatigue	10 (12.5 %)	7	3	1	0	0
Headache	10 (12.5 %)	5	4	2	1	0
Upper respiratory tract infection	9 (11.3 %)	4	1	3	1	0
Abdominal pain	8 (10.0 %)	4	1	3	0	0
Arthralgia	8 (10.0 %)	2	4	3	0	0
Pyrexia	8 (10.0 %)	4	2	2	1	0
Urinary tract infection	7 (8.8 %)	1	3	3	0	0
Hypertension	6 (7.5 %)	3	2	1	1	0
Injection site pruritus	6 (7.5 %)	3	3	0	1	0
Oral herpes	6 (7.5 %)	3	2	3	1	0
Oropharyngeal pain	6 (7.5 %)	1	4	1	0	0
Pain in extremity	6 (7.5 %)	3	3	0	1	0
Thrombocytopenia	6 (7.5 %)	5	1	0	1	0
Asthenia	5 (6.3 %)	3	2	2	0	0
Back pain	5 (6.3 %)	4	1	1	0	0
Contusion	5 (6.3 %)	3	1	1	0	0
Injection site bruising	5 (6.3 %)	3	2	1	1	0
Injection site induration	5 (6.3 %)	5	4	3	3	0
Injection site reaction	5 (6.3 %)	5	1	0	0	0
Injection site swelling	5 (6.3 %)	4	3	0	0	0
Myalgia	5 (6.3 %)	1	3	1	0	0
Abdominal distension	4 (5.0 %)	1	1	2	0	0
Acute kidney injury	4 (5.0 %)	0	2	2	1	0
Anxiety	4 (5.0 %)	0	3	1	0	0
Epistaxis	4 (5.0 %)	0	2	2	0	0
Erythema	4 (5.0 %)	3	0	1	1	0
Gastroenteritis	4 (5.0 %)	3	0	1	0	0
Injection site pain	4 (5.0 %)	3	2	2	1	0
Sinusitis	4 (5.0 %)	0	2	2	0	0
Vaccination complication	4 (5.0 %)	2	2	0	0	0
Alanine aminotransferase increased	3 (3.8 %)	2	1	0	0	0
Angina pectoris	3 (3.8 %)	0	1	2	0	0
Dizziness	3 (3.8 %)	1	2	0	1	0
Dyspnoea	3 (3.8 %)	1	2	0	0	0
Haematuria	3 (3.8 %)	1	2	1	1	0

	Overall APL-2 Monotherapy (RCP+OLA)					
	Total	To Month 3	Month 4 to 6	Month 7 to 9	Month 10 to 12	Month 13 or later
Hyperbilirubinaemia	3 (3.8 %)	0	2	1	1	0
Influenza like illness	3 (3.8 %)	1	1	1	0	0
Injection site haemorrhage	3 (3.8 %)	2	3	0	0	0
Muscle spasms	3 (3.8 %)	2	1	0	0	0
Nausea	3 (3.8 %)	2	2	1	0	0
Neck pain	3 (3.8 %)	3	0	0	0	0
Neutropenia	3 (3.8 %)	1	1	1	0	0
Oedema	3 (3.8 %)	2	0	1	0	0
Pain	3 (3.8 %)	1	2	2	1	0
Peripheral swelling	3 (3.8 %)	3	0	0	0	0
Rhinitis	3 (3.8 %)	2	1	0	0	0
Serum ferritin increased	3 (3.8 %)	2	0	1	0	0
Vomiting	3 (3.8 %)	1	1	1	0	0
Abdominal discomfort	2 (2.5 %)	2	0	0	0	0
Abdominal pain upper	2 (2.5 %)	1	2	0	0	0
Acute respiratory failure	2 (2.5 %)	1	1	1	1	0
Anaemia	2 (2.5 %)	1	0	0	1	0
Basal cell carcinoma	2 (2.5 %)	0	2	0	0	0
Blood creatinine increased	2 (2.5 %)	1	0	1	0	0
Blood lactate dehydrogenase increased	2 (2.5 %)	0	1	0	1	0
Chest pain	2 (2.5 %)	1	1	0	0	0
Cholelithiasis	2 (2.5 %)	2	0	0	0	0
Chromaturia	2 (2.5 %)	2	0	0	0	0
Constipation	2 (2.5 %)	1	0	1	0	0
Decreased appetite	2 (2.5 %)	1	1	0	0	0
Dental caries	2 (2.5 %)	1	1	0	1	0
Dyspepsia	2 (2.5 %)	2	0	0	0	0
Ear discomfort	2 (2.5 %)	2	0	0	0	0
Febrile infection	2 (2.5 %)	0	1	1	0	0
Gastrointestinal haemorrhage	2 (2.5 %)	0	2	0	0	0
Gastrointestinal infection	2 (2.5 %)	2	0	0	0	0
Haemolytic anaemia	2 (2.5 %)	0	0	2	0	0
Hiccups	2 (2.5 %)	0	0	1	1	0
Hyperthermia	2 (2.5 %)	0	0	1	1	0
Hypoalbuminaemia	2 (2.5 %)	1	0	1	0	0
Hypokalaemia	2 (2.5 %)	0	1	0	1	0
Nasal congestion	2 (2.5 %)	2	1	0	0	0
Night sweats	2 (2.5 %)	0	2	0	0	0
Non-cardiac chest pain	2 (2.5 %)	1	0	1	0	0
Ocular icterus	2 (2.5 %)	2	1	0	0	0
Respiratory tract infection	2 (2.5 %)	0	1	1	0	0
Rhinitis allergic	2 (2.5 %)	0	0	2	0	0
Sciatica	2 (2.5 %)	0	0	1	1	0
Sleep disorder	2 (2.5 %)	0	1	0	1	0
Vertigo	2 (2.5 %)	2	1	0	0	0

Source: pmda_m274_t_teaesum_3m_302W48.SAS 2022-02-10T14:51:00 Z9FRBE.

Abbreviations: ECU, Eculizumab; OLA, Open label APL-2; RCP, Randomized controlled.

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.

Preferred terms are only included for AEs occuring in at least 2% of patients in the total column. Catagorization of AEs include all occurring AEs.

A subject is included until the last date of APL-2 treatment in OLA + 30 days or to the end of study participation, what ever comes first.

表 2.7.4-56 年齢（65 歳以下、65 歳超）による TEAE の部分集団解析（APL2-302 試験：安全性解析対象集団）

Table 3.10.1 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Age group (Safety Set) - CSR Table 14.3.1.1.4 - Age group: <=65 years

	Statistics	APL-2 + Eculizumab [1] (N=63)	APL-2 Group [2] (N=31)	Eculizumab Group [2] (N=32)	Total OLP APL-2 Group [3] (N=61)	Overall APL-2 Monotherapy (RCP+OLP) (N=63)
Any TEAEs	n (%)	56 (88.9)	28 (90.3)	29 (90.6)	55 (90.2)	61 (96.8)
Total Events	n	304	224	126	547	773
Total Unique Events	n	102	81	64	161	196
TEAEs by Closest Relationship to APL-2						
Related	n (%)	38 (60.3)	9 (29.0)	NA	25 (41.0)	29 (46.0)
Unrelated	n (%)	18 (28.6)	19 (61.3)	NA	30 (49.2)	32 (50.8)
TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	4 (6.3)	NA	6 (18.8)	NA	NA
Unrelated	n (%)	52 (82.5)	NA	23 (71.9)	NA	NA

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted] and [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4a1.sas
Output: t-14-3-1-1-4a1. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:10 Page 1/4

Table 3.10.1 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Age group (Safety Set) - CSR Table 14.3.1.1.4 - Age group: <=65 years

	Statistics	APL-2 + Eculizumab [1] (N=63)	APL-2 Group [2] (N=31)	Eculizumab Group [2] (N=32)	Total OLP APL-2 Group [3] (N=61)	Overall APL-2 Monotherapy (RCP+OLP) (N=63)
TEAEs by Closest Relationship to Infusion						
Related	n (%)	29 (46.0)	5 (16.1)	0	9 (14.8)	12 (19.0)
Unrelated	n (%)	27 (42.9)	23 (74.2)	29 (90.6)	46 (75.4)	49 (77.8)
Serious TEAEs	n (%)	4 (6.3)	6 (19.4)	4 (12.5)	12 (19.7)	18 (28.6)
Total Events	n	4	7	8	16	23
Total Unique Events	n	3	6	8	12	16
Serious TEAEs by Closest Relationship to APL-2						
Related	n (%)	1 (1.6)	1 (3.2)	NA	2 (3.3)	3 (4.8)
Unrelated	n (%)	3 (4.8)	5 (16.1)	NA	10 (16.4)	15 (23.8)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4a1.sas
Output: t-14-3-1-1-4a1. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:10 Page 2/4

Table 3.10.1 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Age group (Safety Set) - CSR Table 14.3.1.1.4 - Age group: <=65 years

	Statistics	APL-2 + Eculizumab [1] (N=63)	APL-2 Group [2] (N=31)	Eculizumab Group [2] (N=32)	Total OLP APL-2 Group [3] (N=61)	Overall APL-2 Monotherapy (RCP+OLP) (N=63)
Serious TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	4 (6.3)	NA	4 (12.5)	NA	NA
Serious TEAEs by Closest Relationship to Infusion						
Related	n (%)	0	0	0	0	0
Unrelated	n (%)	4 (6.3)	6 (19.4)	4 (12.5)	12 (19.7)	18 (28.6)
TEAEs by Maximum Severity						
Mild	n (%)	41 (65.1)	14 (45.2)	11 (34.4)	26 (42.6)	25 (39.7)
Moderate	n (%)	11 (17.5)	8 (25.8)	14 (43.8)	15 (24.6)	18 (28.6)
Severe	n (%)	4 (6.3)	6 (19.4)	4 (12.5)	14 (23.0)	18 (28.6)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4a1.sas
Output: t-14-3-1-1-4a1. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:10 Page 3/4

Table 3.10.1 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Age group (Safety Set) - CSR Table 14.3.1.1.4 - Age group: <=65 years

	Statistics	APL-2 + Eculizumab [1] (N=63)	APL-2 Group [2] (N=31)	Eculizumab Group [2] (N=32)	Total OLP APL-2 Group [3] (N=61)	Overall APL-2 Monotherapy (RCP+OLP) (N=63)
Injection Site Reaction	n (%)	38 (60.3)	10 (32.3)	1 (3.1)	15 (24.6)	22 (34.9)
TEAEs Leading to Study Discontinuation	n (%)	0	2 (6.5)	0	6 (9.8)	8 (12.7)
TEAEs Leading to Death	n (%)	0	0	0	1 (1.6)	1 (1.6)
TEAEs Due to COVID-19	n (%)	0	0	0	1 (1.6)	1 (1.6)
TEAEs Beyond Week 48	n (%)	0	0	0	3 (4.9)	3 (4.8)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], [redacted], [redacted], [redacted], [redacted], [redacted] and [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4a1.sas
Output: t-14-3-1-1-4a1. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:10 Page 4/4

Table 3.10.1 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Age group (Safety Set) - CSR Table 14.3.1.1.4 - Age group: >65 years

	Statistics	APL-2 + Eculizumab [1] (N=17)	APL-2 Group [2] (N=10)	Eculizumab Group [2] (N=7)	Total OLP APL-2 Group [3] (N=16)	Overall APL-2 Monotherapy (RCP+OLP) (N=17)
Any TEAEs	n (%)	15 (88.2)	8 (80.0)	7 (100.0)	16 (100.0)	17 (100.0)
Total Events	n	79	48	36	149	198
Total Unique Events	n	42	35	29	95	111
TEAEs by Closest Relationship to APL-2						
Related	n (%)	8 (47.1)	5 (50.0)	NA	9 (56.3)	10 (58.8)
Unrelated	n (%)	7 (41.2)	3 (30.0)	NA	7 (43.8)	7 (41.2)
TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	1 (14.3)	NA	NA
Unrelated	n (%)	15 (88.2)	NA	6 (85.7)	NA	NA

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4a2.sas
Output: t-14-3-1-1-4a2. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:10 Page 1/4

Table 3.10.1 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Age group (Safety Set) - CSR Table 14.3.1.1.4 - Age group: >65 years

	Statistics	APL-2 + Eculizumab [1] (N=17)	APL-2 Group [2] (N=10)	Eculizumab Group [2] (N=7)	Total OLP APL-2 Group [3] (N=16)	Overall APL-2 Monotherapy (RCP+OLP) (N=17)
TEAEs by Closest Relationship to Infusion						
Related	n (%)	6 (35.3)	4 (40.0)	0	3 (18.8)	5 (29.4)
Unrelated	n (%)	9 (52.9)	4 (40.0)	7 (100.0)	13 (81.3)	12 (70.6)
Serious TEAEs	n (%)	0	1 (10.0)	1 (14.3)	6 (37.5)	6 (35.3)
Total Events	n	0	1	1	14	15
Total Unique Events	n	0	1	1	14	15
Serious TEAEs by Closest Relationship to APL-2						
Related	n (%)	0	0	NA	2 (12.5)	2 (11.8)
Unrelated	n (%)	0	1 (10.0)	NA	4 (25.0)	4 (23.5)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4a2.sas
Output: t-14-3-1-1-4a2. Data Cut: [redacted]. Run Date/Time: 09FEB2022/09:10 Page 2/4

Table 3.10.1 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Age group (Safety Set) - CSR Table 14.3.1.1.4 - Age group: >65 years

	Statistics	APL-2 + Eculizumab [1] (N=17)	APL-2 Group [2] (N=10)	Eculizumab Group [2] (N=7)	Total OLP APL-2 Group [3] (N=16)	Overall APL-2 Monotherapy (RCP+OLP) (N=17)
Serious TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	0	NA	1 (14.3)	NA	NA
Serious TEAEs by Closest Relationship to Infusion						
Related	n (%)	0	0	0	0	0
Unrelated	n (%)	0	1 (10.0)	1 (14.3)	6 (37.5)	6 (35.3)
TEAEs by Maximum Severity						
Mild	n (%)	10 (58.8)	4 (40.0)	4 (57.1)	7 (43.8)	7 (41.2)
Moderate	n (%)	5 (29.4)	2 (20.0)	3 (42.9)	5 (31.3)	5 (29.4)
Severe	n (%)	0	2 (20.0)	0	4 (25.0)	5 (29.4)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Table 3.10.1 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Age group (Safety Set) - CSR Table 14.3.1.1.4 - Age group: >65 years

	Statistics	APL-2 + Eculizumab [1] (N=17)	APL-2 Group [2] (N=10)	Eculizumab Group [2] (N=7)	Total OLP APL-2 Group [3] (N=16)	Overall APL-2 Monotherapy (RCP+OLP) (N=17)
Injection Site Reaction	n (%)	9 (52.9)	5 (50.0)	0	5 (31.3)	7 (41.2)
TEAEs Leading to Study Discontinuation	n (%)	0	1 (10.0)	0	3 (18.8)	4 (23.5)
TEAEs Leading to Death	n (%)	0	0	0	0	0
TEAEs Due to COVID-19	n (%)	0	0	0	0	0
TEAEs Beyond Week 48	n (%)	0	0	0	0	0

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4a2.sas
Output: t-14-3-1-1-4a2. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:10 Page 4/4

表 2.7.4-57 人種（アジア人、黒人又はアフリカ系アメリカ人、白人、報告なし、その他）による TEAE の部分集団解析（APL2-302 試験：安全性解析対象集団）

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Asian

	Statistics	APL-2 + Eculizumab [1] (N=12)	APL-2 Group [2] (N=5)	Eculizumab Group [2] (N=7)	Total OLP APL-2 Group [3] (N=12)	Overall APL-2 Monotherapy (RCP+OLP) (N=12)
Any TEAEs	n (%)	11 (91.7)	4 (80.0)	5 (71.4)	12 (100.0)	12 (100.0)
Total Events	n	98	76	14	257	333
Total Unique Events	n	32	14	11	26	31
TEAEs by Closest Relationship to APL-2						
Related	n (%)	11 (91.7)	4 (80.0)	NA	8 (66.7)	8 (66.7)
Unrelated	n (%)	0	0	NA	4 (33.3)	4 (33.3)
TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	1 (14.3)	NA	NA
Unrelated	n (%)	11 (91.7)	NA	4 (57.1)	NA	NA

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r1.sas
Output: t-14-3-1-1-4r1. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 1/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Asian

	Statistics	APL-2 + Eculizumab [1] (N=12)	APL-2 Group [2] (N=5)	Eculizumab Group [2] (N=7)	Total OLP APL-2 Group [3] (N=12)	Overall APL-2 Monotherapy (RCP+OLP) (N=12)
TEAEs by Closest Relationship to Infusion						
Related	n (%)	7 (58.3)	3 (60.0)	0	5 (41.7)	6 (50.0)
Unrelated	n (%)	4 (33.3)	1 (20.0)	5 (71.4)	7 (58.3)	6 (50.0)
Serious TEAEs	n (%)	2 (16.7)	1 (20.0)	1 (14.3)	1 (8.3)	2 (16.7)
Total Events	n	2	1	1	1	2
Total Unique Events	n	2	1	1	1	2
Serious TEAEs by Closest Relationship to APL-2						
Related	n (%)	0	0	NA	0	0
Unrelated	n (%)	2 (16.7)	1 (20.0)	NA	1 (8.3)	2 (16.7)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r1.sas
Output: t-14-3-1-1-4r1. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 2/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Asian

	Statistics	APL-2 + Eculizumab [1] (N=12)	APL-2 Group [2] (N=5)	Eculizumab Group [2] (N=7)	Total OLP APL-2 Group [3] (N=12)	Overall APL-2 Monotherapy (RCP+OLP) (N=12)
Serious TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	2 (16.7)	NA	1 (14.3)	NA	NA
Serious TEAEs by Closest Relationship to Infusion						
Related	n (%)	0	0	0	0	0
Unrelated	n (%)	2 (16.7)	1 (20.0)	1 (14.3)	1 (8.3)	2 (16.7)
TEAEs by Maximum Severity						
Mild	n (%)	6 (50.0)	4 (80.0)	3 (42.9)	9 (75.0)	9 (75.0)
Moderate	n (%)	4 (33.3)	0	1 (14.3)	3 (25.0)	3 (25.0)
Severe	n (%)	1 (8.3)	0	1 (14.3)	0	0

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r1.sas
Output: t-14-3-1-1-4r1. Data Cut: [redacted]. Run Date/Time: 09FEB2022/09:11 Page 3/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Asian

	Statistics	APL-2 + Eculizumab [1] (N=12)	APL-2 Group [2] (N=5)	Eculizumab Group [2] (N=7)	Total OLP APL-2 Group [3] (N=12)	Overall APL-2 Monotherapy (RCP+OLP) (N=12)
Injection Site Reaction	n (%)	11 (91.7)	4 (80.0)	1 (14.3)	6 (50.0)	7 (58.3)
TEAEs Leading to Study Discontinuation	n (%)	0	0	0	0	0
TEAEs Leading to Death	n (%)	0	0	0	0	0
TEAEs Due to COVID-19	n (%)	0	0	0	0	0
TEAEs Beyond Week 48	n (%)	0	0	0	1 (8.3)	1 (8.3)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r1.sas
Output: t-14-3-1-1-4r1. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 4/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Black or African American

	Statistics	APL-2 + Eculizumab [1] (N=2)	APL-2 Group [2] (N=2)	Eculizumab Group [2] (N=0)	Total OLP APL-2 Group [3] (N=2)	Overall APL-2 Monotherapy (RCP+OLP) (N=2)
Any TEAEs	n (%)	2 (100.0)	2 (100.0)	0	2 (100.0)	2 (100.0)
Total Events	n	8	4	0	4	8
Total Unique Events	n	8	4	0	3	7
TEAEs by Closest Relationship to APL-2						
Related	n (%)	1 (50.0)	0	NA	0	0
Unrelated	n (%)	1 (50.0)	2 (100.0)	NA	2 (100.0)	2 (100.0)
TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	2 (100.0)	NA	0	NA	NA

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r2.sas
Output: t-14-3-1-1-4r2. Data Cut: [redacted]. Run Date/Time: 09FEB2022/09:11 Page 1/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Black or African American

	Statistics	APL-2 + Eculizumab [1] (N=2)	APL-2 Group [2] (N=2)	Eculizumab Group [2] (N=0)	Total OLP APL-2 Group [3] (N=2)	Overall APL-2 Monotherapy (RCP+OLP) (N=2)
TEAEs by Closest Relationship to Infusion						
Related	n (%)	1 (50.0)	0	0	0	0
Unrelated	n (%)	1 (50.0)	2 (100.0)	0	2 (100.0)	2 (100.0)
Serious TEAEs	n (%)	1 (50.0)	0	0	0	0
Total Events	n	1	0	0	0	0
Total Unique Events	n	1	0	0	0	0
Serious TEAEs by Closest Relationship to APL-2						
Related	n (%)	1 (50.0)	0	NA	0	0
Unrelated	n (%)	0	0	NA	0	0

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r2.sas
Output: t-14-3-1-1-4r2. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 2/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Black or African American

	Statistics	APL-2 + Eculizumab [1] (N=2)	APL-2 Group [2] (N=2)	Eculizumab Group [2] (N=0)	Total OLP APL-2 Group [3] (N=2)	Overall APL-2 Monotherapy (RCP+OLP) (N=2)
Serious TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	1 (50.0)	NA	0	NA	NA
Serious TEAEs by Closest Relationship to Infusion						
Related	n (%)	0	0	0	0	0
Unrelated	n (%)	1 (50.0)	0	0	0	0
TEAEs by Maximum Severity						
Mild	n (%)	0	1 (50.0)	0	2 (100.0)	1 (50.0)
Moderate	n (%)	1 (50.0)	1 (50.0)	0	0	1 (50.0)
Severe	n (%)	1 (50.0)	0	0	0	0

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r2.sas
Output: t-14-3-1-1-4r2. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 3/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Black or African American

	Statistics	APL-2 + Eculizumab [1] (N=2)	APL-2 Group [2] (N=2)	Eculizumab Group [2] (N=0)	Total OLP APL-2 Group [3] (N=2)	Overall APL-2 Monotherapy (RCP+OLP) (N=2)
Injection Site Reaction	n (%)	1 (50.0)	1 (50.0)	0	0	1 (50.0)
TEAEs Leading to Study Discontinuation	n (%)	0	0	0	0	0
TEAEs Leading to Death	n (%)	0	0	0	0	0
TEAEs Due to COVID-19	n (%)	0	0	0	0	0
TEAEs Beyond Week 48	n (%)	0	0	0	0	0

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], [redacted], [redacted], [redacted], [redacted], [redacted] and [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r2.sas
Output: t-14-3-1-1-4r2. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 4/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: White

	Statistics	APL-2 + Eculizumab [1] (N=49)	APL-2 Group [2] (N=24)	Eculizumab Group [2] (N=25)	Total OLP APL-2 Group [3] (N=46)	Overall APL-2 Monotherapy (RCP+OLP) (N=49)
Any TEAEs	n (%)	44 (89.8)	23 (95.8)	24 (96.0)	42 (91.3)	48 (98.0)
Total Events	n	237	155	116	323	481
Total Unique Events	n	96	67	66	154	184
TEAEs by Closest Relationship to APL-2						
Related	n (%)	28 (57.1)	10 (41.7)	NA	21 (45.7)	26 (53.1)
Unrelated	n (%)	16 (32.7)	13 (54.2)	NA	21 (45.7)	22 (44.9)
TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	4 (8.2)	NA	5 (20.0)	NA	NA
Unrelated	n (%)	40 (81.6)	NA	19 (76.0)	NA	NA

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r3.sas
Output: t-14-3-1-1-4r3. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 1/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: White

	Statistics	APL-2 + Eculizumab [1] (N=49)	APL-2 Group [2] (N=24)	Eculizumab Group [2] (N=25)	Total OLP APL-2 Group [3] (N=46)	Overall APL-2 Monotherapy (RCP+OLP) (N=49)
TEAEs by Closest Relationship to Infusion						
Related	n (%)	23 (46.9)	6 (25.0)	0	6 (13.0)	10 (20.4)
Unrelated	n (%)	21 (42.9)	17 (70.8)	24 (96.0)	36 (78.3)	38 (77.6)
Serious TEAEs	n (%)	1 (2.0)	5 (20.8)	2 (8.0)	10 (21.7)	14 (28.6)
Total Events	n	1	6	2	18	24
Total Unique Events	n	1	5	2	15	18
Serious TEAEs by Closest Relationship to APL-2						
Related	n (%)	0	1 (4.2)	NA	0	1 (2.0)
Unrelated	n (%)	1 (2.0)	4 (16.7)	NA	10 (21.7)	13 (26.5)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r3.sas
Output: t-14-3-1-1-4r3. Data Cut: [redacted]. Run Date/Time: 09FEB2022/09:11 Page 2/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: White

	Statistics	APL-2 + Eculizumab [1] (N=49)	APL-2 Group [2] (N=24)	Eculizumab Group [2] (N=25)	Total OLP APL-2 Group [3] (N=46)	Overall APL-2 Monotherapy (RCP+OLP) (N=49)
Serious TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	1 (2.0)	NA	2 (8.0)	NA	NA
Serious TEAEs by Closest Relationship to Infusion						
Related	n (%)	0	0	0	0	0
Unrelated	n (%)	1 (2.0)	5 (20.8)	2 (8.0)	10 (21.7)	14 (28.6)
TEAEs by Maximum Severity						
Mild	n (%)	36 (73.5)	12 (50.0)	10 (40.0)	18 (39.1)	19 (38.8)
Moderate	n (%)	6 (12.2)	7 (29.2)	12 (48.0)	13 (28.3)	15 (30.6)
Severe	n (%)	2 (4.1)	4 (16.7)	2 (8.0)	11 (23.9)	14 (28.6)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r3.sas
Output: t-14-3-1-1-4r3. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 3/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: White

	Statistics	APL-2 + Eculizumab [1] (N=49)	APL-2 Group [2] (N=24)	Eculizumab Group [2] (N=25)	Total OLP APL-2 Group [3] (N=46)	Overall APL-2 Monotherapy (RCP+OLP) (N=49)
Injection Site Reaction	n (%)	30 (61.2)	10 (41.7)	0	13 (28.3)	20 (40.8)
TEAEs Leading to Study Discontinuation	n (%)	0	3 (12.5)	0	5 (10.9)	8 (16.3)
TEAEs Leading to Death	n (%)	0	0	0	0	0
TEAEs Due to COVID-19	n (%)	0	0	0	0	0
TEAEs Beyond Week 48	n (%)	0	0	0	2 (4.3)	2 (4.1)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r3.sas
Output: t-14-3-1-1-4r3. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 4/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Not Reported

	Statistics	APL-2 + Eculizumab [1] (N=16)	APL-2 Group [2] (N=10)	Eculizumab Group [2] (N=6)	Total OLP APL-2 Group [3] (N=16)	Overall APL-2 Monotherapy (RCP+OLP) (N=16)
Any TEAEs	n (%)	13 (81.3)	7 (70.0)	6 (100.0)	14 (87.5)	15 (93.8)
Total Events	n	37	37	28	110	147
Total Unique Events	n	30	32	22	76	95
TEAEs by Closest Relationship to APL-2						
Related	n (%)	5 (31.3)	0	NA	5 (31.3)	5 (31.3)
Unrelated	n (%)	8 (50.0)	7 (70.0)	NA	9 (56.3)	10 (62.5)
TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	1 (16.7)	NA	NA
Unrelated	n (%)	13 (81.3)	NA	5 (83.3)	NA	NA

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r4.sas
Output: t-14-3-1-1-4r4. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 1/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Not Reported

	Statistics	APL-2 + Eculizumab [1] (N=16)	APL-2 Group [2] (N=10)	Eculizumab Group [2] (N=6)	Total OLP APL-2 Group [3] (N=16)	Overall APL-2 Monotherapy (RCP+OLP) (N=16)
TEAEs by Closest Relationship to Infusion						
Related	n (%)	3 (18.8)	0	0	1 (6.3)	1 (6.3)
Unrelated	n (%)	10 (62.5)	7 (70.0)	6 (100.0)	13 (81.3)	14 (87.5)
Serious TEAEs	n (%)	0	1 (10.0)	2 (33.3)	6 (37.5)	7 (43.8)
Total Events	n	0	1	6	10	11
Total Unique Events	n	0	1	6	10	11
Serious TEAEs by Closest Relationship to APL-2						
Related	n (%)	0	0	NA	4 (25.0)	4 (25.0)
Unrelated	n (%)	0	1 (10.0)	NA	2 (12.5)	3 (18.8)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r4.sas
Output: t-14-3-1-1-4r4. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 2/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Not Reported

	Statistics	APL-2 + Eculizumab [1] (N=16)	APL-2 Group [2] (N=10)	Eculizumab Group [2] (N=6)	Total OLP APL-2 Group [3] (N=16)	Overall APL-2 Monotherapy (RCP+OLP) (N=16)
Serious TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	0	NA	2 (33.3)	NA	NA
Serious TEAEs by Closest Relationship to Infusion						
Related	n (%)	0	0	0	0	0
Unrelated	n (%)	0	1 (10.0)	2 (33.3)	6 (37.5)	7 (43.8)
TEAEs by Maximum Severity						
Mild	n (%)	8 (50.0)	1 (10.0)	1 (16.7)	4 (25.0)	3 (18.8)
Moderate	n (%)	5 (31.3)	2 (20.0)	4 (66.7)	3 (18.8)	3 (18.8)
Severe	n (%)	0	4 (40.0)	1 (16.7)	7 (43.8)	9 (56.3)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r4.sas
Output: t-14-3-1-1-4r4. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 3/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Not Reported

	Statistics	APL-2 + Eculizumab [1] (N=16)	APL-2 Group [2] (N=10)	Eculizumab Group [2] (N=6)	Total OLP APL-2 Group [3] (N=16)	Overall APL-2 Monotherapy (RCP+OLP) (N=16)
Injection Site Reaction	n (%)	4 (25.0)	0	0	1 (6.3)	1 (6.3)
TEAEs Leading to Study Discontinuation	n (%)	0	0	0	4 (25.0)	4 (25.0)
TEAEs Leading to Death	n (%)	0	0	0	1 (6.3)	1 (6.3)
TEAEs Due to COVID-19	n (%)	0	0	0	1 (6.3)	1 (6.3)
TEAEs Beyond Week 48	n (%)	0	0	0	0	0

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r4.sas
Output: t-14-3-1-1-4r4. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 4/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Other

	Statistics	APL-2 + Eculizumab [1] (N=1)	APL-2 Group [2] (N=0)	Eculizumab Group [2] (N=1)	Total OLP APL-2 Group [3] (N=1)	Overall APL-2 Monotherapy (RCP+OLP) (N=1)
Any TEAEs	n (%)	1 (100.0)	0	1 (100.0)	1 (100.0)	1 (100.0)
Total Events	n	3	0	4	2	2
Total Unique Events	n	3	0	4	2	2
TEAEs by Closest Relationship to APL-2						
Related	n (%)	1 (100.0)	0	NA	0	0
Unrelated	n (%)	0	0	NA	1 (100.0)	1 (100.0)
TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	1 (100.0)	NA	1 (100.0)	NA	NA

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r5.sas
Output: t-14-3-1-1-4r5. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:13 Page 1/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Other

	Statistics	APL-2 + Eculizumab [1] (N=1)	APL-2 Group [2] (N=0)	Eculizumab Group [2] (N=1)	Total OLP APL-2 Group [3] (N=1)	Overall APL-2 Monotherapy (RCP+OLP) (N=1)
TEAEs by Closest Relationship to Infusion						
Related	n (%)	1 (100.0)	0	0	0	0
Unrelated	n (%)	0	0	1 (100.0)	1 (100.0)	1 (100.0)
Serious TEAEs	n (%)	0	0	0	1 (100.0)	1 (100.0)
Total Events	n	0	0	0	1	1
Total Unique Events	n	0	0	0	1	1
Serious TEAEs by Closest Relationship to APL-2						
Related	n (%)	0	0	NA	0	0
Unrelated	n (%)	0	0	NA	1 (100.0)	1 (100.0)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r5.sas
Output: t-14-3-1-1-4r5. Data Cut: [redacted]. Run Date/Time: 09FEB2022/09:13 Page 2/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Other

	Statistics	APL-2 + Eculizumab [1] (N=1)	APL-2 Group [2] (N=0)	Eculizumab Group [2] (N=1)	Total OLP APL-2 Group [3] (N=1)	Overall APL-2 Monotherapy (RCP+OLP) (N=1)
Serious TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	0	NA	0	NA	NA
Serious TEAEs by Closest Relationship to Infusion						
Related	n (%)	0	0	0	0	0
Unrelated	n (%)	0	0	0	1 (100.0)	1 (100.0)
TEAEs by Maximum Severity						
Mild	n (%)	1 (100.0)	0	1 (100.0)	0	0
Moderate	n (%)	0	0	0	1 (100.0)	1 (100.0)
Severe	n (%)	0	0	0	0	0

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r5.sas
Output: t-14-3-1-1-4r5. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:13 Page 3/4

Table 3.10.5 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Race (Safety Set) - CSR
Table 14.3.1.1.4 - Race: Other

	Statistics	APL-2 + Eculizumab [1] (N=1)	APL-2 Group [2] (N=0)	Eculizumab Group [2] (N=1)	Total OLP APL-2 Group [3] (N=1)	Overall APL-2 Monotherapy (RCP+OLP) (N=1)
Injection Site Reaction	n (%)	1 (100.0)	0	0	0	0
TEAEs Leading to Study Discontinuation	n (%)	0	0	0	0	0
TEAEs Leading to Death	n (%)	0	0	0	0	0
TEAEs Due to COVID-19	n (%)	0	0	0	0	0
TEAEs Beyond Week 48	n (%)	0	0	0	0	0

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4r5.sas
Output: t-14-3-1-1-4r5. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:13 Page 4/4

表 2.7.4-58 性別（男性、女性）による TEAE の部分集団解析（APL2-302 試験：安全性解析対象集団）

Table 3.10.3 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Sex (Safety Set) - CSR
Table 14.3.1.1.4 - Sex: Male

	Statistics	APL-2 + Eculizumab [1] (N=31)	APL-2 Group [2] (N=14)	Eculizumab Group [2] (N=17)	Total OLP APL-2 Group [3] (N=30)	Overall APL-2 Monotherapy (RCP+OLP) (N=31)
Any TEAEs	n (%)	26 (83.9)	13 (92.9)	16 (94.1)	27 (90.0)	29 (93.5)
Total Events	n	103	74	79	225	299
Total Unique Events	n	56	42	52	140	159
TEAEs by Closest Relationship to APL-2						
Related	n (%)	13 (41.9)	5 (35.7)	NA	12 (40.0)	13 (41.9)
Unrelated	n (%)	13 (41.9)	8 (57.1)	NA	15 (50.0)	16 (51.6)
TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	1 (5.9)	NA	NA
Unrelated	n (%)	26 (83.9)	NA	15 (88.2)	NA	NA

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4s1.sas
Output: t-14-3-1-1-4s1. Data Cut: [redacted]. Run Date/Time: 09FEB2022/09:11 Page 1/4

Table 3.10.3 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Sex (Safety Set) - CSR
Table 14.3.1.1.4 - Sex: Male

	Statistics	APL-2 + Eculizumab [1] (N=31)	APL-2 Group [2] (N=14)	Eculizumab Group [2] (N=17)	Total OLP APL-2 Group [3] (N=30)	Overall APL-2 Monotherapy (RCP+OLP) (N=31)
TEAEs by Closest Relationship to Infusion						
Related	n (%)	8 (25.8)	3 (21.4)	0	3 (10.0)	4 (12.9)
Unrelated	n (%)	18 (58.1)	10 (71.4)	16 (94.1)	24 (80.0)	25 (80.6)
Serious TEAEs	n (%)	2 (6.5)	3 (21.4)	4 (23.5)	10 (33.3)	12 (38.7)
Total Events	n	2	3	8	20	23
Total Unique Events	n	1	3	7	17	19
Serious TEAEs by Closest Relationship to APL-2						
Related	n (%)	1 (3.2)	1 (7.1)	NA	3 (10.0)	4 (12.9)
Unrelated	n (%)	1 (3.2)	2 (14.3)	NA	7 (23.3)	8 (25.8)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4s1.sas
Output: t-14-3-1-1-4s1. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 2/4

Table 3.10.3 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Sex (Safety Set) - CSR
Table 14.3.1.1.4 - Sex: Male

	Statistics	APL-2 + Eculizumab [1] (N=31)	APL-2 Group [2] (N=14)	Eculizumab Group [2] (N=17)	Total OLP APL-2 Group [3] (N=30)	Overall APL-2 Monotherapy (RCP+OLP) (N=31)
Serious TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	2 (6.5)	NA	4 (23.5)	NA	NA
Serious TEAEs by Closest Relationship to Infusion						
Related	n (%)	0	0	0	0	0
Unrelated	n (%)	2 (6.5)	3 (21.4)	4 (23.5)	10 (33.3)	12 (38.7)
TEAEs by Maximum Severity						
Mild	n (%)	18 (58.1)	6 (42.9)	6 (35.3)	11 (36.7)	10 (32.3)
Moderate	n (%)	6 (19.4)	4 (28.6)	8 (47.1)	6 (20.0)	7 (22.6)
Severe	n (%)	2 (6.5)	3 (21.4)	2 (11.8)	10 (33.3)	12 (38.7)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Table 3.10.3 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Sex (Safety Set) - CSR
Table 14.3.1.1.4 - Sex: Male

	Statistics	APL-2 + Eculizumab [1] (N=31)	APL-2 Group [2] (N=14)	Eculizumab Group [2] (N=17)	Total OLP APL-2 Group [3] (N=30)	Overall APL-2 Monotherapy (RCP+OLP) (N=31)
Injection Site Reaction	n (%)	13 (41.9)	5 (35.7)	1 (5.9)	5 (16.7)	7 (22.6)
TEAEs Leading to Study Discontinuation	n (%)	0	1 (7.1)	0	4 (13.3)	5 (16.1)
TEAEs Leading to Death	n (%)	0	0	0	0	0
TEAEs Due to COVID-19	n (%)	0	0	0	0	0
TEAEs Beyond Week 48	n (%)	0	0	0	1 (3.3)	1 (3.2)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4s1.sas
Output: t-14-3-1-1-4s1. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 4/4

Table 3.10.3 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Sex (Safety Set) - CSR
Table 14.3.1.1.4 - Sex: Female

	Statistics	APL-2 + Eculizumab [1] (N=49)	APL-2 Group [2] (N=27)	Eculizumab Group [2] (N=22)	Total OLP APL-2 Group [3] (N=47)	Overall APL-2 Monotherapy (RCP+OLP) (N=49)
Any TEAEs	n (%)	45 (91.8)	23 (85.2)	20 (90.9)	44 (93.6)	49 (100.0)
Total Events	n	280	198	83	471	672
Total Unique Events	n	99	78	50	124	158
TEAEs by Closest Relationship to APL-2						
Related	n (%)	33 (67.3)	9 (33.3)	NA	22 (46.8)	26 (53.1)
Unrelated	n (%)	12 (24.5)	14 (51.9)	NA	22 (46.8)	23 (46.9)
TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	4 (8.2)	NA	6 (27.3)	NA	NA
Unrelated	n (%)	41 (83.7)	NA	14 (63.6)	NA	NA

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4s2.sas
Output: t-14-3-1-1-4s2. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 1/4

Table 3.10.3 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Sex (Safety Set) - CSR
Table 14.3.1.1.4 - Sex: Female

	Statistics	APL-2 + Eculizumab [1] (N=49)	APL-2 Group [2] (N=27)	Eculizumab Group [2] (N=22)	Total OLP APL-2 Group [3] (N=47)	Overall APL-2 Monotherapy (RCP+OLP) (N=49)
TEAEs by Closest Relationship to Infusion						
Related	n (%)	27 (55.1)	6 (22.2)	0	9 (19.1)	13 (26.5)
Unrelated	n (%)	18 (36.7)	17 (63.0)	20 (90.9)	35 (74.5)	36 (73.5)
Serious TEAEs	n (%)	2 (4.1)	4 (14.8)	1 (4.5)	8 (17.0)	12 (24.5)
Total Events	n	2	5	1	10	15
Total Unique Events	n	2	5	1	9	12
Serious TEAEs by Closest Relationship to APL-2						
Related	n (%)	0	0	NA	1 (2.1)	1 (2.0)
Unrelated	n (%)	2 (4.1)	4 (14.8)	NA	7 (14.9)	11 (22.4)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Table 3.10.3 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Sex (Safety Set) - CSR
Table 14.3.1.1.4 - Sex: Female

	Statistics	APL-2 + Eculizumab [1] (N=49)	APL-2 Group [2] (N=27)	Eculizumab Group [2] (N=22)	Total OLP APL-2 Group [3] (N=47)	Overall APL-2 Monotherapy (RCP+OLP) (N=49)
Serious TEAEs by Closest Relationship to Eculizumab						
Related	n (%)	0	NA	0	NA	NA
Unrelated	n (%)	2 (4.1)	NA	1 (4.5)	NA	NA
Serious TEAEs by Closest Relationship to Infusion						
Related	n (%)	0	0	0	0	0
Unrelated	n (%)	2 (4.1)	4 (14.8)	1 (4.5)	8 (17.0)	12 (24.5)
TEAEs by Maximum Severity						
Mild	n (%)	33 (67.3)	12 (44.4)	9 (40.9)	22 (46.8)	22 (44.9)
Moderate	n (%)	10 (20.4)	6 (22.2)	9 (40.9)	14 (29.8)	16 (32.7)
Severe	n (%)	2 (4.1)	5 (18.5)	2 (9.1)	8 (17.0)	11 (22.4)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev¥Pegcetacoplan¥PNH¥PMDA Submission W48¥D-Deliverables¥C-TLFs¥A-Tables¥A-Production¥Programs¥t-14-3-1-1-4s2.sas
Output: t-14-3-1-1-4s2. Data Cut: [redacted]20[redacted]. Run Date/Time: 09FEB2022/09:11 Page 3/4

Table 3.10.3 Overview of Treatment Emergent Adverse Events by Study Periods and Treatment Group, by Sex (Safety Set) - CSR
Table 14.3.1.1.4 - Sex: Female

	Statistics	APL-2 + Eculizumab [1] (N=49)	APL-2 Group [2] (N=27)	Eculizumab Group [2] (N=22)	Total OLP APL-2 Group [3] (N=47)	Overall APL-2 Monotherapy (RCP+OLP) (N=49)
Injection Site Reaction	n (%)	34 (69.4)	10 (37.0)	0	15 (31.9)	22 (44.9)
TEAEs Leading to Study Discontinuation	n (%)	0	2 (7.4)	0	5 (10.6)	7 (14.3)
TEAEs Leading to Death	n (%)	0	0	0	1 (2.1)	1 (2.0)
TEAEs Due to COVID-19	n (%)	0	0	0	1 (2.1)	1 (2.0)
TEAEs Beyond Week 48	n (%)	0	0	0	2 (4.3)	2 (4.1)

Treatment-emergent adverse events are AEs that started or increased in severity on or after the first APL-2 dose of the Run-in Period and within 30 days after the last APL-2 dose of the study.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count. The total unique events is a count of unique preferred terms.
Unlikely related and not related AEs are classified as Unrelated AEs. All other AEs are classified as Related AEs.
[1] The APL-2 + Eculizumab column includes TEAEs that started during the Run-in period or the Open-label Run-in period.
[2] The APL-2 column only includes TEAEs that started during APL-2 monotherapy in the Randomized Controlled Period. The Eculizumab Group column only includes TEAEs that started during eculizumab monotherapy in the Randomized Controlled Period.
[3] The Total OLP APL-2 Group column includes TEAEs that started during APL-2 monotherapy in the Open-label Period or within 30 days after the last APL-2 dose. The TEAEs of Subjects [redacted], who received eculizumab concomitantly with APL-2 during the last weeks of the Open-label Period, are also counted in this column.

Program: Dev\Pegcetacoplan\PNH\PMDA Submission W48\D-Deliverables\C-TLFs\A-Tables\A-Production\Programs\t-14-3-1-1-4s2.sas
Output: t-14-3-1-1-4s2. Data Cut: [redacted]. Run Date/Time: 09FEB2022/09:11 Page 4/4

2.7.4.8.3.2　APL2-307 試験

表 2.7.4-59　有害事象により中止した被験者の一覧（APL2-307 試験：安全性解析対象集団）

Protocol APL2-307
Systemic IB Update, 2[redacted]

Listing 15.8
Subjects Who Discontinued Study due to Treatment Emergent Adverse Events

Page 1 of 2

Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
[redacted] /M/[redacted]	Haemolysis	2[redacted](67) /20[redacted](79)	Not Related/ Recovered/Resolved/ Y	N
		2[redacted](164) /20[redacted](239)	Not Related/ Recovered/Resolved/ N	Y
	Urinary tract infection	2[redacted](69) /20[redacted](73)	Not Related/ Recovered/Resolved/ N	N
[redacted] /M/[redacted]	Haemolysis	2[redacted](43) /20[redacted](64)	Not Related/ Recovered/Resolved/ Y	N
		2[redacted](92) /20[redacted](253)	Not Related/ Recovered/Resolved/ N	Y
[redacted] /M/[redacted]	Acute kidney injury	2[redacted](99) /20[redacted](107)	Not Related/ Recovered/Resolved/ N	N
	Anaemia	2[redacted](100) /ONGOING	Not Related/ Not Recovered/Not Resolved/ N	N
	Haemolysis	2[redacted](89) /20[redacted](108)	Not Related/ Recovered/Resolved/ Y	Y
		2[redacted](109) /20[redacted](128)	Not Related/ Recovered/Resolved/ N	N
		2[redacted](129) /20[redacted](136)	Not Related/ Recovered/Resolved/ N	N
	Respiratory tract infection	2[redacted](99) /20[redacted](108)	Unlikely Related/ Recovered/Resolved/ Y	N

Data cut as of 20[redacted]s used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events from 1 subject who died in the study are not included.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_ae_disc.sas

Run time: 08OCT21:10:59

Protocol APL2-307
Systemic IB Update, 20[redacted]

Listing 15.8
Subjects Who Discontinued Study due to Treatment Emergent Adverse Events

Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date|Day| /End Date|Day|	Causality/ Action Taken/ Serious	Event Caused Discontinuation
[redacted] /M/[redacted]	Dizziness	20[redacted]|130| /20[redacted]|131|	Not Related/ Recovered/Resolved/ N	N
[redacted] /F/[redacted]	Abdominal pain	20[redacted]|418| /20[redacted]|455|	Not Related/ Recovered/Resolved/ N	Y
	Chest discomfort	20[redacted]|418| /20[redacted]|455|	Not Related/ Recovered/Resolved/ N	Y
	Dyspnoea	20[redacted]|436| /20[redacted]|436|	Not Related/ Recovered/Resolved/ N	N
	Haemolysis	20[redacted]|459| /20[redacted]|473|	Not Related/ Recovered/Resolved/ Y	N
	Headache	20[redacted]|266| /20[redacted]|268|	Not Related/ Recovered/Resolved/ N	N
	Oropharyngeal discomfort	20[redacted]|418| /20[redacted]|455|	Not Related/ Recovered/Resolved/ N	Y
	Pleuritic pain	20[redacted]|182| /20[redacted]|188|	Not Related/ Recovered/Resolved/ N	N
	Pruritus	20[redacted]|417| /20[redacted]|455|	Not Related/ Recovered/Resolved/ N	Y
	Rash	20[redacted]|436| /20[redacted]|436|	Not Related/ Recovered/Resolved/ N	N

Data cut as of 20[redacted]s used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events from 1 subject who died in the study are not included.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_ae_disc.sas

Run time: 08OCT21:10:59

表 2.7.4-60　重篤な有害事象の一覧（APL2-307 試験：安全性解析対象集団）

Protocol APL2-307
Systemic IB Update, 20[redacted]

Listing 15.10
Serious Adverse Events (Safety Set)

Page 1 of 10

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
[redacted] /M[redacted]	20[redacted](96) /20[redacted](97)	Blood and lymphatic system disorders/ Anaemia/ Worsening of Anaemia	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
	20[redacted](188) /20[redacted](189)	Renal and urinary disorders/ Paroxysmal nocturnal haemoglobinuria/ Worsening PNH	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	20[redacted](249) /20[redacted](255)	Renal and urinary disorders/ Paroxysmal nocturnal haemoglobinuria/ Worsening PNH	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
	20[redacted](274) /20[redacted](277)	Renal and urinary disorders/ Paroxysmal nocturnal haemoglobinuria/ Worsening of PNH	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
	20[redacted](295) /20[redacted](299)	Renal and urinary disorders/ Paroxysmal nocturnal haemoglobinuria/ Worsening of PNH	N/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
[redacted] /F[redacted]	20[redacted](165) /20[redacted](167)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough hemolysis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Moderate	N
[redacted] /M[redacted]	20[redacted](111) /20[redacted](137)	Infections and infestations/ COVID-19/ Covid 19	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	20[redacted](292) /20[redacted](332)	Blood and lymphatic system disorders/ Haemolysis/ hemolysis	N/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N

Data cut as of 20[redacted]s used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:10:59

Protocol APL2-307
Systemic IB Update, 20[redacted]

Listing 15.10
Serious Adverse Events (Safety Set)

Page 2 of 10

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
[redacted] /F/[redacted]	20[redacted] (191) /20[redacted] (200)	Infections and infestations/ Viral infection/ Acute Viral Syndrome	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
[redacted] /M/[redacted]	20[redacted] (430) /ONGOING	Renal and urinary disorders/ Chronic kidney disease/ Chronic Kidney Disease	N/N	Dose Not Changed/ Not Recovered/Not Resolved	Not Related	Moderate	N
[redacted] /F/[redacted]	20[redacted] (206) /20[redacted] (209)	Blood and lymphatic system disorders/ Haemolysis/ hemolysis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Severe	N
	20[redacted] (364) /20[redacted] (367)	Blood and lymphatic system disorders/ Haemolysis/ Acute Hemolysis probable related to Infection	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
[redacted] /M/[redacted]	20[redacted] (151) /20[redacted] (240)	Infections and infestations/ COVID-19/ COVID-19	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
[redacted] /F/[redacted]	20[redacted] (333) /20[redacted] (365)	Blood and lymphatic system disorders/ Intravascular haemolysis/ intravascular haemolysis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Moderate	N
[redacted] /F/[redacted]	20[redacted] (255) /20[redacted] (337)	Injury, poisoning and procedural complications/ Rib fracture/ Fracture left 4th rib	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
[redacted] /M/[redacted]	20[redacted] (29) /20[redacted] (94)	Nervous system disorders/ Cerebral infarction/ Cerebral infarction	Y/N	Dose Not Changed/ Recovered/Resolved with Sequelea	Unlikely Related	Moderate	N

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:10:59

Protocol APL2-307
Systemic IB Update, 2[redacted]

Listing 15.10
Serious Adverse Events (Safety Set)

Page 3 of 10

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
[redacted] /M/[redacted]	20[redacted](577) /ONGOING	Renal and urinary disorders/ Paroxysmal nocturnal haemoglobinuria/ Exacerbation of PNH	N/N	Not Applicable/ Recovering/Resolving	Not Related	Severe	N
[redacted] /M/[redacted]	20[redacted](493) /20[redacted](502)	Infections and infestations/ Groin abscess/ Left Groin Abscess	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	20[redacted](503) /20[redacted](512)	Infections and infestations/ Infection/ Recurrent infection from left groin abscess	Y/N	Dose Increased/ Recovered/Resolved	Possibly Related	Moderate	N
	20[redacted](503) /20[redacted](513)	UNCODED AE/ UNCODED AE/ Breakthrough Haemolysis	Y/N	Dose Increased/ Recovered/Resolved	Possibly Related	Moderate	N
[redacted] /F/[redacted]	20[redacted](106) /20[redacted](127)	Blood and lymphatic system disorders/ Haemolysis/ Haemolysis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Severe	N
[redacted] /M/[redacted]	20[redacted](307) /20[redacted](309)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough Haemolysis	Y/N	Dose Increased/ Recovered/Resolved	Unlikely Related	Severe	N
[redacted] /M/[redacted]	20[redacted](67) /20[redacted](79)	Blood and lymphatic system disorders/ Haemolysis/ breakthrough hemolysis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Severe	N
[redacted] /M/[redacted]	20[redacted](43) /20[redacted](64)	Blood and lymphatic system disorders/ Haemolysis/ breakthrough hemolysis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Severe	N

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:10:59

Protocol APL2-307
Systemic IB Update, 2[redacted]

Listing 15.10
Serious Adverse Events (Safety Set)

Page 4 of 10

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
[redacted] /F/[redacted]	20[redacted] (343) /20[redacted] (358)	Psychiatric disorders/ Anxiety/ exacerbation of anxiety disorder/depressive episode	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
[redacted] /M/[redacted]	20[redacted] (99) /20[redacted] (108)	Blood and lymphatic system disorders/ Haemolysis/ Hemolysis	Y/Y	Drug Withdrawn/ Recovered/Resolved	Not Related	Severe	N
		Infections and infestations/ Respiratory tract infection/ infection of respiratory	Y/N	Dose Not Changed/ Recovered/Resolved	Unlikely Related	Moderate	N
[redacted] /F/[redacted]	20[redacted] (270) /20[redacted] (399)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Transitional cell carcinoma/ Urothelial tumor	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
[redacted] /F/[redacted]	20[redacted] (313) /20[redacted] (326)	Psychiatric disorders/ Panic attack/ Panic attack	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	20[redacted] (421) /ONGOING	Psychiatric disorders/ Anxiety/ Anxiety	Y/N	Dose Not Changed/ Not Recovered/Not Resolved	Not Related	Moderate	N
[redacted] /F/[redacted]	20[redacted] (230) /20[redacted] (242)	Blood and lymphatic system disorders/ Haemolysis/ hemolytic crisis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Moderate	N
[redacted] /M/[redacted]	20[redacted] -26) /20[redacted] (150)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough hemolysis	N/N	Dose Increased/ Recovered/Resolved	Not Related	Moderate	N

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:10:59

Protocol APL2-307
Systemic IB Update, 2[redacted]

Listing 15.10
Serious Adverse Events (Safety Set)

Page 5 of 10

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
[redacted] /F/[redacted]	20[redacted](20) /20[redacted](86)	Infections and infestations/ Pharyngitis/ pharyngitis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
	20[redacted](603) /20[redacted](604)	Infections and infestations/ Skin infection/ skin infection	Y/N	Unknown/ Recovered/Resolved	Not Related	Moderate	N
[redacted] /F/[redacted]	20[redacted](389) /20[redacted](393)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough Hemolysis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Severe	N
	20[redacted](572) /20[redacted](578)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough Hemolysis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Severe	N
	20[redacted](585) /20[redacted](588)	Blood and lymphatic system disorders/ Haemolysis/ Hemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
	20[redacted](610) /20[redacted](620)	Infections and infestations/ Urinary tract infection/ Urinary Tract Infection	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
[redacted] /M/[redacted]	20[redacted](274) /20[redacted](285)	Blood and lymphatic system disorders/ Intravascular haemolysis/ intravascular hemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
	20[redacted](423) /ONGOING	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough hemolysis	Y/N	Dose Not Changed/ Recovering/Resolving	Not Related	Moderate	N

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:10:59

Protocol APL2-307
Systemic IB Update, 2[redacted]

Listing 15.10
Serious Adverse Events (Safety Set)

Page 6 of 10

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
[redacted] /F/[redacted]	20[redacted] (635) /ONGOING	Blood and lymphatic system disorders/ Anaemia/ Anemia	N/N	Dose Not Changed/ Not Recovered/Not Resolved	Not Related	Severe	N
	20[redacted] (655) /20[redacted] (673)	Blood and lymphatic system disorders/ Haemolysis/ Hemolysis	N/Y	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
[redacted] /F/[redacted]	20[redacted] -27) /20[redacted] (28)	Injury, poisoning and procedural complications/ Rib fracture/ Fracture of ribs	N/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
[redacted] /F/[redacted]	20[redacted] (106) /20[redacted] (134)	Infections and infestations/ Infection/ Infection	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	20[redacted] (155) /20[redacted] (170)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough haemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	20[redacted] (184) /20[redacted] (233)	Infections and infestations/ Ear infection/ Otitis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	20[redacted] (188) /20[redacted] (232)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough haemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	20[redacted] (244) /20[redacted] (268)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough haemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:10:59

Protocol APL2-307
Systemic IB Update, 2[redacted]

Listing 15.10
Serious Adverse Events (Safety Set)

Page 7 of 10

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
[redacted] /F/[redacted]	2[redacted] (286)/ 2[redacted] (359)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough hemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	2[redacted] (317)/ 2[redacted] (359)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough haemolysis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Severe	N
	2[redacted] (409)/ 2[redacted] (608)	Blood and lymphatic system disorders/ Haemolysis/ breakthrough haemolisis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	2[redacted] (426)/ 2[redacted] (446)	Infections and infestations/ COVID-19/ COVID 19	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	2[redacted] (446)/ 2[redacted] (608)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough haemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	2[redacted] (501)/ 2[redacted] (608)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough haemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	2[redacted] (549)/ 2[redacted] (608)	Respiratory, thoracic and mediastinal disorders/ Pulmonary mass/ Right lung mass	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
	2[redacted] (594)/ 2[redacted] (608)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough haemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N

Data cut as of 2[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:10:59

Protocol APL2-307
Systemic IB Update, 2[redacted]

Listing 15.10
Serious Adverse Events (Safety Set)

Page 8 of 10

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
[redacted] /F/[redacted]	2[redacted] (328) /20[redacted] (331)	Blood and lymphatic system disorders/ Haemolysis/ Acute hemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
	2[redacted] (349) /20[redacted] (352)	Blood and lymphatic system disorders/ Haemolysis/ Acute hemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
	2[redacted] (359) /20[redacted] (363)	Blood and lymphatic system disorders/ Haemolysis/ Acute hemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
[redacted] /M/[redacted]	2[redacted] (246) /20[redacted] (301)	Renal and urinary disorders/ Acute kidney injury/ acute kidney injury due to hemolysis	Y/N	Dose Increased/ Recovered/Resolved	Unlikely Related	Severe	N
[redacted] /F/[redacted]	20[redacted] (459) /20[redacted] (473)	Blood and lymphatic system disorders/ Haemolysis/ severe hemolysis	Y/N	Not Applicable/ Recovered/Resolved	Not Related	Severe	N
[redacted] /F/[redacted]	20[redacted] (39) /20[redacted] (60)	Infections and infestations/ Dengue fever/ severe dengue infection	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Severe	N
[redacted] /F/[redacted]	2[redacted] (653) /ONGOING	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough Hemolysis	N/N	Dose Not Changed/ Recovering/Resolving	Not Related	Severe	N
[redacted] /M/[redacted]	2[redacted] (266) /20[redacted] (278)	Infections and infestations/ Dengue fever/ Dengue	Y/N	Drug Interrupted/ Recovered/Resolved	Not Related	Severe	N

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:10:59

Protocol APL2-307
Systemic IB Update, 2[redacted]

Listing 15.10
Serious Adverse Events (Safety Set)

Page 9 of 10

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
[redacted] /F/[redacted]	20[redacted] (449) /20[redacted] (603)	Infections and infestations/ Chikungunya virus infection/ Chikungunya infection	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Severe	N
	20[redacted] (591) /20[redacted] (595)	Blood and lymphatic system disorders/ Haemolysis/ Acute hemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
[redacted] /F/[redacted]	20[redacted] (39) /20[redacted] (58)	Infections and infestations/ Urinary tract infection/ URINARY TRACT INFECTION	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
	20[redacted] (44) /20[redacted] (49)	Blood and lymphatic system disorders/ Haemolytic anaemia/ HEMOLYTIC ANEMIA	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
[redacted] /M/[redacted]	20[redacted] (330) /20[redacted] (333)	Gastrointestinal disorders/ Food poisoning/ Food poisioning	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Moderate	N
[redacted] /F/[redacted]	20[redacted] (146) /20[redacted] (150)	Endocrine disorders/ Goitre/ Multinodule goiter	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N
[redacted] /M/[redacted]	20[redacted] (69) /20[redacted] (69)	General disorders and administration site conditions/ Sudden cardiac death/ Sudden Cardiac Death	Y/Y	Dose Not Changed/ Fatal	Not Related	Severe	Y
[redacted] /M/[redacted]	20[redacted] (185) /20[redacted] (187)	Blood and lymphatic system disorders/ Haemolytic anaemia/ Hemolytic Anemia	Y/N	Dose Not Changed/ Recovered/Resolved	Not Related	Severe	N

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:10:59

Protocol APL2-307
Systemic IB Update, 2[redacted]

Listing 15.10
Serious Adverse Events (Safety Set)

Page 10 of 10

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
[redacted] /M/[redacted]	2[redacted]403| /20[redacted]411|	Blood and lymphatic system disorders/ Haemolysis/ Hemolysis	Y/N	Dose Increased/ Recovered/Resolved	Not Related	Moderate	N
	2[redacted]587| /20[redacted]591|	Blood and lymphatic system disorders/ Haemolysis/ Haemolysis	Y/N	Dose Not Changed/ Recovered/Resolved with Sequelea	Unlikely Related	Moderate	N
	2[redacted]592| /20[redacted]617|	Blood and lymphatic system disorders/ Haemolysis/ Haemolysis	Y/N	Dose Not Changed/ Recovered/Resolved	Unlikely Related	Moderate	N
	2[redacted]756| /ONGOING	Blood and lymphatic system disorders/ Haemolysis/ Haemolysis	N/N	Dose Not Changed/ Not Recovered/Not Resolved	Unlikely Related	Moderate	N

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.
/Biometrics/pnh/pnh-307/csr/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:10:59

表 2.7.4-61　重篤な有害事象（APL2-307 試験：安全性解析対象集団）

Table 15.15
Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Set

System Organ Class/ Preferred Term	Statistics	Pegcetacoplan (N=137)
Number of subjects with at least one Serious TEAE	n (%)	35 (25.5)
Blood and lymphatic system disorders	n (%)	19 (13.9)
Haemolysis	n (%)	15 (10.9)
Haemolytic anaemia	n (%)	2 (1.5)
Intravascular haemolysis	n (%)	2 (1.5)
Anaemia	n (%)	1 (0.7)
Infections and infestations	n (%)	12 (8.8)
COVID-19	n (%)	3 (2.2)
Dengue fever	n (%)	2 (1.5)
Infection	n (%)	2 (1.5)
Urinary tract infection	n (%)	2 (1.5)
Chikungunya virus infection	n (%)	1 (0.7)
Ear infection	n (%)	1 (0.7)
Groin abscess	n (%)	1 (0.7)
Pharyngitis	n (%)	1 (0.7)
Respiratory tract infection	n (%)	1 (0.7)
Skin infection	n (%)	1 (0.7)
Viral infection	n (%)	1 (0.7)
Psychiatric disorders	n (%)	2 (1.5)
Anxiety	n (%)	2 (1.5)
Panic attack	n (%)	1 (0.7)

Table 15.15
Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Set

System Organ Class/ Preferred Term	Statistics	Pegcetacoplan (N=137)
Renal and urinary disorders	n (%)	2 (1.5)
Acute kidney injury	n (%)	1 (0.7)
Paroxysmal nocturnal haemoglobinuria	n (%)	1 (0.7)
Endocrine disorders	n (%)	1 (0.7)
Goitre	n (%)	1 (0.7)
Gastrointestinal disorders	n (%)	1 (0.7)
Food poisoning	n (%)	1 (0.7)
General disorders and administration site conditions	n (%)	1 (0.7)
Sudden cardiac death	n (%)	1 (0.7)
Injury, poisoning and procedural complications	n (%)	1 (0.7)
Rib fracture	n (%)	1 (0.7)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	n (%)	1 (0.7)
Transitional cell carcinoma	n (%)	1 (0.7)
Nervous system disorders	n (%)	1 (0.7)
Cerebral infarction	n (%)	1 (0.7)
Respiratory, thoracic and mediastinal disorders	n (%)	1 (0.7)
Pulmonary mass	n (%)	1 (0.7)
UNCODED AE(Breakthrough Haemolysis)	n (%)	1 (0.7)
UNCODED AE|Breakthrough Haemolysis)	n (%)	1 (0.7)

表 2.7.4-62　治験薬と関連のある重篤な有害事象（APL2-307 試験：安全性解析対象集団）

Protocol APL2-307
Systemic IB Update, 20[redacted]

Page 1 of 1

Table 15.16
Drug Related Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Set

System Organ Class Preferred Term	Statistics	Pegcetacoplan (N=137)
Number of subjects with at least one Serious TEAE related to Pegcetacoplan	n (%)	1 (0.7)
Infections and infestations	n (%)	1 (0.7)
Infection	n (%)	1 (0.7)
Uncoded Drug Related AE - Breakthrough Haemolysis	n (%)	1 (0.7)
Uncoded Drug Related AE - Breakthrough Haemolysis	n (%)	1 (0.7)

Data cut as of 20[redacted] is used
Source: Listing 15.10
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count.
Run time: 08OCT21:10:59

2.7.4.8.3.3 APL2-CP-AIHA-208 試験

表 2.7.4-63 重篤な有害事象の一覧（APL2-CP-AIHA-208 試験：安全性解析対象集団）

Protocol APL2-CP-AIHA-208
Systemic IB Update, 20[redacted]

Page 1 of 4

Listing 15.8
Serious Adverse Events (Safety Set)

Cohort/ Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/SAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
Cohort 1 /[redacted] /F/[redacted]	20[redacted] (855) /ONGOING	Musculoskeletal and connective tissue disorders/ Systemic lupus erythematosus/ SYSTEMIC LUPUS ERYTHEMATOSUS	Y/Y/N	DRUG INTERRUPTED/ NOT RECOVERED/NOT RESOLVED	UNLIKELY RELATED	SEVERE	
Cohort 1 /[redacted] /F/[redacted]	20[redacted] 01:00(16) /20[redacted] 23)	Blood and lymphatic system disorders/ Autoimmune haemolytic anaemia/ WORSENING OF AIHA	Y/Y/N	DRUG INTERRUPTED/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
	20[redacted] 01:13(416) /20[redacted] 419)	Blood and lymphatic system disorders/ Autoimmune haemolytic anaemia/ WORSENING AIHA	Y/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	MODERATE	
Cohort 1 /[redacted] /M/[redacted]	20[redacted] 42) /20[redacted] 48)	Blood and lymphatic system disorders/ Autoimmune haemolytic anaemia/ WORSENING WAIHA	Y/Y/Y	DRUG WITHDRAWN/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
Cohort 1 /[redacted] /M/[redacted]	20[redacted] 10) /20[redacted] 318)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Squamous cell carcinoma/ SQUAMOUS CELL CARCINOMA	Y/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
Cohort 1 /[redacted] /M/[redacted]	20[redacted] 16:33(7) /20[redacted] 36)	Blood and lymphatic system disorders/ Haemolysis/ WORSENING HEMOLYSIS	Y/Y/Y	DRUG WITHDRAWN/ RECOVERED/RESOLVED	UNLIKELY RELATED	SEVERE	
Cohort 1 /[redacted] /M/[redacted]	20[redacted] 10:30(87) /20[redacted] 122)	Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ THROMBOEMBOLIC EVENT (PULMONARY EMBOLUS)	Y/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	MODERATE	

Data cut as of 20[redacted]s used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose. SAE is the abbreviation for a serious adverse event.
Adverse events are coded to system organ class and preferred term using MedDRA Version 20.0.
Study Day (day) is the number of days relative to date of first dose.

/Biometrics/aiha/aiha-208/csr_partb/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:13:56

Listing 15.8
Serious Adverse Events (Safety Set)

Cohort/ Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/SAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
Cohort 2 /[redacted] /M[redacted]	20[redacted](-15) /20[redacted](-7)	Blood and lymphatic system disorders/ Autoimmune haemolytic anaemia/ EPISODE OF WORSENING AIHA	N/Y/N	NONE/ RECOVERED/RESOLVED WITH SEQUELAE	UNRELATED	SEVERE	
	20[redacted](20) /20[redacted](53)	Infections and infestations/ Urinary tract infection/ URINARY TRACT INFECTION	Y/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	MODERATE	
	20[redacted](33) /20[redacted](51)	Injury, poisoning and procedural complications/ Multiple injuries/ FALL / FRACTURE OF SACRUM/ L5 / PUBIC RAMUS / PELVIC HEMATOMA / ALL FALL RELATED	Y/Y/N	DRUG INTERRUPTED/ RECOVERED/RESOLVED	UNRELATED	MODERATE	
	20[redacted](67) /20[redacted](113)	Blood and lymphatic system disorders/ Autoimmune haemolytic anaemia/ EPISODE OF WORSENING OF AUTO IMMUNE HEMOLYTIC ANEMIA	Y/Y/Y	DRUG WITHDRAWN/ FATAL	UNRELATED	SEVERE	Y
Cohort 2 /[redacted] /F[redacted]	20[redacted]22:00|1| /20[redacted](8)	Respiratory, thoracic and mediastinal disorders/ Dyspnoea/ SHORTNESS OF BREATH DUE TO PULMONARY EDEMA	Y/Y/N	DRUG INTERRUPTED/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
Cohort 2 /[redacted] /F[redacted]	20[redacted](148) /20[redacted](155)	Hepatobiliary disorders/ Cholecystitis acute/ ACUTE CHOLECYSTITIS	Y/Y/N	DRUG INTERRUPTED/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
	20[redacted](403) /20[redacted](415)	Blood and lymphatic system disorders/ Autoimmune haemolytic anaemia/ WORSENING OF AUTO IMMUNE HEMOLYTIC ANEMIA (AIHA)	Y/Y/N	DRUG INTERRUPTED/ RECOVERED/RESOLVED	UNRELATED	SEVERE	

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose. SAE is the abbreviation for a serious adverse event.
Adverse events are coded to system organ class and preferred term using MedDRA Version 20.0.
Study Day (day) is the number of days relative to date of first dose.

Listing 15.8
Serious Adverse Events (Safety Set)

Cohort/ Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/SAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
Cohort 2 /[redacted] /F/[redacted]	20[redacted](403) /20[redacted](422)	Infections and infestations/ Gastroenteritis/ GASTROENTERITIS	Y/Y/N	DRUG INTERRUPTED/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
	20[redacted]00:08|441) /20[redacted](444)	Investigations/ Haemoglobin decreased/ LOW HEMOGLOBIN	Y/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	MODERATE	
	20[redacted]23:00|466) /20[redacted](478)	Investigations/ Haemoglobin decreased/ LOW HEMOGLOBIN	Y/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	MODERATE	
	20[redacted]14:50|506) /ONGOING	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Non-Hodgkin's lymphoma/ NON-HODGKIN'S LYMPHOMA	Y/Y/N	NONE/ RECOVERING/RESOLVING	UNRELATED	SEVERE	
	20[redacted]534) /20[redacted](732)	Infections and infestations/ Corona virus infection/ COVID 19	Y/Y/N	NOT APPLICABLE/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
Cohort 2 /[redacted] /F/[redacted]	20[redacted]08:00|6| /20[redacted](9)	Infections and infestations/ Pneumonia/ COMMUNITY ACQUIRED PNEUMONIA	Y/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
Cohort 2 /[redacted] /F/[redacted]	20[redacted]16:00|25| /20[redacted](31)	Investigations/ Blood calcium increased/ HIGH CALCIUM	Y/Y/Y	DRUG WITHDRAWN/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
		Investigations/ Blood creatinine increased/ HIGH CREATININE	Y/Y/Y	DRUG WITHDRAWN/ RECOVERED/RESOLVED	UNRELATED	SEVERE	

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose. SAE is the abbreviation for a serious adverse event.
Adverse events are coded to system organ class and preferred term using MedDRA Version 20.0.
Study Day (day) is the number of days relative to date of first dose.

Listing 15.8
Serious Adverse Events (Safety Set)

Cohort/ Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/SAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
Cohort 2 /[redacted] /M[redacted]	20[redacted](423) /20[redacted](424)	Surgical and medical procedures/ Hip arthroplasty/ LEFT HIP REPLACEMENT	Y/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
	20[redacted](428) /20[redacted](459)	Blood and lymphatic system disorders/ Haemolytic anaemia/ ACUTE HEMOLYTIC ANEMIA	Y/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
Cohort 2 /[redacted] /M[redacted]	20[redacted](16:35|423) /20[redacted](431)	Cardiac disorders/ Cardiac failure congestive/ ACUTE ON CHRONIC CONGESTIVE HEART FAILURE	N/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
Cohort 2 /[redacted] /F[redacted]	20[redacted](652) /20[redacted](657)	Infections and infestations/ Diverticulitis/ ACUTE DIVER?ICULITIS	Y/Y/N	NONE/ RECOVERED/RESOLVED	UNRELATED	SEVERE	
	20[redacted](871) /20[redacted](871)	Cardiac disorders/ Cardiac arrest/ CARDIAC ARREST	Y/Y/Y	DRUG WITHDRAWN/ FATAL	UNRELATED	SEVERE	Y

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose. SAE is the abbreviation for a serious adverse event.
Adverse events are coded to system organ class and preferred term using MedDRA Version 20.0.
Study Day (day) is the number of days relative to date of first dose.

表 2.7.4-64　有害事象により中止した被験者の一覧（APL2-CP-AIHA-208 試験：安全性解析対象集団）

Protocol APL2-CP-AIHA-208
Systemic IB Update, 20[redacted]

Page 1 of 9

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
Cohort 1 [redacted] /M[redacted]	Autoimmune haemolytic anaemia	20[redacted]42) /20[redacted]48)	UNRELATED/ RECOVERED/RESOLVED/ Y	Y
	Cough	20[redacted]25) /20[redacted]65)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Diarrhoea	20[redacted]14) /20[redacted]28)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Dyspnoea	20[redacted]42) /20[redacted]43)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Flushing	20[redacted]10:20|1) /20[redacted]10:22|1)	PROBABLY RELATED/ RECOVERED/RESOLVED/ N	N
	Nausea	20[redacted]43) /20[redacted]48)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Pain	20[redacted]27) /20[redacted]65)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Pyrexia	20[redacted]27) /20[redacted]28)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Wheezing	20[redacted]28) /ONGOING	UNLIKELY RELATED/ UNKNOWN/ N	N
Cohort 1 [redacted] /M[redacted]	Acute kidney injury	20[redacted]16:33|7) /20[redacted]12)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N

Data cut as of 20[redacted]s used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
* For subjects [redacted] and [redacted] this event resulted in discontinuation from both the treatment and the study. For other subjects listed, the adverse events resulted in discontinuation from the treatment, only.
Adverse events from the two subjects who died during the course of the study were not included in this table.

/Biometrics/aiha/aiha-208/csr_partb/sasdev/programs/tfl/l_ae_disc.sas

Run time: 08OCT21:13:56

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
Cohort 1 [redacted] /M/[redacted]	Acute kidney injury	20[redacted](24) /20[redacted]36)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N
	Anaemia	20[redacted](1) /20[redacted]24)	UNRELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted]10:47(24) /20[redacted]00:19(26)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](26) /20[redacted](35)	UNRELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](36) /20[redacted]49)	UNRELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](50) /ONGOING	UNRELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Dyspepsia	20[redacted]00:15(11) /20[redacted]00:15(11)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N
	Haemolysis	20[redacted]16:33(7) /20[redacted]36)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ Y	Y*
	Neck pain	20[redacted](13) /20[redacted](17)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N
	Pneumonia	20[redacted](7) /20[redacted]10)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Pyrexia	20[redacted]04:10(9) /20[redacted]06:23(9)	POSSIBLY RELATED/ RECOVERED/RESOLVED/ N	N

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
* For subjects [redacted] and [redacted] this event resulted in discontinuation from both the treatment and the study. For other subjects listed, the adverse events resulted in discontinuation from the treatment, only.
Adverse events from the two subjects who died during the course of the study were not included in this table.

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
Cohort 1 /[redacted] /M/[redacted]	Anaemia	20[redacted](87) /20[redacted](88)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](129) /ONGOING	UNRELATED/ NOT RECOVERED/NOT RESOLVED/ N	Y
	Atrial fibrillation	20[redacted](88) /20[redacted](91)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Dyspnoea	20[redacted](84) /20[redacted](92)	UNRELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](115) /20[redacted](151)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Fatigue	20[redacted](84) /20[redacted](93)	UNRELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](150) /20[redacted](151)	PROBABLY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](152) /ONGOING	POSSIBLY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Hiccups	20[redacted](87) /20[redacted](88)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Hyponatraemia	20[redacted](87) /20[redacted](99)	POSSIBLY RELATED/ RECOVERED/RESOLVED/ N	N
	Influenza	20[redacted](88) /20[redacted](93)	UNRELATED/ RECOVERED/RESOLVED/ N	N

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
* For subjects[redacted] and [redacted] this event resulted in discontinuation from both the treatment and the study. For other subjects listed, the adverse events resulted in discontinuation from the treatment, only.
Adverse events from the two subjects who died during the course of the study were not included in this table.

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
Cohort 1 [redacted] /M[redacted]	Nasal congestion	20[redacted](54) /20[redacted](149)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Oedema peripheral	20[redacted](150) /20[redacted](157)	POSSIBLY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](154) /20[redacted](267)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Pneumonitis	20[redacted]T10:30(87) /20[redacted](97)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Productive cough	20[redacted](54) /20[redacted](154)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Pulmonary embolism	20[redacted]T10:30(87) /20[redacted](122)	UNRELATED/ RECOVERED/RESOLVED/ Y	N
	Pyrexia	20[redacted](4) /20[redacted](19)	POSSIBLY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](56) /20[redacted](57)	UNRELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](147) /20[redacted](148)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
* For subjects [redacted] and [redacted] this event resulted in discontinuation from both the treatment and the study. For other subjects listed, the adverse events resulted in discontinuation from the treatment, only.
Adverse events from the two subjects who died during the course of the study were not included in this table.

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
Cohort 2 [redacted] /F/[redacted]	Abdominal pain	20[redacted](1) /2[redacted]419)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](390) /ONGOING	UNLIKELY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Depression	20[redacted](390) /ONGOING	UNRELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Diarrhoea	20[redacted](1) /ONGOING	UNLIKELY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Dry mouth	20[redacted](481) /ONGOING	UNLIKELY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Dysuria	20[redacted](6) /2[redacted](24)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N
	Fatigue	20[redacted](86) /ONGOING	UNLIKELY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Gastric polyps	20[redacted](297) /2[redacted](297)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Injection site bruising	20[redacted](24) /2[redacted]25)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N
			UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
* For subjects [redacted] and [redacted] this event resulted in discontinuation from both the treatment and the study. For other subjects listed, the adverse events resulted in discontinuation from the treatment, only.
Adverse events from the two subjects who died during the course of the study were not included in this table.

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
Cohort 2 [redacted] /F/[redacted]	Lichenoid keratosis	20[redacted](251) /2[redacted](429)	POSSIBLY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](429) /2[redacted](443)	POSSIBLY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](443) /2[redacted](484)	POSSIBLY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](484) /ONGOING	POSSIBLY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	Y*
	Nasal congestion	20[redacted](55) /ONGOING	POSSIBLY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Nausea	20[redacted](6) /2[redacted](9)	UNLIKELY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](481) /ONGOING	POSSIBLY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Neuropathy peripheral	20[redacted](298) /ONGOING	UNRELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Ocular hypertension	20[redacted](163) /ONGOING	UNLIKELY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Oedema	20[redacted](30) /2[redacted](115)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Pneumonia	20[redacted]08:00(6) /2[redacted](9)	UNRELATED/ RECOVERED/RESOLVED/ Y	N

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
* For subjects [redacted] and [redacted] this event resulted in discontinuation from both the treatment and the study. For other subjects listed, the adverse events resulted in discontinuation from the treatment, only.
Adverse events from the two subjects who died during the course of the study were not included in this table.

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
Cohort 2 [redacted] /F/[redacted]	Pruritus	20[redacted](25) /ONGOING	UNLIKELY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Skin warm	20[redacted](25) /2[redacted](146)	POSSIBLY RELATED/ RECOVERED/RESOLVED/ N	N
	Weight decreased	20[redacted](429) /2[redacted](542)	POSSIBLY RELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted](512) /ONGOING	UNLIKELY RELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
Cohort 2 [redacted] /F/[redacted]	Blood calcium increased	20[redacted]T16:00(25) /2[redacted]31)	UNRELATED/ RECOVERED/RESOLVED/ Y	Y
	Blood creatinine increased	20[redacted]T16:00(25) /2[redacted]31)	UNRELATED/ RECOVERED/RESOLVED/ Y	Y
	Bone pain	20[redacted](25) /2[redacted]29)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Confusional state	20[redacted]T15:57(25) /2[redacted]25)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Constipation	20[redacted](22) /2[redacted]31)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Contusion	20[redacted](25) /2[redacted](127)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Decreased appetite	20[redacted](25) /2[redacted]28)	UNRELATED/ RECOVERED/RESOLVED/ N	N

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
* For subjects [redacted] and [redacted] this event resulted in discontinuation from both the treatment and the study. For other subjects listed, the adverse events resulted in discontinuation from the treatment, only.
Adverse events from the two subjects who died during the course of the study were not included in this table.

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
Cohort 2 [redacted] /F,[redacted]	Diverticulum	20[redacted]T17:02(26) /ONGOING	UNRELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Dizziness	20[redacted](2) /2[redacted]25)	UNRELATED/ RECOVERED/RESOLVED/ N	N
		20[redacted]15:57(25) /2[redacted]25)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Dyspnoea	20[redacted](29) /2[redacted]35)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Gastrocesophageal reflux disease	20[redacted](6) /ONGOING	UNRELATED/ UNKNOWN/ N	N
	Hypertension	20[redacted]T01:30(26) /2[redacted]26)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Hyperuricaemia	20[redacted](25) /2[redacted]29)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Hypoxia	20[redacted](30) /2[redacted]30)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Lymphadenopathy	20[redacted]T17:02(26) /ONGOING	UNRELATED/ NOT RECOVERED/NOT RESOLVED/ N	N
	Oedema	20[redacted](25) /2[redacted]35)	UNRELATED/ UNKNOWN/ N	N
	Oral candidiasis	20[redacted](25) /2[redacted]74)	UNRELATED/ RECOVERED/RESOLVED/ N	N

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
* For subjects [redacted] and [redacted] this event resulted in discontinuation from both the treatment and the study. For other subjects listed, the adverse events resulted in discontinuation from the treatment, only.
Adverse events from the two subjects who died during the course of the study were not included in this table.

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
Cohort 2 [redacted] /F/[redacted]	Pollakiuria	20[redacted](29) /20[redacted]35)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Renal injury	20[redacted](25) /20[redacted]35)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	Viral upper respiratory tract infection	20[redacted](22) /20[redacted]35)	UNRELATED/ RECOVERED/RESOLVED/ N	N
	White blood cell count decreased	20[redacted](9) /20[redacted]108)	UNRELATED/ RECOVERED/RESOLVED/ N	N

Data cut as of 20[redacted] is used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
* For subjects[redacted] and [redacted] this event resulted in discontinuation from both the treatment and the study. For other subjects listed, the adverse events resulted in discontinuation from the treatment, only.
Adverse events from the two subjects who died during the course of the study were not included in this table.

表 2.7.4-65　治験薬と関連のある重篤な有害事象（APL2-CP-AIHA-208 試験：安全性解析対象集団）

Protocol APL2-CP-AIHA-208
Systemic IB Update, 20[redacted]

Page 1 of 1

Table 15.20
Drug Related Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Set

System Organ Class Preferred Term	Statistics	Cohort 1 wAIHA (N=11)	Cohort 2 CAD (N=13)	Overall (N=24)
No subject had a serious related adverse event as of [redacted], 20[redacted]				

Data cut as of 20[redacted]s used
Source: Listing 15.8
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Related events are those adverse events that are considered Definitely Related, Probably Related or Possibly Related.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count.

/Biometrics/aiha/aiha-208/csr_partb/sasdev/programs/tfl/t_sae_related.sas

Run time: 08OCT21:13:56

表 2.7.4-66 重篤な有害事象（APL2-CP-AIHA-208 試験：安全性解析対象集団）

Table 15.21
Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Set)

System Organ Class Preferred Term	Statistics	Cohort 1 wAIHA (N=11)	Cohort 2 CAD (N=13)	Overall (N=24)
Number of subjects with at least one Serious TEAE	n (%)	6 (54.5)	7 (53.8)	13 (54.2)
Blood and lymphatic system disorders	n (%)	3 (27.3)	3 (23.1)	6 (25.0)
Autoimmune haemolytic anaemia	n (%)	2 (18.2)	2 (15.4)	4 (16.7)
Haemolysis	n (%)	1 (9.1)	0	1 (4.2)
Haemolytic anaemia	n (%)	0	1 (7.7)	1 (4.2)
Infections and infestations	n (%)	0	4 (30.8)	4 (16.7)
Corona virus infection	n (%)	0	1 (7.7)	1 (4.2)
Diverticulitis	n (%)	0	1 (7.7)	1 (4.2)
Gastroenteritis	n (%)	0	1 (7.7)	1 (4.2)
Pneumonia	n (%)	0	1 (7.7)	1 (4.2)
Urinary tract infection	n (%)	0	1 (7.7)	1 (4.2)
Investigations	n (%)	0	2 (15.4)	2 (8.3)
Blood calcium increased	n (%)	0	1 (7.7)	1 (4.2)
Blood creatinine increased	n (%)	0	1 (7.7)	1 (4.2)
Haemoglobin decreased	n (%)	0	1 (7.7)	1 (4.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	n (%)	1 (9.1)	1 (7.7)	2 (8.3)
Non-Hodgkin's lymphoma	n (%)	0	1 (7.7)	1 (4.2)
Squamous cell carcinoma	n (%)	1 (9.1)	0	1 (4.2)

Data cut as of 20[redacted]s used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count.

Table 15.21
Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Set)

System Organ Class Preferred Term	Statistics	Cohort 1 wAIHA (N=11)	Cohort 2 CAD (N=13)	Overall (N=24)
Respiratory, thoracic and mediastinal disorders	n (%)	1 (9.1)	1 (7.7)	2 (8.3)
Dyspnoea	n (%)	0	1 (7.7)	1 (4.2)
Pulmonary embolism	n (%)	1 (9.1)	0	1 (4.2)
Cardiac disorders	n (%)	0	1 (7.7)	1 (4.2)
Cardiac arrest	n (%)	0	1 (7.7)	1 (4.2)
Hepatobiliary disorders	n (%)	0	1 (7.7)	1 (4.2)
Cholecystitis acute	n (%)	0	1 (7.7)	1 (4.2)
Injury, poisoning and procedural complications	n (%)	0	1 (7.7)	1 (4.2)
Multiple injuries	n (%)	0	1 (7.7)	1 (4.2)
Musculoskeletal and connective tissue disorders	n (%)	1 (9.1)	0	1 (4.2)
Systemic lupus erythematosus	n (%)	1 (9.1)	0	1 (4.2)
Surgical and medical procedures	n (%)	0	1 (7.7)	1 (4.2)
Hip arthroplasty	n (%)	0	1 (7.7)	1 (4.2)

Data cut as of 20[redacted]s used
Cohort 1 is composed of subjects with Warm Antibody Autoimmune Hemolytic Anemia (wAIHA). Cohort 2 is composed of subjects with Cold Agglutinin Disease (CAD).
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count.

2.7.4.8.3.4 APL2-201 試験

表 2.7.4-67 重篤な有害事象の一覧（APL2-201 試験：安全性解析対象集団）

Protocol APL2-201
Systemic IB Update, 20[redacted]

Page 1 of 2

Listing 15.8
Serious Adverse Events (Safety Set)

Cohort/ Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/SAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
LN [redacted] /M[redacted]	20[redacted]623) /20[redacted]652)	Blood and lymphatic system disorders/ Anaemia/ Worsening of chronic anemia	Y/Y/N	Not Applicable/ Recovered/resolved	Not Related	Moderate	
		Metabolism and nutrition disorders/ Metabolic acidosis/ Metabolic Acidosis	Y/Y/N	Not Applicable/ Recovered/resolved	Not Related	Severe	
		Renal and urinary disorders/ Acute kidney injury/ Acute Kidney Injury	Y/Y/N	Not Applicable/ Recovered/resolved	Not Related	Severe	
		Renal and urinary disorders/ End stage renal disease/ End Stage Renal Disease	Y/Y/N	Not Applicable/ Recovered/resolved with sequelae	Not Related	Severe	
Primary MN [redacted] /M[redacted]	20[redacted]104) /20[redacted]148)	Renal and urinary disorders/ Acute kidney injury/ Acute kidney injury on chronic kidney disease	Y/Y/N	Dose Not Changed/ Recovered/resolved with sequelae	Not Related	Moderate	
Primary MN [redacted] /F[redacted]	20[redacted]104) /20[redacted]151)	Metabolism and nutrition disorders/ Fluid overload/ Fluid Overload	Y/Y/N	Not Applicable/ Recovered/resolved	Not Related	Moderate	
		Renal and urinary disorders/ Acute kidney injury/ Acute Renal Failure	Y/Y/N	Drug Interrupted/ Recovered/resolved	Unlikely Related	Moderate	
	20[redacted]104) /20[redacted]155)	Renal and urinary disorders/ Nephrotic syndrome/ Worsening Nephrotic Syndrome	Y/Y/N	Not Applicable/ Recovered/resolved	Unlikely Related	Moderate	

Data cut as of 20[redacted]s used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose. SAE is the abbreviation for a serious adverse event.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.

/Biometrics/nephrology/neph-201/csr_partb/sasdev/programs/tfl/l_sae.sas

Run time: 08OCT21:13:57

Listing 15.8
Serious Adverse Events (Safety Set)

Cohort/ Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/SAE/ Discontinue due to AE	Action Taken / Outcome	Relation to APL2	Severity	Death from Event
Primary MN /[redacted] /M[redacted]	20[redacted] (144) /20[redacted] (155)	Respiratory, thoracic and mediastinal disorders/ Chronic obstructive pulmonary disease/ copd exacerbation	Y/Y/N	Not Applicable/ Recovered/resolved	Not Related	Moderate	
Primary MN /[redacted] /M[redacted]	20[redacted] (108) /20[redacted] (114)	Hepatobiliary disorders/ Cholecystitis/ Cholecystitis	Y/Y/N	Drug Interrupted/ Recovered/resolved	Not Related	Severe	
Primary MN /[redacted] /M[redacted]	20[redacted] (24) /20[redacted] (29)	Metabolism and nutrition disorders/ Hypercalcaemia/ Hypercalcemia	Y/Y/N	Not Applicable/ Recovered/resolved	Not Related	Moderate	
		Renal and urinary disorders/ Acute kidney injury/ Acute on Chronic Kidney Injury	Y/Y/N	Drug Interrupted/ Recovered/resolved	Not Related	Severe	
	20[redacted] (174) /20[redacted] (185)	Respiratory, thoracic and mediastinal disorders/ Acute respiratory failure/ Acute on Chronic Respiratory Failure	Y/Y/N	Drug Interrupted/ Recovered/resolved	Not Related	Severe	
	20[redacted] (340) /20[redacted] (343)	Respiratory, thoracic and mediastinal disorders/ Acute respiratory failure/ Acute on Chronic Hypoxic Respiratory Failure	N/Y/N	Not Applicable/ Recovered/resolved	Not Related	Severe	
C3G /[redacted] /M[redacted]	20[redacted] (603) /20[redacted] (609)	General disorders and administration site conditions/ Pyrexia/ Fever	Y/Y/N	Dose Not Changed/ Recovered/resolved	Possibly Related	Moderate	
	20[redacted] (603) /20[redacted] (610)	Renal and urinary disorders/ Acute kidney injury/ Acute Kidney Injury	Y/Y/N	Dose Not Changed/ Recovered/resolved	Unlikely Related	Moderate	

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose. SAE is the abbreviation for a serious adverse event.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.

表 2.7.4-68　有害事象により中止した被験者の一覧（APL2-201 試験：安全性解析対象集団）

Protocol APL2-201
Systemic IB Update, 2[redacted]

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date|Day| /End Date(Day|	Causality/ Outcome/ Serious	Event Caused Discontinuation
IgAN [redacted] /M[redacted]	Chronic kidney disease	2[redacted]772| /ONGOING	Not Related/ Not recovered/not resolved/ N	Y
	Gamma-glutamyltransferase increased	2[redacted]29| /2[redacted]421|	Not Related/ Recovered/resolved/ N	N
	Injection site bruising	2[redacted]736| /2[redacted]753|	Not Related/ Recovered/resolved/ N	N
	Polypectomy	2[redacted]494| /2[redacted]498|	Not Related/ Recovered/resolved/ N	N
LN [redacted] /M[redacted]	Acne	2[redacted]48| /ONGOING	Not Related/ Not recovered/not resolved/ N	N
		2[redacted]490| /ONGOING	Not Related/ Not recovered/not resolved/ N	N
	Acne cystic	2[redacted]522| /ONGOING	Not Related/ Recovering/resolving/ N	N
	Acute kidney injury	2[redacted]623| /2[redacted]632|	Not Related/ Recovered/resolved/ Y	N
	Anaemia	2[redacted]623| /2[redacted]632|	Not Related/ Recovered/resolved/ Y	N
	Arthritis	2[redacted]71| /ONGOING	Possibly Related/ Not recovered/not resolved/ N	N
	Chronic kidney disease-mineral and bone disorder	2[redacted]623| /ONGOING	Not Related/ Recovered/resolved/ N	N

Data cut as of 2[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
No subjects died during the course of this study.
For subject 1005001, the event above led to a discontinuation from both the treatment and the study.

/Biometrics/nephrology/neph-201/csr_partb/sasdev/programs/tlf/l_ae_disc.sas

Run time: 11OCT21:13:31

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Outcome/ Serious	Event Caused Discontinuation
LN [redacted] /M[redacted]	Constipation	20[redacted](626) /2[redacted](632)	Not Related/ Recovered/resolved/ N	N
	Dry mouth	20[redacted](1) /2[redacted](31)	Possibly Related/ Recovered/resolved/ N	N
	End stage renal disease	20[redacted](623) /2[redacted](632)	Not Related/ Recovered/resolved with sequelae/ Y	N
	Erosive duodenitis	20[redacted](626) /2[redacted](632)	Unlikely Related/ Recovered/resolved/ N	N
	Gastritis erosive	20[redacted](626) /2[redacted](632)	Unlikely Related/ Recovered/resolved/ N	N
	Headache	20[redacted](2) /2[redacted](31)	Not Related/ Recovered/resolved/ N	N
		20[redacted](360) /2[redacted](360)	Possibly Related/ Recovered/resolved/ N	N
		20[redacted](490) /2[redacted](503)	Unlikely Related/ Recovered/resolved/ N	N
		20[redacted](626) /2[redacted](632)	Not Related/ Recovered/resolved/ N	N
	Hypertensive urgency	20[redacted](623) /2[redacted](632)	Not Related/ Recovered/resolved/ N	
	Hypothyroidism	20[redacted](561) /ONGOING	Not Related/ Not recovered/not resolved/ N	N

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
No subjects died during the course of this study.
For subject 1005001, the event above led to a discontinuation from both the treatment and the study.

Listing 15.9
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Cohort /Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Outcome/ Serious	Event Caused Discontinuation
LN /[redacted] /M[redacted]	Joint swelling	20[redacted](219) /21[redacted](223)	Not Related/ Recovered/resolved/ N	N
	Metabolic acidosis	20[redacted](623) /21[redacted](632)	Not Related/ Recovered/resolved/ Y	N
	Nausea	20[redacted](625) /21[redacted](626)	Not Related/ Recovered/resolved/ N	N
	Peripheral swelling	20[redacted](617) /ONGOING	Not Related/ Not recovered/not resolved/ N	N
	Renal impairment	20[redacted](611) /ONGOING	Unlikely Related/ Not recovered/not resolved/ N	Y
	Tooth infection	20[redacted](549) /21[redacted](561)	Unlikely Related/ Recovered/resolved/ N	N

Data cut as of 20[redacted] is used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
No subjects died during the course of this study.
For subject 1005001, the event above led to a discontinuation from both the treatment and the study.

表 2.7.4-69　治験薬と関連のある重篤な有害事象（APL2-201 試験：安全性解析対象集団）

Protocol APL2-201
Systemic IB Update, 20[redacted]

Page 1 of 1

Table 15.17
Drug Related Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Set

System Organ Class Preferred Term	Statistics	IgAN (N=6)	LN (N=2)	Primary MN (N=5)	C3G (N=8)	Overall (N=21)
Any TEAE	n (%)	0	0	0	1 (12.5)	1 (4.8)
General disorders and administration site conditions	n (%)	0	0	0	1 (12.5)	1 (4.8)
Pyrexia	n (%)	0	0	0	1 (12.5)	1 (4.8)

Data cut as of 20[redacted]s used
Source: Listing 15.8
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
Related events are those adverse events that are considered Definitely Related, Probably Related or Possibly Related.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count.

/Biometrics/nephrology/neph-201/csr_partb/sasdev/programs/tlf/t_sae_related.sas

Run time: 08OCT21:13:57

表 2.7.4-70　重篤な有害事象（APL2-201 試験：安全性解析対象集団）

Protocol APL2-201
Adhocs for Type II Variation

Page 1 of 1

Table 15.18
Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Set)

System Organ Class Preferred Term	Statistics	IgAN (N=6)	LN (N=2)	Primary MN (N=5)	C3G (N=8)	Overall (N=21)
Number of subjects with at least one Serious TEAE	n (%)	0	1 (50.0)	4 (80.0)	1 (12.5)	6 (28.6)
Renal and urinary disorders	n (%)	0	1 (50.0)	3 (60.0)	1 (12.5)	5 (23.8)
Acute kidney injury	n (%)	0	1 (50.0)	3 (60.0)	1 (12.5)	5 (23.8)
End stage renal disease	n (%)	0	1 (50.0)	0	0	1 (4.8)
Nephrotic syndrome	n (%)	0	0	1 (20.0)	0	1 (4.8)
Metabolism and nutrition disorders	n (%)	0	1 (50.0)	2 (40.0)	0	3 (14.3)
Fluid overload	n (%)	0	0	1 (20.0)	0	1 (4.8)
Hypercalcaemia	n (%)	0	0	1 (20.0)	0	1 (4.8)
Metabolic acidosis	n (%)	0	1 (50.0)	0	0	1 (4.8)
Respiratory, thoracic and mediastinal disorders	n (%)	0	0	2 (40.0)	0	2 (9.5)
Acute respiratory failure	n (%)	0	0	1 (20.0)	0	1 (4.8)
Chronic obstructive pulmonary disease	n (%)	0	0	1 (20.0)	0	1 (4.8)
Blood and lymphatic system disorders	n (%)	0	1 (50.0)	0	0	1 (4.8)
Anaemia	n (%)	0	1 (50.0)	0	0	1 (4.8)
General disorders and administration site conditions	n (%)	0	0	0	1 (12.5)	1 (4.8)
Pyrexia	n (%)	0	0	0	1 (12.5)	1 (4.8)
Hepatobiliary disorders	n (%)	0	0	1 (20.0)	0	1 (4.8)
Cholecystitis	n (%)	0	0	1 (20.0)	0	1 (4.8)

Data cut as of 20[redacted]s used
A treatment-emergent adverse event (TEAE) is defined as an adverse event that commenced on or after the time of first study drug administration through 30 days beyond the last dose.
If a subject has multiple occurrences of a TEAE, the subject is presented only once in the subject count.

/Biometrics/nephrology/neph-201/csr_partb/sasdev/programs/tfl/t_sae_typell.sas

Run time: 18OCT21:15:34

2.7.4.8.3.5 APL2-206 試験

表 2.7.4-71 全ての有害事象の一覧（APL2-206 試験：安全性解析対象集団）

Protocol ALS-206
Systemic IB Update, 20[redacted]

Page 1 of 3

Listing 15.9
All Adverse Events (Safety Set)

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/SAE/ Discontinue due to AE	Action Taken / Outcome	Relation to Study Drug	Severity	Death from Event
[redacted] /M[redacted]	20[redacted] (104) /ONGOING	Psychiatric disorders/ Insomnia/ INSOMNIA	Y/N/N	DOSE NOT CHANGED/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	MILD	
	20[redacted] 104) /20[redacted] 109)	Cardiac disorders/ Angina pectoris/ CARDIAC CHEST PAIN	Y/Y/N	DOSE NOT CHANGED/ RECOVERED/RESOLVED	NOT RELATED	MODERATE	N
		Infections and infestations/ Urinary tract infection/ ASYMPTOMATIC URINARY TRACT INFECTION	Y/Y/N	DOSE NOT CHANGED/ RECOVERED/RESOLVED	NOT RELATED	MILD	N
	20[redacted] 143) /20[redacted] 147)	Infections and infestations/ Cystitis/ CYSTITIS	Y/N/N	DOSE NOT CHANGED/ RECOVERED/RESOLVED	NOT RELATED	MODERATE	
		Infections and infestations/ Pneumonia/ PNEUMONIA	Y/Y/N	DRUG WITHDRAWN/ RECOVERED/RESOLVED	POSSIBLY RELATED	SEVERE	N
[redacted] /F[redacted]	20[redacted] 154) /20[redacted] 154)	Nervous system disorders/ Amyotrophic lateral sclerosis/ DEATH DUE TO COMPLICATIONS OF ALS	Y/Y/Y	DRUG WITHDRAWN/ FATAL	UNLIKELY RELATED	SEVERE	Y
[redacted] /F[redacted]	20[redacted] 29) /20[redacted] -29)	Gastrointestinal disorders/ Vomiting/ VOMITING	N/N/N	NOT APPLICABLE/ RECOVERED/RESOLVED	NOT RELATED	MILD	
		Musculoskeletal and connective tissue disorders/ Pain in extremity/ LIMB PAIN	N/N/N	NOT APPLICABLE/ RECOVERED/RESOLVED	NOT RELATED	MILD	

Data cut as of 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is defined as an adverse event that starts or deteriorates on or after the date of the first dose of investigational product until the study follow-up visit or the early termination follow-up visit.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.

/Biometrics/neurology/ALS-206/csr/sasdev/programs/tfl/l_ae_ib.sas

Run time: 03NOV21:15:24

Listing 15.9
All Adverse Events (Safety Set)

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/SAE/ Discontinue due to AE	Action Taken / Outcome	Relation to Study Drug	Severity	Death from Event
[redacted] /F/[redacted]	20[redacted] (-7) /20[redacted] (-6)	Gastrointestinal disorders/ Nausea/ NAUSEA	N/N/N	NOT APPLICABLE/ RECOVERED/RESOLVED	NOT RELATED	MILD	
	20[redacted] (-7) /20[redacted] (-3)	Musculoskeletal and connective tissue disorders/ Pain in extremity/ ARM PAIN	N/N/N	NOT APPLICABLE/ RECOVERED/RESOLVED	NOT RELATED	MILD	
[redacted] /M/[redacted]	20[redacted] (9) /ONGOING	Gastrointestinal disorders/ Salivary hypersecretion/ SIALORRHEA	Y/N/N	DOSE NOT CHANGED/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	MILD	
[redacted] /M/[redacted]	20[redacted] (-34) /20[redacted] (-28)	General disorders and administration site conditions/ Malaise/ SICKNESS	N/N/N	NOT APPLICABLE/ RECOVERED/RESOLVED	NOT RELATED	MILD	
		Nervous system disorders/ Dizziness/ DIZZINESS	N/N/N	NOT APPLICABLE/ RECOVERED/RESOLVED	NOT RELATED	MILD	
	20[redacted] (1) /20[redacted] (1)	Gastrointestinal disorders/ Abdominal discomfort/ DISCOMFORT IN THE UPPER ABDOMEN	Y/N/N	DOSE NOT CHANGED/ RECOVERED/RESOLVED	POSSIBLY RELATED	MILD	
		General disorders and administration site conditions/ Malaise/ SICKNESS	Y/N/N	DOSE NOT CHANGED/ RECOVERED/RESOLVED	POSSIBLY RELATED	MILD	
[redacted] /F/[redacted]	20[redacted] (1) /ONGOING	Investigations/ Blood creatine phosphokinase increased/ CK INCREASE	Y/N/N	DOSE NOT CHANGED/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	MILD	

Data cut as of 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is defined as an adverse event that starts or deteriorates on or after the date of the first dose of investigational product until the study follow-up visit or the early termination follow-up visit.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.

Listing 15.9
All Adverse Events (Safety Set)

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/SAE/ Discontinue due to AE	Action Taken / Outcome	Relation to Study Drug	Severity	Death from Event
[redacted] /F/[redacted]	2[redacted]4) /ONGOING	Nervous system disorders/ Dizziness/ DIZZINES	Y/N/N	DOSE NOT CHANGED/ NOT RECOVERED/NOT RESOLVED	POSSIBLY RELATED	MILD	
	2[redacted]5) /20[redacted]5)	Injury, poisoning and procedural complications/ Fall/ FALL	Y/N/N	DOSE NOT CHANGED/ RECOVERED/RESOLVED	NOT RELATED	MODERATE	
		Injury, poisoning and procedural complications/ Nasal injury/ NOSE TRAUMA	Y/N/N	DOSE NOT CHANGED/ RECOVERED/RESOLVED	NOT RELATED	MILD	

Data cut as of 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is defined as an adverse event that starts or deteriorates on or after the date of the first dose of investigational product until the study follow-up visit or the early termination follow-up visit.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.

表 2.7.4-72　重篤な有害事象の一覧（APL2-206 試験：安全性解析対象集団）

Protocol ALS-206
Systemic IB Update, 20[redacted]

Page 1 of 1

Listing 15.10
Serious Adverse Event (Safety Set)

Subject/ Gender/age	Onset Date(Day)/ End Date(Day)	System Organ Class/ Preferred Term/ Verbatim Term	TEAE/SAE/ Discontinue due to AE	Action Taken / Outcome	Relation to Study Drug	Severity	Death from Event
[redacted] /M[redacted]	20[redacted] 104) /20[redacted] 109)	Cardiac disorders/ Angina pectoris/ CARDIAC CHEST PAIN	Y/Y/N	DOSE NOT CHANGED/ RECOVERED/RESOLVED	NOT RELATED	MODERATE	N
		Infections and infestations/ Urinary tract infection/ ASYMPTOMATIC URINARY TRACT INFECTION	Y/Y/N	DOSE NOT CHANGED/ RECOVERED/RESOLVED	NOT RELATED	MILD	N
	20[redacted] 143) /20[redacted] 147)	Infections and infestations/ Pneumonia/ PNEUMONIA	Y/Y/N	DRUG WITHDRAWN/ RECOVERED/RESOLVED	POSSIBLY RELATED	SEVERE	N
[redacted] /F[redacted]	20[redacted] 154) /20[redacted] 154)	Nervous system disorders/ Amyotrophic lateral sclerosis/ DEATH DUE TO COMPLICATIONS OF ALS	Y/Y/Y	DRUG WITHDRAWN/ FATAL	UNLIKELY RELATED	SEVERE	Y

Data cut as of 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is defined as an adverse event that starts or deteriorates on or after the date of the first dose of investigational product until the study follow-up visit or the early termination follow-up visit.
Adverse events are coded to system organ class and preferred term using MedDRA Version 23.0.
Study Day (day) is the number of days relative to date of first dose.

/Biometrics/neurology/ALS-206/csr/sasdev/programs/tfl/l_sae_ib.sas

Run time: 03NOV21:15:24

表 2.7.4-73　有害事象により中止した被験者の一覧（APL2-206 試験：安全性解析対象集団）

Protocol ALS-206
Systemic IB Update, 20[redacted]

Page 1 of 1

Listing 15.11
Subjects Who Discontinued due to Treatment Emergent Adverse Events

Subject /Gender/age	Adverse Event (Preferred Term)	Onset Date(Day) /End Date(Day)	Causality/ Action Taken/ Serious	Event Caused Discontinuation
	No subject had a TEAE leading to a study or treatment discontinuation as of [redacted] 20[redacted]			

Data cut as of 20[redacted] were used.
Source: Listing 15.9
A treatment-emergent adverse event (TEAE) is defined as an adverse event that starts or deteriorates on or after the date of the first dose of investigational product until the study follow-up visit or the early termination follow-up visit.
Adverse events from the two subjects who died during the course of the study were not included in this table.

/Biometrics/neurology/ALS-206/csr/sasdev/programs/tfl/l_ae_disc_ib.sas

Run time: 08OCT21:14:01

表 2.7.4-74　治験薬と関連のある重篤な有害事象（APL2-206 試験：安全性解析対象集団）

Protocol ALS-206
Systemic IB Update, 20[redacted]

Page 1 of 1

Table 15.2
Drug Related Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Set

System Organ Class Preferred Term	Statistics	Total* (N=18)
Any TEAE	n (%)	1 (5.6)
Infections and infestations	n (%)	1 (5.6)
Pneumonia	n (%)	1 (5.6)

Data cut as of 20[redacted] were used.
Source: Listing 15.10
*Study data is currently blinded so overall counts are presented as Total.
A treatment-emergent adverse event (TEAE) is defined as an adverse event that starts or deteriorates on or after the date of the first dose of investigational product until the study follow-up visit or the early termination follow-up visit.
Related events are those adverse events that are considered Definitely Related or Possibly Related.

/Biometrics/neurology/ALS-206/csr/sasdev/programs/tfl/t_sae_related_ib.sas

Run time: 08OCT21:14:01

表 2.7.4-75　重篤な有害事象（APL2-206 試験：安全性解析対象集団）

Protocol ALS-206
Adhocs for Type II Variation

Page 1 of 1

Table 15.3
Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Set)
Safety Set

System Organ Class Preferred Term	Statistics	Total* (N=18)
Number of subjects with at least one Serious TEAE	n (%)	2 (11.1)
Cardiac disorders	n (%)	1 (5.6)
Angina pectoris	n (%)	1 (5.6)
Infections and infestations	n (%)	1 (5.6)
Pneumonia	n (%)	1 (5.6)
Urinary tract infection	n (%)	1 (5.6)
Nervous system disorders	n (%)	1 (5.6)
Amyotrophic lateral sclerosis	n (%)	1 (5.6)

Data cut as of 20[redacted]were used.

*Study data is currently blinded so overall counts are presented as Total.
A treatment-emergent adverse event (TEAE) is defined as an adverse event that starts or deteriorates on or after the date of the first dose of investigational product until the study follow-up visit or the early termination follow-up visit.

/Biometrics/neurology/ALS-206/csr/sasdev/programs/tfl/t_sae_typeII.sas

Run time: 18OCT21:15:34

2.7.4.8.4　継続中の全身投与試験の叙述

継続中の全身投与試験でペグセタコプラン又は盲検下の治験薬と関連のある重篤な有害事象を発現した被験者の叙述を以下に示した。

被験者番号 APL2-ALS-206-[redacted]

Study ID: APL2-ALS-206 A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Pegcetacoplan in Subjects With Amyotrophic Lateral Sclerosis (ALS) Subject ID: APL2-ALS-206-[redacted] Treatment group: Blinded Study medication: Blinded	
Serious/selected adverse event verbatim term (Preferred Term)	肺炎（肺炎）
Dose at adverse event onset (route/frequency):	Blinded
Age/sex/race/ethnicity:	[redacted] years/male (race and ethnicity not reported)
Amyotrophic lateral sclerosis diagnosis date:	29 September 同年*
Relevant medical history:	Alcohol consumption from 19[redacted], hypertension from 20[redacted], obstructive sleep apnea syndrome from 20[redacted], seasonal allergy from 20[redacted], and hypokalaemia from 20[redacted]
Relevant concomitant medications:	Amitriptyline hydrochloride, 25 mg Amlodipine besilate, 5 mg and 2.5 mg Cetirizine hydrochloride, 10 mg Hydrochlorothiazide, 25 mg Acetylsalicylic acid, 81 mg Baclofen, 10 mg
Date study drug first administered (Study Day):	17 November 20[redacted] (Day 1)
Date study drug last administered (Study Day):	19 March 翌年* (Day 123)
Date of study completion (Study Day):	Not available

SAE Preferred Term/verbatim term	Start date (Study Day)	End date (Study Day)	Severity	Relationship to study drug/ relationship to infusion procedure	Outcome	Selected TEAE Y/N	SAE Y/N
肺炎/ 肺炎	08 April 翌年* (143)	12 April 翌年* (147)	Severe	Not related/ notrelated	Recovered /resolved	Y	Y

Abbreviations: N = no; SAE = serious adverse event; TEAE = treatment-emergent adverse event; Y = yes.

有害事象の叙述：

本被験者は、[redacted]歳の男性であった。生命を脅かす肺炎の重篤な有害事象を発現し、入院を要した。

関連する病歴及び併用薬は上記の表を参照のこと。

同年* 年 11 月 17 日（Day 1）、治験薬投与を開始した。翌年* 年 2 月 26 日（Day 102）、被験者は、肺炎の発現前の直近の治験薬投与を受けた。

肺炎

翌年* 年 4 月 8 日（Day 143）、本被験者は再入院し、肺炎と診断された。この肺炎は重度と判定され、生命を脅かすものであり入院に至ったことから重篤な有害事象と判断された。本被験者は、本事象に対する治療として Zosyn（piperacillin/tazobactam 注射剤）、vancomycin HCl、acetaminophen、sodium chloride を処方された。

同日、本被験者は中等度の膀胱炎（非重篤）を発現した。肺炎に対して胸部 X 線検査、血液培養、痰培養及び心電図検査が実施され、膀胱炎に対して尿培養が実施された。また、本被験者は造影剤の静脈内投与を用いた腹部及び骨盤のコンピュータ断層撮影（CT）検査を受けたが、本報告時点で検査結果は未入手であった。治療には、Zosyn（piperacillin/tazobactam 注射剤）3.375 mg の単回静脈内投与、vancomycin HCl 1000 mg の単回静脈内投与、acetaminophen 1000 mg の単回静脈内投与、並びに sodium chloride 2100 mL 及び 250 mL の持続静脈内投与が含まれた。

翌年* 年 4 月 12 日（Day 147）、本被験者は肺炎及び膀胱炎から回復した。

治験担当医師は、肺炎と治験薬との因果関係を「関連なし（not related）」と判断した。

治験依頼者は、治験担当医師の判断に同意した。

備考：治験担当医師は、データカットオフ日以降に、因果関係の判断を「関連あり」から「関

連なし」に変更した（情報の受領日：＊年 8 月 16 日）。そのため、本申請での解析時点では、この肺炎は治験薬との関連ありと判断されていた。

＊新薬承認情報提供時に置換

被験者番号 APL2-307-[redacted]

Study ID: APL2-307 An Open-Label, Nonrandomized, Multicenter Extension Study to Evaluate the Long-Term Safety and Efficacy ofPegcetacoplan in the Treatment of Paroxysmal Nocturnal Hemoglobinuria (PNH) Subject ID: APL2-307-[redacted] Treatment group: Pegcetacoplan Study medication: 54 mg/mL, subcutaneous	
Serious/selected adverse event verbatim term (Preferred Term)	左単径部膿瘍（単径部膿瘍）、左単径部膿瘍からの回帰性感染（単径部膿瘍）、ブレイクスルー溶血（ブレイクスルー溶血）
Dose at adverse event onset (route/frequency):	54 mg/mL, subcutaneous
Age/sex/race/ethnicity:	[redacted] years/male (race and ethnicity not reported)
Paroxysmal nocturnal haemoglobinuria diagnosis date:	Not available
Relevant medical history:	Hypertension from 30 November 20[redacted], drug hypersensitivity(start date not reported)
Relevant concomitant medications:	Penicillin V 500 mg twice daily
Date study drug first administered (Study Day):	30 March 20[redacted] (Day 1)
Date study drug last administered (Study Day):	Not available
Date of study completion (Study Day):	Not available

SAE Preferred Term/verbatim term	Start date (Study Day)	End date (Study Day)	Severity	Relationship to pegcetacoplan/ relationship to infusion procedure	Outcome	Selected TEAE Y/N	SAE Y/N
鼡径部膿瘍/左鼡径部膿瘍	04 August 翌年* (493)	13 August 翌年* (502)	Severe	Not related/ not related	Recovered /resolved	Y	Y
鼡径部膿瘍/左鼡径部膿瘍からの回帰性感染	14 August 翌年* (503)	23 August 翌年* (512)	Moderate	Possibly related/ not related	Recovered /resolved	N	Y
ブレイクスルー溶血/ブレイクスルー溶血	14 August 翌年* (503)	24 August 翌年* (513)	Moderate	Definitely related/not related	Recovered /resolved	Y	Y

Abbreviations: N = no; SAE = serious adverse event; TEAE = treatment-emergent adverse event; Y = yes.

有害事象の叙述：

本被験者は、[redacted]歳の男性であった。重篤な有害事象の鼡径部膿瘍 2 件（左鼡径部膿瘍及び左鼡径部膿瘍からの回帰性感染）及びブレイクスルー溶血を発現した。

関連する病歴及び併用薬は上記の表を参照のこと。

同年* 年 3 月 30 日（Day 1）、ペグセタコプランの週 2 回の皮下投与を開始した。翌年* 年 8 月 2 日（Day 491）、被験者は、左鼡径部膿瘍の発現前の直近のペグセタコプラン投与を受けた。

左鼡径部膿瘍：

翌年* 年 8 月 4 日（Day 493）、本被験者は左鼡径部膿瘍の有害事象を発現した。この鼡径部膿瘍は重度と判定され、入院に至ったことから重篤な有害事象と判断された。本事象に対する治療として、levofloxacin、phenoxymethylpenicillin、folic acid 及び lercanidipine hydrochloride が処方された。

翌年* 年 8 月 4 日（Day 493）、本被験者は発熱、全身の不快感及び下痢を訴えて病院を受診した。本被験者は 10 日前から左鼡径部膿瘍の症状があり、Co-amoxiclav による 7 日間の治療を完了していた。本被験者の膿瘍は排膿があり、C 反応性蛋白は基準値範囲内で定常状態であった。本被験者のヘモグロビン値は基準値範囲内であり、溶血のエビデンスは認められなかった。本被験者は、髄膜炎菌感染症又は敗血症の可能性がなくなった 翌年* 年 8 月 6 日（Day 495）までの間、cefotaxime 2 g 及び amoxicillin 2 g の静脈内投与を受けた。

翌年* 年 8 月 6 日（Day 495）、髄膜炎菌及び肺炎球菌のポリメラーゼ連鎖反応（PCR）検査結果は陰性であった。本被験者は退院し、levofloxacin 500 mg 錠の 1 日 2 回 7 日間経口投与及び phenoxymethylpenicillin 500 mg 錠の 1 日 2 回経口投与が処方された。また、翌年* 年 8 月 7 日（Day 496）から、folic acid 5 mg 1 日 1 回経口投与及び lercanidipine hydrochloride（10 mg 錠）20 mg 1 日 1 回経口投与も開始された。本被験者は、発熱及び全身の不快感を自宅治療するよう勧められ、必要に応じて、また 翌年* 年 8 月 9 日（Day 498）には血液再検査のため病院を再受診するよう告げられた。

翌年* 年 8 月 13 日（Day 502）、本被験者は鼡径部膿瘍から回復した。ペグセタコプランの投与変更はなかった。

治験責任医師は、鼡径部膿瘍とペグセタコプラン又は注入手順との因果関係を「関連なし（not related）」と判断した。

治験依頼者は、治験責任医師の判断に同意した。

左鼡径部膿瘍からの回帰感染、ブレイクスルー溶血：

翌年* 年 8 月 12 日（Day 501）、本被験者は、左鼡径部膿瘍からの回帰感染及びブレイクスルー溶血の発現前の直近のペグセタコプラン投与を受けた。

翌年* 年 8 月 14 日（Day 503）、本被験者は左鼡径部膿瘍の有害事象を発現した。この鼡径部膿瘍は重度と判定され、入院に至ったことから重篤な有害事象と判断された。本事象に対する治療として、cefotaxime、amoxicillin、Co-amoxiclav 及び経口投与の penicillin が処方された。

翌年* 年 8 月 14 日（Day 503）、本被験者は病院を受診した。体温は 39.4°C で、被験者は強い倦怠感と睡眠の増加を訴えた。Methicillin 耐性の *Staphylococcus aureus*（MRSA）及び敗血症のスクリーニング検査並びに COVID-19 の PCR 検査の結果は陰性であった。本被験者は左鼡径部膿瘍からの回帰感染との診断及びブレイクスルー溶血の症状により再入院した。本被験者の LDH 値は基準値範囲上限の 2 倍超であり、ヘモグロビン値は 91 g/L に低下していた。治療として、cefotaxime 2 g 及び amoxicillin 2 g を 翌年* 年 8 月 16 日（Day 505）まで静脈内投与した。また、2 単位の輸血を受けた。

翌年* 年 8 月 15 日（Day 504）、ヘモグロビン値は 91 g/L に低下しており（軽度のブレイクスルー溶血）、LDH 値は 464 IU/L で、体温は 36.9°C であった。

翌年* 年 8 月 16 日（Day 505）、本被験者の体温は 36.3°C であった。本被験者は退院した。被験者は、翌年* 年 8 月 22 日（Day 511）まで Co-amoxiclav（amoxicillin-clavulanic acid）625 mg 1 日 3 回経口投与及び penicillin 500 mg 1 日 2 回経口投与を処方された。

翌年* 年 8 月 17 日（Day 506）、被験者の臨床検査の結果は、ヘモグロビン値は 111 g/L（基準値範囲：135～180）、白血球数 6.17×10^9 cells/L（基準値範囲：4.00～11.0）、血小板数 252×10^9 cells/L（基準値範囲：150～400）、平均赤血球容積 100 fL（基準値範囲：78～100)ヘマトクリット値 0.37（基準値範囲：0.40～0.52）、赤血球数 3.66×10^{12} cells/L（基準値範囲：4.50～6.50）、平均赤

血球ヘモグロビン量 30.3 pg（基準値範囲：27～32）、赤血球分布幅 16.6（15 未満）、好中球数 4.36 × 10^9 cells/L（基準値範囲：2.00～7.50）、リンパ球数 1.26 × 10^9 cells/L（基準値範囲：1.00～4.50）、単球数 0.39 × 10^9 cells/L（基準値範囲：0.20～0.80）、好酸球数 0.04 × 10^9 cells/L（0.04～0.40）、好塩基球 0.02 × 10^9 cells/L（基準値範囲：0.10 未満）、大型非染色球 0.11 × 10^9 cells/L（基準値範囲：0.60 未満）、低色素性細胞 19%、網赤血球数 110 × 10^9 cells/L（20～80）、網赤血球の割合 3%（基準値範囲：0.8～1.8）、網赤血球ヘモグロビン含量 31.3 pg（基準値範囲：27.0～33.0）であった。（いずれも基準値範囲の単位不明）。

翌年* 年 8 月 21 日（Day 510）、被験者がブレイクスルー溶血から完全に回復していなかったため、ペグセタコプランが増量された。

翌年* 年 8 月 23 日（Day 512）、被験者は左鼡径部膿瘍からの回帰感染から回復した。

翌年* 年 8 月 24 日（Day 513）、被験者はブレイクスルー溶血から回復した。

治験担当医師は、左鼡径部膿瘍からの回帰感染とペグセタコプランの因果関係を「関連あり（possibly related）」、注入手順との因果関係を「関連なし」と判断した。治験責任医師によれば、鼡径部膿瘍に関連する感染は埋没毛に起因しており、ペグセタコプランと関連なしとのことであった。感染が長引いたため、感染の長期化はペグセタコプランに起因する可能性があると報告された。

治験担当医師は、ブレイクスルー溶血とペグセタコプランとの因果関係を「関連あり（definitely related）」、注入手順との因果関係を「関連なし」と判断した。治験責任医師によれば、ブレイクスルー溶血は感染により引き起こされたものであるが、ペグセタコプラン投与がブレイクスルー溶血の予防に不十分であったことから、ブレイクスルー溶血はペグセタコプランと関連ありとした。

治験依頼者は、ブレイクスルー溶血及び鼡径部膿瘍は原疾患である発作性夜間ヘモグロビン尿症及び局所感染（溶血を引き起こす）の医学的状況に起因するため、ブレイクスルー溶血及び鼡径部膿瘍とペグセタコプランとの因果関係を「関連なし」とした。加えて、これらの事象に対してペグセタコプランを増量し、これらの事象は回復した。