Listing 1　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-302 W48

Study/ Randomized Treatment/ Actual treatment	Subject/ Age/Sex/ Race	Study phase/ Onset Date/Time (Day)/ End Date/Time (Day)/ Duration	Latest Treatment/ Latest APL-2 Date/time/ Latest ECU Date/time	System Organ Class/ Preferred Term/ Verbatim Term	Serious/ Treatment emergent	Severity	Relationship to APL2/ Eculizumab/ Infusion	Outcome/ Action Taken with APL2/ Eculizumab	Date of Death
APL-302 W48/ APL2/APL2	[redacted] /M/ White	OLA/ 20[redacted] (270)/ 20[redacted] (295)/ 26	APL-2 1080 mg/ 20[redacted] T09:00/ 20[redacted] T12:30	感染症および寄生虫症/ 上気道感染/ infection upper airways	Yes/Yes	SEVERE	Unlikely Related / Not Applicable / Not Related	RECOVERED/RESOLVED / DOSE INCREASED / NOT APPLICABLE	
		OLA/ 20[redacted] (270)/ 20[redacted] (344)/ 75	APL-2 1080 mg/ 20[redacted] T09:00/ 20[redacted] T12:30	血液およびリンパ系障害/ 溶血/ Break through hemolysis	Yes/Yes	SEVERE	Not Related / Not Applicable / Not Related	RECOVERED/RESOLVED / DOSE INCREASED / NOT APPLICABLE	
APL-302 W48/ ECU/ECU	[redacted] /M/	RCP/ 20[redacted] (99)/ 20[redacted] (103)/ 5	Eculizumab/ 20[redacted] T12:41/ 20[redacted] T15:05	血液およびリンパ系障害/ 溶血/ Hemolysis crisis	Yes/Yes	SEVERE	Not Related / Not Related / Not Related	RECOVERED/RESOLVED / NOT APPLICABLE / DOSE NOT CHANGED	
		RCP/ 20[redacted] (105)/ 20[redacted] (110)/ 6	Eculizumab/ 20[redacted] T12:41/ 20[redacted] T15:05	肝胆道系障害/ 肝細胞損傷/ hepatic cytolisis	Yes/Yes	SEVERE	Not Related / Not Related / Not Related	RECOVERED/RESOLVED / NOT APPLICABLE / DOSE NOT CHANGED	
		RCP/ 20[redacted] (105)/ 20[redacted] (110)/ 6	Eculizumab/ 20[redacted] T12:41/ 20[redacted] T15:05	肝胆道系障害/ 高ビリルビン血症/ hyperbilirubinemia	Yes/Yes	SEVERE	Not Related / Not Related / Not Related	RECOVERED/RESOLVED / NOT APPLICABLE / DOSE NOT CHANGED	
		RCP/ 20[redacted] (105)/ 20[redacted] (110)/ 6	Eculizumab/ 20[redacted] T12:41/ 20[redacted] T15:05	肝胆道系障害/ 黄疸/ icterus	Yes/Yes	SEVERE	Not Related / Not Related / Not Related	RECOVERED/RESOLVED / NOT APPLICABLE / DOSE NOT CHANGED	

Listing 1　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-302 W48

Study/ Randomized Treatment/ Actual treatment	Subject/ Age/Sex/ Race	Study phase/ Onset Date/Time (Day)/ End Date/Time (Day)/ Duration	Latest Treatment/ Latest APL-2 Date/time/ Latest ECU Date/time	System Organ Class/ Preferred Term/ Verbatim Term	Serious/ Treatment emergent	Severity	Relationship to APL2/ Eculizumab/ Infusion	Outcome/ Action Taken with APL2/ Eculizumab	Date of Death
		RCP/ 20[redacted] (105)/ 20[redacted] (148)/ 44	Eculizumab/ 20[redacted] T12:41/ 20[redacted] T15:05	胃腸障害/ 腹痛/ Abdominal pain	Yes/Yes	MILD	Not Related / Not Related / Not Related	RECOVERED/RESOLVED / NOT APPLICABLE / DOSE NOT CHANGED	
		OLA/ 20[redacted] (177)/ 20[redacted] (187)/ 11	APL-2 1080 mg/ 20[redacted] / 20[redacted]	感染症および寄生虫症/ 処置後敗血症/ Sepsis post-surgery	Yes/Yes	SEVERE	Not Related / Not Applicable / Not Related	RECOVERED/RESOLVED / DOSE NOT CHANGED / NOT APPLICABLE	
		FU/ 20[redacted] (248)/ 20[redacted] (261)/ 14	APL-2 1080 mg/ 20[redacted] / 20[redacted]	胃腸障害/ 腸管虚血/ Mesenteric ischemia	Yes/Yes	SEVERE	Possibly Related / Not Related / Not Related	RECOVERED/RESOLVED / DRUG WITHDRAWN / DOSE NOT CHANGED	
APL-302 W48/ APL2/APL2	[redacted] /[redacted]/F/	OLA/ 20[redacted] (324)/ 20[redacted] (333)/ 10	APL-2 1080 mg/ 20[redacted] T12:00/ 20[redacted]	感染症および寄生虫症/ COVID-19/ Covid infection	Yes/Yes	SEVERE	Not Related / Not Applicable / Not Related	FATAL / DRUG WITHDRAWN / DOSE INCREASED	20[redacted]
APL-302 W48/ APL2/APL2	[redacted] /[redacted]/M/	OLA/ 20[redacted] (245)/ 20[redacted] (246)/ 2	APL-2 1080 mg/ 20[redacted] T08:02/ 20[redacted] T13:32	免疫系障害/ 免疫グロブリン療法アレルギー/ Reaction to intravenous immunoglobulin treatment for the matching duration	Yes/Yes	MODERATE	Not Related / Not Applicable / Not Related	RECOVERED/RESOLVED / DOSE NOT CHANGED / NOT APPLICABLE	
APL-302 W48/ APL2/APL2	[redacted] /[redacted]/M/	OLA/ 20[redacted] (210)/ 20[redacted] (216)/ 7	APL-2 1080 mg/ 20[redacted] T09:30/ 20[redacted] T12:10	感染症および寄生虫症/ 胆道性敗血症/ Sepsis undocumented from biliary origin	Yes/Yes	SEVERE	Possibly Related / Not Applicable / Not Related	RECOVERED/RESOLVED / DOSE INCREASED / NOT APPLICABLE	

Listing 1　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-302 W48

Study/ Randomized Treatment/ Actual treatment	Subject/ Age/Sex/ Race	Study phase/ Onset Date/Time (Day)/ End Date/Time (Day)/ Duration	Latest Treatment/ Latest APL-2 Date/time/ Latest ECU Date/time	System Organ Class/ Preferred Term/ Verbatim Term	Serious/ Treatment emergent	Severity	Relationship to APL2/ Eculizumab/ Infusion	Outcome/ Action Taken with APL2/ Eculizumab	Date of Death
		OLA/ 20[redacted] (210)/ 20[redacted] (244)/ 35	APL-2 1080 mg/ 20[redacted] T09:30/ 20[redacted] T12:10	腎および尿路障害/ 急性腎障害/ Acute Kidney failure	Yes/Yes	SEVERE	Not Related / Not Applicable / Not Related	RECOVERED/RESOLVED / DOSE INCREASED / NOT APPLICABLE	
		OLA/ 20[redacted] (210)/ 20[redacted] (247)/ 38	APL-2 1080 mg/ 20[redacted] T09:30/ 20[redacted] T12:10	血液およびリンパ系障害/ 溶血/ Hemolysis breakthrough	Yes/Yes	SEVERE	Not Related / Not Applicable / Not Related	RECOVERED/RESOLVED / DOSE INCREASED / DOSE INCREASED	
		FU/ 20[redacted] (241)/ 20[redacted] (384)/ 144	APL-2 1080 mg and Eculizumab/ 20[redacted] / 20[redacted]	筋骨格系および結合組織障害/ 筋肉内血腫/ psoas hematoma	Yes/Yes	SEVERE	Not Related / Not Related / Not Related	RECOVERED/RESOLVED / DOSE NOT CHANGED / NOT APPLICABLE	
APL-302 W48/ APL2/APL2	[redacted] /[redacted]F/	RCP/ 20[redacted] (73)/ 20[redacted] (74)/ 2	APL-2 1080 mg/ 20[redacted] T11:38/ 20[redacted] T11:15	呼吸器、胸郭および縦隔障害/ 呼吸困難/ Dyspnea	Yes/Yes	SEVERE	Not Related / Not Related / Not Related	RECOVERED/RESOLVED / DOSE NOT CHANGED / NOT APPLICABLE	
APL-302 W48/ ECU/ECU	[redacted] /[redacted]M/	RCP/ 20[redacted] T12:00 (47)/ 20[redacted] (50)/ 4	Eculizumab/ 20[redacted] T10:45/ 20[redacted]	一般・全身障害および投与部位の状態/ 高体温症/ hyperthermia	Yes/Yes	MODERATE	Not Related / Not Related / Not Related	RECOVERED/RESOLVED / NOT APPLICABLE / DOSE NOT CHANGED	

Listing 1　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-302 W48

Study/ Randomized Treatment/ Actual treatment	Subject/ Age/Sex/ Race	Study phase/ Onset Date/Time (Day)/ End Date/Time (Day)/ Duration	Latest Treatment/ Latest APL-2 Date/time/ Latest ECU Date/time	System Organ Class/ Preferred Term/ Verbatim Term	Serious/ Treatment emergent	Severity	Relationship to APL2/ Eculizumab/ Infusion	Outcome/ Action Taken with APL2/ Eculizumab	Date of Death
APL-302 W48/ ECU/ECU	[redacted] /M/	OLA/ 20[redacted] (202)/ 20[redacted] (294)/ 93	APL-2 1080 mg/ 20[redacted] T09:38/ 20[redacted] T13:21	呼吸器、胸郭および縦隔障害/ 過敏性肺臓炎/ HYPERSENSITIVITY PNEUMONITIS	Yes/Yes	SEVERE	Possibly Related / Not Applicable / Not Related	RECOVERED/RESOLVED WITH SEQUELAE / DRUG WITHDRAWN / NOT APPLICABLE	
APL-302 W48/ ECU/ECU	[redacted] /F/	OLA/ 20[redacted] (357)/ 20[redacted] (377)/ 21	APL-2 1080 mg/ 20[redacted] T08:51/ 20[redacted] T09:14	血液およびリンパ系障害/ 溶血性貧血/ HEMOLYTIC ANEMIA	Yes/Yes	SEVERE	Possibly Related / Not Applicable / Unlikely Related	RECOVERED/RESOLVED / DRUG WITHDRAWN / NOT APPLICABLE	
APL-302 W48/ ECU/ECU	[redacted] /F/ White	OLA/ 20[redacted] (194)/ 20[redacted] (196)/ 3	APL-2 1080 mg/ 20[redacted] T07:00/ 20[redacted] T11:50	感染症および寄生虫症/ 胃腸炎/ Gastroenteritis	Yes/Yes	SEVERE	Unlikely Related / Not Applicable / Not Related	RECOVERED/RESOLVED / DOSE NOT CHANGED / NOT APPLICABLE	
APL-302 W48/ ECU/ECU	[redacted] /M/ White	OLA/ 20[redacted] (217)/ 20[redacted] (238)/ 22	APL-2 1080 mg/ 20[redacted] T10:00/ 20[redacted] T12:20	胃腸障害/ 浮腫性膵炎/ Acute Pancreatitis Edematous Form	Yes/Yes	SEVERE	Not Related / Not Applicable / Not Related	RECOVERED/RESOLVED / DOSE INCREASED / NOT APPLICABLE	
		OLA/ 20[redacted] (239)/ 20[redacted] T09:00 (239)/ 1	APL-2 1080 mg/ 20[redacted] T10:00/ 20[redacted] T12:20	肝胆道系障害/ 胆石症/ Gallstone disease	Yes/Yes	MODERATE	Not Related / Not Applicable / Not Related	RECOVERED/RESOLVED / NOT APPLICABLE / NOT APPLICABLE	

Listing 1　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-302 W48

Study/ Randomized Treatment/ Actual treatment	Subject/ Age/Sex/ Race	Study phase/ Onset Date/Time (Day)/ End Date/Time (Day)/ Duration	Latest Treatment/ Latest APL-2 Date/time/ Latest ECU Date/time	System Organ Class/ Preferred Term/ Verbatim Term	Serious/ Treatment emergent	Severity	Relationship to APL2/ Eculizumab/ Infusion	Outcome/ Action Taken with APL2/ Eculizumab	Date of Death
		OLA/ 20[redacted] (338)/ -- (--)/	APL-2 1080 mg/ 20[redacted] T18:05/ 20[redacted] T12:20	血液およびリンパ系障害/ 溶血/ Breakthrough hemolysis	Yes/Yes	MODERATE	Not Related / Not Applicable / Not Related	NOT RECOVERED/NOT RESOLVED / DOSE INCREASED / NOT APPLICABLE	

Source: pmda_m274_l_sae_dth_302W48.SAS 2022-02-09T08:16:58 Z9FRBE.

Abbreviations: ECU, Eculizumab; FU, Follow-up; OLA, Open label APL2; OLR, Open label run-in; RCP, Randomized controlled; RI, Run-in; SCR, Screening.

A treatment-emergent adverse event is defined as an adverse event that commenced on or after the time of first study drug administration.

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 randomization.

表 2.7.4-47　死亡又は重篤な有害事象を発現した被験者の一覧（APL2-202 試験）

Listing 3　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-202

Study/ Treatment/ Subject ID	Race/ Sex/ Age	Adverse Event Verbatim/ System Organ Class/ Preferred Term	Severity/ Seriousness	Onset Date (Part)/ Onset Time (D)/ End Date (Part)/ End Time (D)	Onset Time since Last Dose (Hours)	Event Duration (Hours)	Relationship to Study Drug	Action Taken with Study Drug	Outcome
APL2-202/ APL-2 270 mg/ [redacted]	WHITE/ Female/ [redacted]	Fracture Of Ribs/ 傷害、中毒および処置合併症/ 肋骨骨折	Severe/ SERIOUS	[redacted]-20[redacted] (Part 2B)/ 15:45 (338)/ [redacted]-20[redacted] (Part 2B)/ - (392)	2.53	1304.25	Not Related	Dose Not Changed / Other-Concurrent Meds	Recovered/ Resolved

Source: pmda_m274_1_sae_dth_202.SAS 2022-02-07T17:12:03 U103097.
Study Day 1 corresponds the date of first dose of study drug

表 2.7.4-48　死亡又は重篤な有害事象を発現した被験者の一覧（APL2-CP-PNH-204 試験）

Listing 4　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-204

Unique Subject Identifier/ Cohort	Subject ID/ Treatment	Race/ Sex/ Age	Adverse Event Verbatim/ System Organ Class/ Preferred Term	Severity/ Seriousness	Onset Date (Part)/ Onset Time (D)/ End Date (Part)/ End Time (D)	Onset Time since Last Dose (Hours)	Event Duration (Hours)	Relation-ship to Study Drug	Action Taken with Study Drug	Outcome
APL2-CP-PNH-204-[redacted]/ Cohort 1	[redacted]/ APL-2 180 mg	WHITE/ Male/ [redacted]	Hypersensitivity Reaction/ 免疫系障害/ 過敏症	Moderate/ SERIOUS	[redacted]-20[redacted] (Part 1)/ 14:08 (1)/ [redacted]-20[redacted] (Part 1)/ - (5)	4.88	105.87	Probably Related	Drug Withdrawn / Other-Hospitalisation And Con Meds	Recovered/ Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 1	[redacted]/ APL-2 180 mg	WHITE/ Male/ [redacted]	Perineal Abcess With Fistula/ 生殖系および乳房障害/ 会陰瘻	Moderate/ SERIOUS	[redacted]-20[redacted] (Part 3)/ - (39)/ Ongoing (Part 3)	912		Not Related	Not Applicable / Other-Hospitalisation And Con Meds	Not Recovered/ Not Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	WHITE/ Female/ [redacted]	Intra-Abdominal Malignancy/ 良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 腹部新生物	Severe/ SERIOUS	[redacted]-20[redacted] (Part 2B)/ - (231)/ Ongoing (Part 2B)	24		Not Related	Drug Withdrawn / Other-Medications Given And Non Medication Treatment Given. Investigation Colonoscopy Ultrasound And Blood Transfusion	Not Recovered/ Not Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	[redacted]/ Male/ [redacted]	Aplastic Anaemia/ 血液およびリンパ系障害/ 再生不良性貧血	Death related to AE/ SERIOUS	[redacted]-20[redacted] (Part 2C)/ - (367)/ [redacted]-20[redacted] (Part 2C)/ - (463)	24	2328	Not Related	Drug Withdrawn / Other-Hospitalisation / Prolongation Of Hospitalisation Medications Given, Non-Medication Treatment Bone Marrow Biopsy	Fatal

Listing 4　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-204

Unique Subject Identifier/ Cohort	Subject ID/ Treatment	Race/ Sex/ Age	Adverse Event Verbatim/ System Organ Class/ Preferred Term	Severity/ Seriousness	Onset Date (Part)/ Onset Time (D)/ End Date (Part)/ End Time (D)	Onset Time since Last Dose (Hours)	Event Duration (Hours)	Relation-ship to Study Drug	Action Taken with Study Drug	Outcome
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	ASIAN/ Male/ [redacted]	Acute Intravascular Hemolysis/ 血液およびリンパ系障害/ 血管内溶血	Severe/ SERIOUS	[redacted]-20[redacted] (Part 2B)/ - (159)/ [redacted]-20[redacted] (Part 2B)/ - (161)	24	72	Not Related	Dose Not Changed / Other-Non-Medication Treatment Given (Blood Transfusion)	Recovered/ Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	ASIAN/ Male/ [redacted]	Acute Kidney Injury / 腎および尿路障害/ 急性腎障害	Severe/ SERIOUS	[redacted]-20[redacted] (Part 2B)/ - (298)/ [redacted]-20[redacted] (Part 2B)/ - (303)	24	144	Not Related	Dose Not Changed / Other-Medical Given To Treat Sae (Aki) As Iv Fluid And Non-Medication Treatment (Prbc) Given.	Recovered/ Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	OTHER: [redacted]/ Male/ [redacted]	Right Shoulder Dislocation (Recurrent)/ 傷害、中毒および処置合併症/ 関節脱臼	Moderate/ SERIOUS	[redacted]-20[redacted] (Part 2A)/ - (34)/ [redacted]-20[redacted] (Part 2A)/ - (36)	120	72	Not Related	Not Applicable	Recovered/ Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	ASIAN/ Male/ [redacted]	Pneumonitis/ 呼吸器、胸郭および縦隔障害/ 肺臓炎	Moderate/ SERIOUS	[redacted]-20[redacted] (Part 2B)/ - (201)/ [redacted]-20[redacted] (Part 2B)/ - (208)	24	192	Not Related	Dose Not Changed / Other-Treated With Antibiotic And Iv Normal Saline Hydration	Recovered/ Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	ASIAN/ Male/ [redacted]	Ongoing Hemolysis/ 血液およびリンパ系障害/ 溶血	Moderate/ SERIOUS	[redacted]-20[redacted] (Part 2B)/ - (233)/ [redacted]-20[redacted] (Part 2B)/ - (243)	24	264	Unlikely Related	Dose Not Changed / Other-Hydration Treatment	Recovered/ Resolved

Listing 4 All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-204

Unique Subject Identifier/ Cohort	Subject ID/ Treatment	Race/ Sex/ Age	Adverse Event Verbatim/ System Organ Class/ Preferred Term	Severity/ Seriousness	Onset Date (Part)/ Onset Time (D)/ End Date (Part)/ End Time (D)	Onset Time since Last Dose (Hours)	Event Duration (Hours)	Relation-ship to Study Drug	Action Taken with Study Drug	Outcome
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	ASIAN/ Male/ [redacted]	Relapse Paroxysmal Nocturnal Haemoglobinuria/ 血液およびリンパ系障害/ 発作性夜間血色素尿症	Moderate/ SERIOUS	[redacted]-20[redacted] (Part 2B)/ 21:00 (276)/ [redacted]-20[redacted] (Part 2B)/ - (286)	13	243	Not Related	Dose Increased / Other-Treat With Hydration	Recovered/ Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	ASIAN/ Male/ [redacted]	Acute Haemolysis/ 血液およびリンパ系障害/ 溶血	Mild/ SERIOUS	[redacted]-20[redacted] (Part 2B)/ 16:00 (298)/ [redacted]-20[redacted] (Part 2B)/ - (317)	8	464	Not Related	Dose Not Changed / Other-Hydration Treatment	Recovered/ Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	ASIAN/ Male/ [redacted]	Acute Cholecystitis/ 肝胆道系障害/ 急性胆嚢炎	Severe/ SERIOUS	[redacted]-20[redacted] (Part 2A)/ - (79)/ [redacted]-20[redacted] (Part 2A)/ - (129)	216	1224	Not Related	Drug Interrupted / Other-Medication Given	Recovered/ Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	ASIAN/ Male/ [redacted]	Hemolysis/ 血液およびリンパ系障害/ 溶血	Severe/ SERIOUS	[redacted]-20[redacted] (Part 2A)/ 14:-- (81)/ [redacted]-20[redacted] (Part 2A)/ - (154)	24	1776	Not Related	Dose Not Changed / Other-Medications Given (Enoxaprin For Prophylasix); Non-Medication Treatment Given (Haemodialysis And Blood Transfusion)	Recovered/ Resolved
APL2-CP-PNH-204-[redacted]/ Cohort 2	[redacted]/ APL-2 270 mg	ASIAN/ Male/ [redacted]	Abdominal Pain / 胃腸障害/ 腹痛	Moderate/ SERIOUS	[redacted]-20[redacted] (Part 2B)/ - (157)/ [redacted]-20[redacted] (Part 2B)/ - (159)	24	72	Unlikely Related	Dose Not Changed / Other-Medication Given	Recovered/ Resolved

Source: pmda_m274_l_sae_dth_204.SAS 2022-02-11T09:02:09 Z9FRBE.
Study Day 1 corresponds the date of first dose of study drug
Subject [redacted] (Cohort 1) also enrolled in Cohort 2 ([redacted]). Unique Subject Identifier is same for both cohorts

表 2.7.4-49　死亡又は重篤な有害事象を発現した被験者の一覧（APL-CP0514 試験）

Listing 5　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL-CP0514

Study/ Cohort/ Subject ID	Race/ Sex/ Age	Dose	Verbatim/ SOC/ Preferred Term	Severity/ Seriousness	AE Start Study Day/ AE Dur-ation (days)	AE Start Multiple Dose Day (Study Part)	Action Taken with Study Drug/ Other Actions Taken	Relationship To Study Drug/ If Unrelated, Cause/ If Related, Expectedness	Severity/ Pattern	Outcome
APL-CP0514/ Cohort 1/ [redacted]	WHITE/ Female/ [redacted]	APL-2-25 mg/5 mg	Intracranial Hemorrhage/ 神経系障害/ 頭蓋内出血	SEVERE/ SERIOUS	34/ 2	#n (SDP)	NONE/ NONE	UNLIKELY RELATED/ THROMBOCYTOPENIA (DUE TO DISEASE)/ N/A	FATAL/ SINGLE EVENT	FATAL
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-270 mg/360 mg	Lower Gastrointestinal Hemorrhage/ 胃腸障害/ 下部消化管出血	MODERATE / SERIOUS	39/ 2	#n (PART 2A)	NONE/ OTHER-COLONOSCOPY, ADMISSION TO HOSPITAL	UNRELATED/ UNKNOWN/ N/A	MODERATE/ SINGLE EVENT	RECOVERED/ RESOLVED
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-270 mg/360 mg	Sepsis/ 感染症および寄生虫症/ 敗血症	SEVERE/ SERIOUS	199/ 8	#n (PART 2B)	DRUG INTERRUPTED / MEDICATIONS GIVEN	UNRELATED/ KIDNEY STENT PLACEMENT, NEPHROSTOMY TUBE/ N/A	SEVERE/ INTERMITTENT	RECOVERED/ RESOLVED WITH SEQUEL
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-270 mg/360 mg	Portal Vein Thrombosis/ 肝胆道系障害/ 門脈血栓症	SEVERE/ SERIOUS	207/ 23	#n (FU)	DRUG INTERRUPTED / MEDICATIONS GIVEN	UNLIKELY RELATED/ N/A	SEVERE/ SINGLE EVENT	RECOVERED/ RESOLVED WITH SEQUEL

Listing 5 All Adverse Events for Subjects with Serious Adverse Events or Death in study APL-CP0514

Study/ Cohort/ Subject ID	Race/ Sex/ Age	Dose	Verbatim/ SOC/ Preferred Term	Severity/ Seriousness	AE Start Study Day/ AE Dur-ation (days)	AE Start Multiple Dose Day (Study Part)	Action Taken with Study Drug/ Other Actions Taken	Relationship To Study Drug/ If Unrelated, Cause/ If Related, Expectedness	Severity/ Pattern	Outcome
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-270 mg/360 mg	Complicated Urinary Tract Infection/ 感染症および寄生虫症/ 尿路感染	SEVERE/ SERIOUS	239/ 9	#n (FU)	DRUG INTERRUPTED / MEDICATIONS GIVEN	UNRELATED/ KIDNEY STONE/ N/A	SEVERE/ INTERMITTENT	RECOVERED/ RESOLVED
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-270 mg/360 mg	Recurrent Urinary Tract Infection/ 感染症および寄生虫症/ 尿路感染	SEVERE/ SERIOUS	254/ 4	#n (FU)	DRUG INTERRUPTED / MEDICATIONS GIVEN	UNRELATED/ RECURRENT URINARY TRACT INFECTION, KIDNEY STONE/ N/A	SEVERE/ INTERMITTENT	RECOVERED/ RESOLVED
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-270 mg/360 mg	Urinary Tract Infection/ 感染症および寄生虫症/ 尿路感染	SEVERE/ SERIOUS	262/ 6	#n (FU)	DRUG INTERRUPTED / MEDICATIONS GIVEN	UNRELATED/ KIDNEY STONE/ N/A	SEVERE/ INTERMITTENT	RECOVERED/ RESOLVED
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-270 mg/360 mg	Fever/ 一般・全身障害および投与部位の状態/ 発熱	SEVERE/ SERIOUS	274/ 12	#n (FU)	DRUG INTERRUPTED / MEDICATIONS GIVEN	UNRELATED/ KIDNEY STONE/ N/A	SEVERE/ INTERMITTENT	RECOVERED/ RESOLVED

Listing 5 All Adverse Events for Subjects with Serious Adverse Events or Death in study APL-CP0514

Study/ Cohort/ Subject ID	Race/ Sex/ Age	Dose	Verbatim/ SOC/ Preferred Term	Severity/ Seriousness	AE Start Study Day/ AE Dur-ation (days)	AE Start Multiple Dose Day (Study Part)	Action Taken with Study Drug/ Other Actions Taken	Relationship To Study Drug/ If Unrelated, Cause/ If Related, Expectedness	Severity/ Pattern	Outcome
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-50 mg/30 mg to APL-2-180 mg to APL-2-270 mg/360 mg	Alanine Aminotransferase Increased/ 臨床検査/ アラニンアミノトランスフェラーゼ増加	SEVERE/ SERIOUS	28/ 25	#n (PART 1)	DRUG INTERRUPTED / OTHER-ADDITIONAL LIVER TESTING	POSSIBLY RELATED/ UNEXPECTED	SEVERE/ CONTINUOUS	RECOVERED/ RESOLVED
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-50 mg/30 mg to APL-2-180 mg to APL-2-270 mg/360 mg	Anemia/ 血液およびリンパ系障害/ 貧血	SEVERE/ SERIOUS	48/ 2	#n (PART 2A)	NONE/ NON-MEDICATION TREATMENT GIVEN	UNRELATED/ DRUG BEING HELD/ N/A	SEVERE/ SINGLE EVENT	RECOVERED/ RESOLVED
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-50 mg/30 mg to APL-2-180 mg to APL-2-270 mg/360 mg	Alanine Aminotransferase Increased/ 臨床検査/ アラニンアミノトランスフェラーゼ増加	SEVERE/ SERIOUS	101/ 13	#n (PART 2B)	NONE/ NONE	POSSIBLY RELATED/ UNEXPECTED	SEVERE/ CONTINUOUS	RECOVERED/ RESOLVED
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-50 mg/30 mg to APL-2-180 mg to APL-2-270 mg/360 mg	Aspartate Aminotransferase Increased/ 臨床検査/ アスパラギン酸アミノトランスフェラーゼ増加	SEVERE/ SERIOUS	101/ 13	#n (PART 2B)	NONE/ NONE	POSSIBLY RELATED/ UNEXPECTED	SEVERE/ CONTINUOUS	RECOVERED/ RESOLVED

Listing 5　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL-CP0514

Study/ Cohort/ Subject ID	Race/ Sex/ Age	Dose	Verbatim/ SOC/ Preferred Term	Severity/ Seriousness	AE Start Study Day/ AE Dur-ation (days)	AE Start Multiple Dose Day (Study Part)	Action Taken with Study Drug/ Other Actions Taken	Relationship To Study Drug/ If Unrelated, Cause/ If Related, Expectedness	Severity/ Pattern	Outcome
APL-CP0514/ Cohort 4/ [redacted]	WHITE/ Female/ [redacted]	APL-2-50 mg/30 mg to APL-2-180 mg to APL-2-270 mg/360 mg	Pancreatitis/ 胃腸障害/ 膵炎	SEVERE/ SERIOUS	103/ 5	#n (PART 2B)	NONE/ MEDICATIONS GIVEN	UNRELATED/ ERCP PROCEDURE/ N/A	SEVERE/ CONTINUOUS	RECOVERED/ RESOLVED

Source: pmda_m274_l_sae_dth_cp0514.SAS 2022-02-11T09:20:04 U103097.

Abbreviations: N/A=Not Applicable; SDP=Single Dose Phase; FU=Follow-Up.

Definitions: Cohort 1=25 mg on Day 1 then 5 mg/day from Day 29 to Day 56; Cohort 2=50 mg on Day 1 then 30 mg/day from Day 29 to Day 56; Cohort 3=180 mg/day from Day 1 to Day 28; Cohort 4=270-360 mg/day from Day 1 to Day 729; For Cohorts 1 and 2, Multiple Dose Day=date relative to first daily dose (Visit 9); For non-ongoing AEs, AE duration = AE start date - AE end date + 1; Refer to Statistical Analysis Plan for imputation of missing dates/partial dates.

Notes: Subject [redacted] (Cohort 2) also enrolled in Cohort 3 ([redacted]) and Cohort 4 ([redacted]), Subject [redacted] died before Multiple Dose Phase.

表 2.7.4-50　死亡又は重篤な有害事象を発現した被験者の一覧（APL2-308 試験）

Listing 6　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-308

Study/ Randomized Treatment/Actual treatment	Subject/ Age/Sex/ Race	Onset Date/Time (Day)/End Date/Time (Day)/Duration	Latest prior Treatment/ Dose of APL2 (mg)/ Date/time of dose	System Organ Class/ Preferred Term/ Verbatim Term	Serious/ Treatment emergent	Severity	Relation to APL2/ Infusion Procedure	Action Taken with APL2/to Treat AEs/Outcome	Date of Death
APL2-308/ APL2/APL2	[redacted]/ [redacted]/F/ Asian	20[redacted] (28)/ 20[redacted] (38)/ 11	APL-2/1080/ 20[redacted] [redacted]T19:20	先天性、家族性および遺伝性障害/ 皮様嚢腫/ Dermoid cysts	Yes/Yes	MILD	NOT RELATED/ NOT RELATED	DOSE NOT CHANGED/Yes/ RECOVERED/RESOLVED	
APL2-308/ SOC/SOC	[redacted]/ [redacted]/M/ Asian	20[redacted] (163)/ 20[redacted] (184)/ 22	Standard of Care	感染症および寄生虫症/ ニューモシスチス・イロベチイ肺炎/ Pneumocystis jiroveci Pneumonia	Yes/Yes	MODERATE	NA/ NA	NOT APPLICABLE/Yes/ RECOVERED/RESOLVED	
		20[redacted] (165)/ 20[redacted] (212)/ 48	Standard of Care	血液およびリンパ系障害/ 血小板減少症/ Thrombocytopenia	Yes/Yes	SEVERE	NA/ NA	NOT APPLICABLE/Yes/ FATAL	20[redacted]
		20[redacted] (192)/ 20[redacted] (212)/ 21	Standard of Care	血液およびリンパ系障害/ 発熱性好中球減少症/ Febrile neutropenia	Yes/Yes	SEVERE	NA/ NA	NOT APPLICABLE/Yes/ FATAL	20[redacted]
		20[redacted] (199)/ 20[redacted] (212)/ 14	Standard of Care	感染症および寄生虫症/ ヘルペスウイルス感染/ Herpes viral infection	Yes/Yes	SEVERE	NA/ NA	NOT APPLICABLE/Yes/ FATAL	20[redacted]
		20[redacted] (202)/ 20[redacted] (212)/ 11	Standard of Care	感染症および寄生虫症/ 尿路感染/ Urinary tract infection	Yes/Yes	SEVERE	NA/ NA	NOT APPLICABLE/Yes/ FATAL	20[redacted]
		20[redacted] (208)/ 20[redacted] (212)/ 5	Standard of Care	感染症および寄生虫症/ 敗血症性ショック/ Septic Shock	Yes/Yes	SEVERE	NA/ NA	NOT APPLICABLE/Yes/ FATAL	20[redacted]
		20[redacted] (209)/ 20[redacted] (212)/ 4	Standard of Care	感染症および寄生虫症/ 肺結核/ Pulmonary Tuberculosis	Yes/Yes	SEVERE	NA/ NA	NOT APPLICABLE/Yes/ FATAL	20[redacted]

Listing 6　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-308

Study/ Randomized Treatment/Actual treatment	Subject/ Age/Sex/ Race	Onset Date/Time (Day)/End Date/Time (Day)/Duration	Latest prior Treatment/ Dose of APL2 (mg)/ Date/time of dose	System Organ Class/ Preferred Term/ Verbatim Term	Serious/ Treatment emergent	Severity	Relation to APL2/ Infusion Procedure	Action Taken with APL2/to Treat AEs/Outcome	Date of Death
		20[redacted] (209)/ 20[redacted] (212)/ 4	Standard of Care	呼吸器、胸郭および縦隔障害/ 呼吸不全/ Respiratory failure	Yes/Yes	SEVERE	NA/ NA	NOT APPLICABLE/Yes/ FATAL	20[redacted]
APL2-308/ SOC/SOC-APL2	[redacted]/ /F/ Asian	20[redacted] (40)/ 20[redacted] (45)/ 6	Standard of Care	代謝および栄養障害/ 代謝性アシドーシス/ Metabolic acidosis	Yes/Yes	MODERATE	NA/ NA	DOSE NOT CHANGED/Yes/ RECOVERED/RESOLVED	
APL2-308/ SOC/SOC-APL2	[redacted]/ /M/ Asian	20[redacted] (160)/ 20[redacted] (162)/ 3	APL-2/1080/ 20[redacted]- [redacted]T10:30	血液およびリンパ系障害/ 貧血/ Symptomatic Anaemia	Yes/Yes	SEVERE	UNLIKELY RELATED/ NOT RELATED	DOSE NOT CHANGED/Yes/ RECOVERED/RESOLVED	
APL2-308/ SOC/SOC-APL2	[redacted]/ /M/ American Indian or Alaska Native	20[redacted] (16)/ 20[redacted] (426)/ 411	Standard of Care	血液およびリンパ系障害/ 骨髄機能不全/ worsening of bone marrow hipoplasia	Yes/Yes	MODERATE	NA/ NA	DOSE NOT CHANGED/Yes/ RECOVERED/RESOLVED	
APL2-308/ APL2/APL2	[redacted]/ /M/ American Indian or Alaska Native	20[redacted] (1)/ 20[redacted] (32)/ 32	APL-2/1080/ 20[redacted]- [redacted]T09:40	血液およびリンパ系障害/ 好中球減少症/ neutropenia	Yes/Yes	SEVERE	NOT RELATED/ NOT RELATED	DOSE NOT CHANGED/Yes/ RECOVERED/RESOLVED	
APL2-308/ APL2/APL2	[redacted]/ /M/ American Indian or Alaska Native	20[redacted] (-4)/ 20[redacted] (-3)/ 2	--	血液およびリンパ系障害/ 貧血/ Severe symptomatic anemia	Yes/No	SEVERE	NOT RELATED/ NOT RELATED	NOT APPLICABLE/Yes/ RECOVERED/RESOLVED	

Listing 6　All Adverse Events for Subjects with Serious Adverse Events or Death in study APL2-308

Study/ Randomized Treatment/Actual treatment	Subject/ Age/Sex/ Race	Onset Date/Time (Day)/End Date/Time (Day)/Duration	Latest prior Treatment/ Dose of APL2 (mg)/ Date/time of dose	System Organ Class/ Preferred Term/ Verbatim Term	Serious/ Treatment emergent	Severity	Relation to APL2/ Infusion Procedure	Action Taken with APL2/to Treat AEs/Outcome	Date of Death
		20[redacted] (1)/ -- (--)/	APL-2/1080/ 20[redacted] T13:20	血液およびリンパ系障害/ 汎血球減少症/ Severe Pancytopenia	Yes/Yes	SEVERE	NOT RELATED/ NOT RELATED	NOT APPLICABLE/Yes/ NOT RECOVERED/NOT RESOLVED	
		20[redacted] (162)/ 20[redacted] (177)/ 16	APL-2/1080/ 20[redacted] T16:06	血液およびリンパ系障害/ 発熱性好中球減少症/ Febrile neutropenia	Yes/Yes	SEVERE	NOT RELATED/ NOT RELATED	DOSE NOT CHANGED/Yes/ RECOVERED/RESOLVED	
		20[redacted] (179)/ 20[redacted] (181)/ 3	APL-2/1080/ 20[redacted] T17:30	感染症および寄生虫症/ 敗血症性ショック/ Septic shock	Yes/Yes	SEVERE	NOT RELATED/ NOT RELATED	DOSE NOT CHANGED/No/ FATAL	20[redacted]
APL2-308/ SOC/SOC-APL2	[redacted]/ /M/ American Indian or Alaska Native	20[redacted] (385)/ 20[redacted] (393)/ 9	APL-2/1080/ 20[redacted] T17:25	肝胆道系障害/ 胆管結石/ Choledocholithiasis	Yes/Yes	SEVERE	NOT RELATED/ NOT RELATED	DOSE NOT CHANGED/Yes/ RECOVERED/RESOLVED	
APL2-308/ APL2/APL2	[redacted]/ /M/ Black or African American	20[redacted] (233)/ 20[redacted] (268)/ 36	APL-2/1080/ 20[redacted] T18:20	血液およびリンパ系障害/ 溶血/ BREAKTHROUGH HEMOLYSIS	Yes/Yes	SEVERE	NOT RELATED/ NOT RELATED	DOSE INCREASED/Yes/ RECOVERED/RESOLVED	

Source: pmda_m274_1_sae_dth_308.SAS 2022-02-09T10:06:36 Z9FRBE.

A treatment-emergent adverse event is defined as an adverse event that commenced on or after the time of first study drug administration.

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 randomization.

2.7.4.8.3　追加解析表

表 2.7.4-51　ペグセタコプランの曝露状況（20[redacted]年[redacted]月[redacted]日時点）

Pegcetacoplan SC Duration of Exposure (as of [redacted])

Population	Study	Number of Subjects with at Least One Pegcetacoplan Dose	Duration of Exposure Category					Cumulative Years on Pegcetacoplan
			> 3 Months	> 6 Months	> 1 Year	> 2 Years	> 3 Years	
PNH	APL2-CP0514	9	6	6	4	4	4	19.0
	APL2-202	4	4	4	4	4	0	10.0
	APL2-CP-PNH-204	22	18	18	18	14	8	46.6
	APL2-302	80	77	75	63	20	1	136.8
	APL2-308	52	51	48	31	0	0	54.8
	Cumulative (PNH)	167	156	151	120	42	13	267.3
Non-PNH	APL2-201	21	21	15	12	9	0	29.4
	APL2-CP-AIHA-208	24	19	18	16	11	1	37.8
	Cumulative (Non-PNH)	45	40	33	28	20	1	67.2
All SC	Cumulative Subjects Studied	212	196	184	148	62	14	334.5

Exposure in the long-term safety study (APL2-307) is included in the parent study.

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2.7.4.8.3.1 APL2-302 試験

表 2.7.4-52 無作為化投与期間又は非盲検投与期間のペグセタコプラン用量漸増の有無による TEAE の概要（APL2-302 試験：安全性解析対象集団）

Protocol APL2-302
EMA Day 120 Response

Table 17.14
Overview of Treatment-Emergent Adverse Events (TEAE) by Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

	Subjects with Any Dosing Escalation			
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Any TEAEs	15 (100.0%)	13 (86.7%)	15 (100.0%)	65 (100.0%)
Total Events	154	106	260	1256
Total Unique Events	93	78	148	261
TEAEs by Closest Relationship to APL-2				
Related	8 (53.3%)	3 (20.0%)	9 (60.0%)	48 (73.8%)
Unrelated	7 (46.7%)	10 (66.7%)	6 (40.0%)	17 (26.2%)
TEAEs by Closest Relationship to Eculizumab				
Related	0	1 (6.7%)	1 (6.7%)	9 (13.8%)
Unrelated	15 (100.0%)	2 (13.3%)	14 (93.3%)	55 (84.6%)
Not Applicable	0	10 (66.7%)	0	1 (1.5%)
TEAEs by Closest Relationship to Infusion				
Related	4 (26.7%)	0	4 (26.7%)	34 (52.3%)
Unrelated	11 (73.3%)	13 (86.7%)	11 (73.3%)	31 (47.7%)
Serious TEAEs	8 (53.3%)	6 (40.0%)	11 (73.3%)	20 (30.8%)
Total Events	15	12	27	24
Total Unique Events	10	12	21	18

Data locked as of [redacted] 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
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.
APL-2 dosing escalation is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation.

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Table 17.14
Overview of Treatment-Emergent Adverse Events (TEAE) by Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

	Subjects with Any Dosing Escalation			
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Serious TEAEs by Closest Relationship to APL-2				
Related	1 (6.7%)	1 (6.7%)	2 (13.3%)	4 (6.2%)
Unrelated	7 (46.7%)	5 (33.3%)	9 (60.0%)	16 (24.6%)
Serious TEAEs by Closest Relationship to Eculizumab				
Related	0	0	0	0
Unrelated	4 (26.7%)	2 (13.3%)	5 (33.3%)	13 (20.0%)
Not Applicable	4 (26.7%)	4 (26.7%)	6 (40.0%)	7 (10.8%)
Serious TEAEs by Closest Relationship to Infusion				
Related	0	0	0	0
Unrelated	8 (53.3%)	6 (40.0%)	11 (73.3%)	20 (30.8%)
TEAEs by Maximum Severity				
Mild	2 (13.3%)	2 (13.3%)	0	20 (30.8%)
Moderate	2 (13.3%)	5 (33.3%)	2 (13.3%)	30 (46.2%)
Severe	11 (73.3%)	6 (40.0%)	13 (86.7%)	15 (23.1%)
Injection Site Reaction	5 (33.3%)	1 (6.7%)	5 (33.3%)	46 (70.8%)
TEAEs Leading to Study Discontinuation	1 (6.7%)	4 (26.7%)	5 (33.3%)	7 (10.8%)

Data locked as of [redacted] 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
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.
APL-2 dosing escalation is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation.

Table 17.14
Overview of Treatment-Emergent Adverse Events (TEAE) by Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

	Subjects with Any Dosing Escalation			
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
TEAEs Leading to Death	0	0	0	1 (1.5%)
TEAEs Due to COVID-19	0	0	0	1 (1.5%)
TEAEs Beyond Week 48	0	0	0	3 (4.6%)

Data locked as of [redacted] 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
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.
APL-2 dosing escalation is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation.

表 2.7.4-53　無作為化投与期間又は非盲検投与期間のペグセタコプラン用量漸増の有無による TEAE（APL2-302 試験：安全性解析対象集団）

Protocol APL2-302
EMA Day 120 Response

Table 17.13
Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Any TEAEs	15 (100.0%)	13 (86.7%)	15 (100.0%)	65 (100.0%)
Blood and lymphatic system disorders	14 (93.3%)	8 (53.3%)	15 (100.0%)	26 (40.0%)
Haemolysis	11 (73.3%)	7 (46.7%)	13 (86.7%)	14 (21.5%)
Anaemia	2 (13.3%)	1 (6.7%)	3 (20.0%)	6 (9.2%)
Eosinophilia	1 (6.7%)	0	1 (6.7%)	0
Haemoglobinaemia	1 (6.7%)	0	1 (6.7%)	0
Haemolytic anaemia	1 (6.7%)	0	1 (6.7%)	2 (3.1%)
Immune thrombocytopenia	0	1 (6.7%)	1 (6.7%)	0
Intravascular haemolysis	0	1 (6.7%)	1 (6.7%)	0
Neutropenia	0	1 (6.7%)	1 (6.7%)	3 (4.6%)
Splenomegaly	1 (6.7%)	0	1 (6.7%)	0
Thrombocytopenia	1 (6.7%)	0	1 (6.7%)	6 (9.2%)
Bone marrow failure	0	0	0	1 (1.5%)
Cytopenia	0	0	0	1 (1.5%)
Extravascular haemolysis	0	0	0	1 (1.5%)
Leukopenia	0	0	0	1 (1.5%)
Lymphadenopathy	0	0	0	1 (1.5%)
Lymphopenia	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.
If a subject has multiple occurrences of a TEAE, the subject is counted only once for a given System Organ Class and Preferred Term.
APL-2 dosing escalation is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation.

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Table 17.13

Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Cardiac disorders	2 (13.3%)	1 (6.7%)	3 (20.0%)	5 (7.7%)
Angina pectoris	0	1 (6.7%)	1 (6.7%)	2 (3.1%)
Myocardial ischaemia	1 (6.7%)	0	1 (6.7%)	0
Palpitations	1 (6.7%)	0	1 (6.7%)	3 (4.6%)
Atrial fibrillation	0	0	0	1 (1.5%)
Extrasystoles	0	0	0	1 (1.5%)
Pericardial effusion	0	0	0	1 (1.5%)
Tachycardia	0	0	0	1 (1.5%)

Data locked as of [redacted] were used.
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.
If a subject has multiple occurrences of a TEAE, the subject is counted only once for a given System Organ Class and Preferred Term.
APL-2 dosing escalation is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation.

Table 17.13

Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Ear and labyrinth disorders	1 (6.7%)	1 (6.7%)	1 (6.7%)	2 (3.1%)
Ear discomfort	1 (6.7%)	0	1 (6.7%)	1 (1.5%)
Ear pain	0	1 (6.7%)	1 (6.7%)	0
Hypoacusis	0	0	0	1 (1.5%)
Tinnitus	0	0	0	1 (1.5%)
Vertigo	0	0	0	2 (3.1%)

Data locked as of [redacted] 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.
If a subject has multiple occurrences of a TEAE, the subject is counted only once for a given System Organ Class and Preferred Term.
APL-2 dosing escalation is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation.

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SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation (N = 65)
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	
Eye disorders	0	1 (6.7%)	1 (6.7%)	5 (7.7%)
Ulcerative keratitis	0	1 (6.7%)	1 (6.7%)	0
Dry eye	0	0	0	1 (1.5%)
Eye haemorrhage	0	0	0	1 (1.5%)
Eye swelling	0	0	0	1 (1.5%)
Ocular hyperaemia	0	0	0	1 (1.5%)
Vision blurred	0	0	0	1 (1.5%)
Visual impairment	0	0	0	1 (1.5%)

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SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	(N = 65)
Gastrointestinal disorders	10 (66.7%)	7 (46.7%)	12 (80.0%)	38 (58.5%)
Diarrhoea	4 (26.7%)	0	4 (26.7%)	22 (33.8%)
Abdominal pain	2 (13.3%)	1 (6.7%)	3 (20.0%)	10 (15.4%)
Abdominal discomfort	2 (13.3%)	0	2 (13.3%)	4 (6.2%)
Abdominal distension	1 (6.7%)	1 (6.7%)	2 (13.3%)	4 (6.2%)
Abdominal pain upper	2 (13.3%)	0	2 (13.3%)	2 (3.1%)
Vomiting	1 (6.7%)	1 (6.7%)	2 (13.3%)	6 (9.2%)
Abdominal wall cyst	0	1 (6.7%)	1 (6.7%)	0
Aerophagia	1 (6.7%)	0	1 (6.7%)	0
Constipation	0	1 (6.7%)	1 (6.7%)	5 (7.7%)
Gastrointestinal haemorrhage	1 (6.7%)	0	1 (6.7%)	1 (1.5%)
Haematochezia	0	1 (6.7%)	1 (6.7%)	0
Intestinal ischaemia	0	1 (6.7%)	1 (6.7%)	0
Lip swelling	0	1 (6.7%)	1 (6.7%)	0
Oedematous pancreatitis	0	1 (6.7%)	1 (6.7%)	0
Pancreatitis	1 (6.7%)	0	1 (6.7%)	0
Small intestinal obstruction	0	1 (6.7%)	1 (6.7%)	0
Abdominal pain lower	0	0	0	2 (3.1%)
Abdominal tenderness	0	0	0	1 (1.5%)
Aphthous ulcer	0	0	0	1 (1.5%)
Dental caries	0	0	0	2 (3.1%)

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	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Dyspepsia	0	0	0	2 (3.1%)
Flatulence	0	0	0	2 (3.1%)
Gastric ulcer	0	0	0	1 (1.5%)
Gastrooesophageal reflux disease	0	0	0	1 (1.5%)
Gingival erythema	0	0	0	1 (1.5%)
Gingival pruritus	0	0	0	1 (1.5%)
Inguinal hernia	0	0	0	1 (1.5%)
Nausea	0	0	0	11 (16.9%)
Paraesthesia oral	0	0	0	1 (1.5%)
Stomatitis	0	0	0	2 (3.1%)
Swollen tongue	0	0	0	1 (1.5%)
Traumatic occlusion	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
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Table 17.13
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SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	(N = 65)
General disorders and administration site conditions	10 (66.7%)	6 (40.0%)	10 (66.7%)	55 (84.6%)
Asthenia	4 (26.7%)	3 (20.0%)	5 (33.3%)	6 (9.2%)
Fatigue	3 (20.0%)	0	3 (20.0%)	16 (24.6%)
Injection site erythema	3 (20.0%)	0	3 (20.0%)	32 (49.2%)
Oedema	0	2 (13.3%)	2 (13.3%)	1 (1.5%)
Pyrexia	2 (13.3%)	1 (6.7%)	2 (13.3%)	11 (16.9%)
Chest pain	1 (6.7%)	0	1 (6.7%)	3 (4.6%)
Chills	0	1 (6.7%)	1 (6.7%)	1 (1.5%)
Hyperthermia	0	1 (6.7%)	1 (6.7%)	2 (3.1%)
Influenza like illness	1 (6.7%)	0	1 (6.7%)	3 (4.6%)
Injection site discolouration	1 (6.7%)	0	1 (6.7%)	0
Injection site pain	1 (6.7%)	1 (6.7%)	1 (6.7%)	7 (10.8%)
Injection site pruritus	1 (6.7%)	0	1 (6.7%)	17 (26.2%)
Injection site rash	1 (6.7%)	0	1 (6.7%)	1 (1.5%)
Injection site reaction	1 (6.7%)	0	1 (6.7%)	9 (13.8%)
Pain	1 (6.7%)	0	1 (6.7%)	4 (6.2%)
Swelling face	0	1 (6.7%)	1 (6.7%)	0
Vaccination site pain	1 (6.7%)	0	1 (6.7%)	3 (4.6%)
Administration site discolouration	0	0	0	1 (1.5%)
Catheter site pain	0	0	0	1 (1.5%)

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SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation (N = 65)
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	
Catheter site related reaction	0	0	0	1 (1.5%)
Chest discomfort	0	0	0	2 (3.1%)
Facial pain	0	0	0	1 (1.5%)
Infusion site bruising	0	0	0	1 (1.5%)
Infusion site erythema	0	0	0	2 (3.1%)
Infusion site induration	0	0	0	1 (1.5%)
Infusion site pain	0	0	0	1 (1.5%)
Infusion site reaction	0	0	0	2 (3.1%)
Infusion site swelling	0	0	0	1 (1.5%)
Infusion site urticaria	0	0	0	1 (1.5%)
Injection site bruising	0	0	0	7 (10.8%)
Injection site haematoma	0	0	0	1 (1.5%)
Injection site haemorrhage	0	0	0	3 (4.6%)
Injection site induration	0	0	0	6 (9.2%)
Injection site mass	0	0	0	1 (1.5%)
Injection site swelling	0	0	0	11 (16.9%)
Malaise	0	0	0	1 (1.5%)
Non-cardiac chest pain	0	0	0	2 (3.1%)
Oedema peripheral	0	0	0	1 (1.5%)
Peripheral swelling	0	0	0	3 (4.6%)
Vaccination site erythema	0	0	0	2 (3.1%)

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SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation (N = 65)
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	
Vaccination site inflammation	0	0	0	1 (1.5%)
Vaccination site joint pain	0	0	0	1 (1.5%)
Vaccination site lymphadenopathy	0	0	0	1 (1.5%)
Vaccination site reaction	0	0	0	2 (3.1%)
Vaccination site swelling	0	0	0	3 (4.6%)

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	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Hepatobiliary disorders	6 (40.0%)	2 (13.3%)	6 (40.0%)	6 (9.2%)
Cholestasis	3 (20.0%)	0	3 (20.0%)	0
Hepatocellular injury	2 (13.3%)	0	2 (13.3%)	0
Hyperbilirubinaemia	2 (13.3%)	0	2 (13.3%)	3 (4.6%)
Biliary colic	1 (6.7%)	0	1 (6.7%)	0
Cholelithiasis	0	1 (6.7%)	1 (6.7%)	1 (1.5%)
Hepatitis	1 (6.7%)	0	1 (6.7%)	0
Jaundice	1 (6.7%)	0	1 (6.7%)	0
Ocular icterus	1 (6.7%)	1 (6.7%)	1 (6.7%)	2 (3.1%)

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SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Immune system disorders	2 (13.3%)	1 (6.7%)	3 (20.0%)	2 (3.1%)
Allergy to arthropod sting	1 (6.7%)	0	1 (6.7%)	0
Allergy to immunoglobulin therapy	0	1 (6.7%)	1 (6.7%)	0
Skin graft rejection	1 (6.7%)	0	1 (6.7%)	0
Allergy to arthropod bite	0	0	0	1 (1.5%)
Seasonal allergy	0	0	0	1 (1.5%)

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SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	(N = 65)
Infections and infestations	11 (73.3%)	8 (53.3%)	13 (86.7%)	43 (66.2%)
Nasopharyngitis	2 (13.3%)	2 (13.3%)	3 (20.0%)	13 (20.0%)
Upper respiratory tract infection	2 (13.3%)	1 (6.7%)	3 (20.0%)	7 (10.8%)
Febrile infection	2 (13.3%)	0	2 (13.3%)	0
Oral herpes	1 (6.7%)	2 (13.3%)	2 (13.3%)	5 (7.7%)
Respiratory tract infection	1 (6.7%)	1 (6.7%)	2 (13.3%)	1 (1.5%)
Sinusitis	1 (6.7%)	1 (6.7%)	2 (13.3%)	5 (7.7%)
Urinary tract infection	0	2 (13.3%)	2 (13.3%)	8 (12.3%)
Bacteriuria	1 (6.7%)	0	1 (6.7%)	0
Biliary sepsis	1 (6.7%)	0	1 (6.7%)	0
Candida infection	0	1 (6.7%)	1 (6.7%)	0
Cellulitis	1 (6.7%)	0	1 (6.7%)	1 (1.5%)
Chronic sinusitis	0	1 (6.7%)	1 (6.7%)	0
Cystitis	0	1 (6.7%)	1 (6.7%)	1 (1.5%)
Enterococcal infection	0	1 (6.7%)	1 (6.7%)	0
Gastroenteritis	1 (6.7%)	0	1 (6.7%)	4 (6.2%)
Gastroenteritis viral	0	1 (6.7%)	1 (6.7%)	0
Pneumonia	0	1 (6.7%)	1 (6.7%)	0
Post procedural sepsis	0	1 (6.7%)	1 (6.7%)	0
Rhinitis	1 (6.7%)	0	1 (6.7%)	2 (3.1%)
Rhinovirus infection	1 (6.7%)	0	1 (6.7%)	0

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SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	(N = 65)
Sepsis	0	1 (6.7%)	1 (6.7%)	2 (3.1%)
Tonsillitis	1 (6.7%)	0	1 (6.7%)	0
Tooth infection	1 (6.7%)	0	1 (6.7%)	1 (1.5%)
Bacterial infection	0	0	0	1 (1.5%)
Bronchitis	0	0	0	1 (1.5%)
COVID-19	0	0	0	1 (1.5%)
Cervicitis	0	0	0	1 (1.5%)
Diverticulitis	0	0	0	1 (1.5%)
Ear infection	0	0	0	1 (1.5%)
Fungal infection	0	0	0	2 (3.1%)
Furuncle	0	0	0	1 (1.5%)
Gastrointestinal infection	0	0	0	2 (3.1%)
Groin infection	0	0	0	1 (1.5%)
Hordeolum	0	0	0	1 (1.5%)
Infection	0	0	0	1 (1.5%)
Laryngitis	0	0	0	1 (1.5%)
Oral infection	0	0	0	1 (1.5%)
Otitis externa	0	0	0	2 (3.1%)
Periodontitis	0	0	0	1 (1.5%)
Pharyngitis	0	0	0	1 (1.5%)
Pilonidal cyst	0	0	0	1 (1.5%)

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	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	
Pulpitis dental	0	0	0	1 (1.5%)
Respiratory tract infection viral	0	0	0	1 (1.5%)
Tinea infection	0	0	0	1 (1.5%)
Tinea pedis	0	0	0	1 (1.5%)
Tonsillitis bacterial	0	0	0	1 (1.5%)
Viral infection	0	0	0	1 (1.5%)
Viral pharyngitis	0	0	0	1 (1.5%)
Vulvovaginal mycotic infection	0	0	0	1 (1.5%)

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SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	(N = 65)
Injury, poisoning and procedural complications	4 (26.7%)	2 (13.3%)	5 (33.3%)	18 (27.7%)
Cartilage injury	1 (6.7%)	1 (6.7%)	1 (6.7%)	0
Chemical peritonitis	0	1 (6.7%)	1 (6.7%)	0
Contusion	1 (6.7%)	0	1 (6.7%)	7 (10.8%)
Muscle strain	1 (6.7%)	0	1 (6.7%)	0
Traumatic haematoma	1 (6.7%)	0	1 (6.7%)	0
Vaccination complication	1 (6.7%)	0	1 (6.7%)	5 (7.7%)
Ankle fracture	0	0	0	1 (1.5%)
Arthropod bite	0	0	0	2 (3.1%)
Fall	0	0	0	1 (1.5%)
Infusion related reaction	0	0	0	1 (1.5%)
Limb injury	0	0	0	1 (1.5%)
Muscle injury	0	0	0	1 (1.5%)
Tooth fracture	0	0	0	1 (1.5%)

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Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	(N = 65)
Investigations	0	3 (20.0%)	3 (20.0%)	18 (27.7%)
Blood bilirubin increased	0	1 (6.7%)	1 (6.7%)	1 (1.5%)
Blood creatinine increased	0	1 (6.7%)	1 (6.7%)	1 (1.5%)
Blood lactate dehydrogenase increased	0	1 (6.7%)	1 (6.7%)	1 (1.5%)
Weight decreased	0	1 (6.7%)	1 (6.7%)	1 (1.5%)
Alanine aminotransferase increased	0	0	0	3 (4.6%)
Aspartate aminotransferase increased	0	0	0	1 (1.5%)
Bilirubin conjugated increased	0	0	0	1 (1.5%)
Blood folate decreased	0	0	0	1 (1.5%)
Blood phosphorus decreased	0	0	0	1 (1.5%)
Body temperature increased	0	0	0	1 (1.5%)
Complement factor C3 increased	0	0	0	2 (3.1%)
Fibrin D dimer increased	0	0	0	1 (1.5%)
International normalised ratio increased	0	0	0	1 (1.5%)
Platelet count decreased	0	0	0	2 (3.1%)
Serum ferritin increased	0	0	0	3 (4.6%)
Weight increased	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.
If a subject has multiple occurrences of a TEAE, the subject is counted only once for a given System Organ Class and Preferred Term.
APL-2 dosing escalation is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation.

Table 17.13

Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Metabolism and nutrition disorders	3 (20.0%)	3 (20.0%)	5 (33.3%)	10 (15.4%)
Hypoalbuminaemia	0	2 (13.3%)	2 (13.3%)	0
Cell death	1 (6.7%)	0	1 (6.7%)	0
Decreased appetite	1 (6.7%)	1 (6.7%)	1 (6.7%)	2 (3.1%)
Hypomagnesaemia	0	1 (6.7%)	1 (6.7%)	1 (1.5%)
Hyponatraemia	0	1 (6.7%)	1 (6.7%)	0
Hypophosphataemia	0	1 (6.7%)	1 (6.7%)	0
Iron overload	1 (6.7%)	0	1 (6.7%)	1 (1.5%)
Malnutrition	0	1 (6.7%)	1 (6.7%)	0
Gout	0	0	0	1 (1.5%)
Hypercalcaemia	0	0	0	1 (1.5%)
Hyperferritinaemia	0	0	0	1 (1.5%)
Hypocalcaemia	0	0	0	1 (1.5%)
Hypokalaemia	0	0	0	2 (3.1%)
Iron deficiency	0	0	0	1 (1.5%)
Vitamin B12 deficiency	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.
If a subject has multiple occurrences of a TEAE, the subject is counted only once for a given System Organ Class and Preferred Term.
APL-2 dosing escalation is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject[redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation.

Table 17.13

Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	(N = 65)
Musculoskeletal and connective tissue disorders	7 (46.7%)	3 (20.0%)	7 (46.7%)	34 (52.3%)
Pain in extremity	4 (26.7%)	0	4 (26.7%)	6 (9.2%)
Arthralgia	1 (6.7%)	2 (13.3%)	3 (20.0%)	8 (12.3%)
Myalgia	2 (13.3%)	0	2 (13.3%)	6 (9.2%)
Haemarthrosis	1 (6.7%)	0	1 (6.7%)	0
Haematoma muscle	1 (6.7%)	1 (6.7%)	1 (6.7%)	0
Joint effusion	0	1 (6.7%)	1 (6.7%)	0
Sacroiliitis	1 (6.7%)	0	1 (6.7%)	0
Arthropathy	0	0	0	1 (1.5%)
Back pain	0	0	0	12 (18.5%)
Bone pain	0	0	0	1 (1.5%)
Bursitis	0	0	0	1 (1.5%)
Joint swelling	0	0	0	1 (1.5%)
Muscle spasms	0	0	0	4 (6.2%)
Muscle twitching	0	0	0	1 (1.5%)
Musculoskeletal chest pain	0	0	0	1 (1.5%)
Musculoskeletal pain	0	0	0	1 (1.5%)
Neck pain	0	0	0	3 (4.6%)
Pain in jaw	0	0	0	2 (3.1%)
Rheumatoid arthritis	0	0	0	1 (1.5%)
Torticollis	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.
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Table 17.13

Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (6.7%)	2 (13.3%)	2 (13.3%)	2 (3.1%)
Acute myeloid leukaemia	0	1 (6.7%)	1 (6.7%)	0
Basal cell carcinoma	1 (6.7%)	0	1 (6.7%)	1 (1.5%)
Diffuse large B-cell lymphoma	0	1 (6.7%)	1 (6.7%)	0
Skin papilloma	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.
If a subject has multiple occurrences of a TEAE, the subject is counted only once for a given System Organ Class and Preferred Term.
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Table 17.13

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SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	(N = 65)
Nervous system disorders	7 (46.7%)	1 (6.7%)	7 (46.7%)	27 (41.5%)
Headache	3 (20.0%)	0	3 (20.0%)	21 (32.3%)
Dizziness	1 (6.7%)	0	1 (6.7%)	9 (13.8%)
Lethargy	1 (6.7%)	0	1 (6.7%)	1 (1.5%)
Parosmia	1 (6.7%)	0	1 (6.7%)	0
Sciatica	0	1 (6.7%)	1 (6.7%)	1 (1.5%)
Somnolence	1 (6.7%)	0	1 (6.7%)	0
Syncope	1 (6.7%)	0	1 (6.7%)	1 (1.5%)
Carpal tunnel syndrome	0	0	0	1 (1.5%)
Complex regional pain syndrome	0	0	0	1 (1.5%)
Disturbance in attention	0	0	0	1 (1.5%)
Facial paralysis	0	0	0	1 (1.5%)
Head discomfort	0	0	0	1 (1.5%)
Paraesthesia	0	0	0	2 (3.1%)
Peripheral sensory neuropathy	0	0	0	1 (1.5%)
Restless legs syndrome	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.
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APL-2 dosing escalation is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation.

Table 17.13

Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	(N = 65)
Psychiatric disorders	1 (6.7%)	0	1 (6.7%)	11 (16.9%)
Sleep disorder	1 (6.7%)	0	1 (6.7%)	2 (3.1%)
Anxiety	0	0	0	5 (7.7%)
Depressed mood	0	0	0	1 (1.5%)
Depression	0	0	0	2 (3.1%)
Insomnia	0	0	0	3 (4.6%)
Irritability	0	0	0	1 (1.5%)
Mental disorder	0	0	0	1 (1.5%)
Restlessness	0	0	0	2 (3.1%)

Data locked as of [redacted] 20[redacted] were used.
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Table 17.13
Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation (N = 65)
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	
Renal and urinary disorders	4 (26.7%)	4 (26.7%)	6 (40.0%)	15 (23.1%)
Acute kidney injury	3 (20.0%)	1 (6.7%)	3 (20.0%)	1 (1.5%)
Haematuria	1 (6.7%)	2 (13.3%)	2 (13.3%)	2 (3.1%)
Chromaturia	0	1 (6.7%)	1 (6.7%)	5 (7.7%)
Renal failure	0	1 (6.7%)	1 (6.7%)	0
Dysuria	0	0	0	1 (1.5%)
Haemoglobinuria	0	0	0	3 (4.6%)
Nephrolithiasis	0	0	0	1 (1.5%)
Renal pain	0	0	0	1 (1.5%)
Urinary tract disorder	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
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Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Reproductive system and breast disorders	0	0	0	8 (12.3%)
Breast pain	0	0	0	1 (1.5%)
Dysmenorrhoea	0	0	0	1 (1.5%)
Genital haemorrhage	0	0	0	1 (1.5%)
Menopausal symptoms	0	0	0	1 (1.5%)
Menstruation irregular	0	0	0	1 (1.5%)
Ovarian cyst	0	0	0	1 (1.5%)
Vaginal discharge	0	0	0	1 (1.5%)
Vaginal haemorrhage	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.
If a subject has multiple occurrences of a TEAE, the subject is counted only once for a given System Organ Class and Preferred Term.
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Table 17.13

Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term by APL-2 Dosing Escalation During the Randomized Controlled and Open-label Periods (Safety Set)

SYSTEM ORGAN CLASS Preferred Term	Subjects with Any Dosing Escalation			Subjects with No Dosing Escalation
	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	(N = 65)
Respiratory, thoracic and mediastinal disorders	6 (40.0%)	5 (33.3%)	9 (60.0%)	23 (35.4%)
Dyspnoea	2 (13.3%)	2 (13.3%)	4 (26.7%)	5 (7.7%)
Cough	3 (20.0%)	0	3 (20.0%)	10 (15.4%)
Epistaxis	1 (6.7%)	2 (13.3%)	3 (20.0%)	3 (4.6%)
Acute respiratory failure	1 (6.7%)	2 (13.3%)	2 (13.3%)	0
Oropharyngeal pain	2 (13.3%)	0	2 (13.3%)	8 (12.3%)
Hiccups	0	1 (6.7%)	1 (6.7%)	1 (1.5%)
Lung disorder	1 (6.7%)	0	1 (6.7%)	0
Pulmonary mass	0	1 (6.7%)	1 (6.7%)	0
Pulmonary oedema	0	1 (6.7%)	1 (6.7%)	0
Rhinorrhoea	1 (6.7%)	0	1 (6.7%)	0
Acute respiratory distress syndrome	0	0	0	1 (1.5%)
Choking sensation	0	0	0	1 (1.5%)
Dyspnoea exertional	0	0	0	1 (1.5%)
Hypersensitivity pneumonitis	0	0	0	1 (1.5%)
Nasal congestion	0	0	0	3 (4.6%)
Productive cough	0	0	0	1 (1.5%)
Respiratory tract congestion	0	0	0	1 (1.5%)
Rhinalgia	0	0	0	1 (1.5%)
Rhinitis allergic	0	0	0	2 (3.1%)
Sinus congestion	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
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	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Skin and subcutaneous tissue disorders	4 (26.7%)	4 (26.7%)	8 (53.3%)	17 (26.2%)
Dermatitis allergic	1 (6.7%)	0	1 (6.7%)	0
Erythema	0	1 (6.7%)	1 (6.7%)	3 (4.6%)
Hyperhidrosis	1 (6.7%)	0	1 (6.7%)	2 (3.1%)
Night sweats	0	1 (6.7%)	1 (6.7%)	2 (3.1%)
Prurigo	1 (6.7%)	0	1 (6.7%)	0
Rash papular	0	1 (6.7%)	1 (6.7%)	0
Skin lesion	1 (6.7%)	0	1 (6.7%)	1 (1.5%)
Urticaria	0	1 (6.7%)	1 (6.7%)	2 (3.1%)
Acne	0	0	0	1 (1.5%)
Dermatitis acneiform	0	0	0	1 (1.5%)
Dry skin	0	0	0	1 (1.5%)
Eczema	0	0	0	1 (1.5%)
Mechanical urticaria	0	0	0	1 (1.5%)
Nail discolouration	0	0	0	1 (1.5%)
Petechiae	0	0	0	1 (1.5%)
Pigmentation disorder	0	0	0	1 (1.5%)
Pruritus	0	0	0	1 (1.5%)
Purpura	0	0	0	1 (1.5%)
Rash	0	0	0	3 (4.6%)

Data locked as of [redacted] 20[redacted] were used.
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Table 17.13
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	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Rash maculo-papular	0	0	0	1 (1.5%)
Skin weeping	0	0	0	1 (1.5%)

Data locked as of [redacted] 20[redacted] were used.
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	Subjects with Any Dosing Escalation			
SYSTEM ORGAN CLASS Preferred Term	Before Dosing Escalation (N = 15)	During or After Dosing Escalation (N = 15)	Total (N = 15)	Subjects with No Dosing Escalation (N = 65)
Vascular disorders	2 (13.3%)	2 (13.3%)	4 (26.7%)	6 (9.2%)
Circulatory collapse	0	1 (6.7%)	1 (6.7%)	0
Deep vein thrombosis	0	1 (6.7%)	1 (6.7%)	0
Hypertension	0	1 (6.7%)	1 (6.7%)	6 (9.2%)
Intermittent claudication	1 (6.7%)	0	1 (6.7%)	0
Jugular vein thrombosis	0	1 (6.7%)	1 (6.7%)	0
Orthostatic hypotension	1 (6.7%)	0	1 (6.7%)	0
Peripheral arterial occlusive disease	1 (6.7%)	0	1 (6.7%)	0

Data locked as of [redacted], 20[redacted] were used.
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
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表 2.7.4-54　無作為化投与期間又は非盲検投与期間の最初のペグセタコプラン用量漸増中又は漸増後に発現した TEAE の一覧（APL2-302 試験：安全性解析対象集団）

Protocol APL2-302
Adhoc Analysis for EMA Type II Variation

Listing 17.13
Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (158)/ Ongoing	Musculoskeletal and connective tissue disorders/ Arthralgia/ Intermittent Hip pain	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (209)/ 20[redacted] (218)	Eye disorders/ Ulcerative keratitis/ Corneal ulcers	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (219)/ Ongoing	Musculoskeletal and connective tissue disorders/ Arthralgia/ Intermittent joint pain	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (222)/ 20[redacted] (230)	Infections and infestations/ Gastroenteritis viral/ Stomach virus	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (236)/ 20[redacted] (239)	Renal and urinary disorders/ Haematuria/ Hematuria	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (236)/ Ongoing	Blood and lymphatic system disorders/ Haemolysis/ Hemolysis	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE INCREASED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (239)/ Ongoing	General disorders and administration site conditions/ Oedema/ Intermittent edema	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Possibly Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

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Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (241)/ Ongoing	General disorders and administration site conditions/ Injection site pain/ Intermittent injection site burning	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ Yes/ (ABDOMEN)	Definitely Related/ Not Applicable/ Not Related
20[redacted] (253)/ Ongoing	Gastrointestinal disorders/ Abdominal distension/ Abdominal bloating	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Possibly Related/ Not Applicable/ Not Related
20[redacted] (256)/ 20[redacted] (324)	Infections and infestations/ Sinusitis/ Intermittent Sinusitis	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (267)/ 20[redacted] (274)	Infections and infestations/ Nasopharyngitis/ Common cold	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (315)/ Ongoing	Injury, poisoning and procedural complications/ Cartilage injury/ Labral hip tear	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (324)/ 20[redacted] (325)	Renal and urinary disorders/ Haematuria/ Hematuria	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

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Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (244)/ 20[redacted] (244)	Respiratory, thoracic and mediastinal disorders/ Epistaxis/ nose bleed	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

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Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (247)/ 20[redacted] (251)	Gastrointestinal disorders/ Small intestinal obstruction/ Ileal obstruction	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	Yes/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (309)/ Ongoing	Blood and lymphatic system disorders/ Neutropenia/ neutropenia	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (331)/ Ongoing	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Acute myeloid leukaemia/ Acute Myeloid Leukaemia	SEVERE	NOT RECOVERED/NOT RESOLVED/ DRUG WITHDRAWN/ NOT APPLICABLE	Yes/ Yes/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

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Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (224)/ 20[redacted] (253)	Renal and urinary disorders/ Chromaturia/ Dark Urine	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (226)/ 20[redacted] (253)	Gastrointestinal disorders/ Lip swelling/ Swelling around lips	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (226)/ 20[redacted] (253)	General disorders and administration site conditions/ Swelling face/ Swelling of lower face	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (226)/ 20[redacted] (277)	Infections and infestations/ Chronic sinusitis/ Chronic sinusitis	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (253)/ Ongoing	Investigations/ Blood bilirubin increased/ High total bilirubin	MILD	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (253)/ Ongoing	Investigations/ Blood lactate dehydrogenase increased/ High LDH	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (273)/ Ongoing	Ear and labyrinth disorders/ Ear pain/ ear ache	MILD	RECOVERING/RESOLVING/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted], 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

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Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (273)/ Ongoing	General disorders and administration site conditions/ Chills/ cold shivery	MODERATE	RECOVERING/RESOLVING/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (275)/ 20[redacted] (283)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough haemolysis	SEVERE	RECOVERED/RESOLVED/ DRUG WITHDRAWN/ NOT APPLICABLE	No/ Yes/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (276)/ 20[redacted] (283)	Infections and infestations/ Urinary tract infection/ Urinary tract infection	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Unlikely Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted], 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

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Protocol APL2-302
Adhoc Analysis for EMA Type II Variation

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (268)/ 20[redacted] (289)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough haemolysis	MODERATE	RECOVERED/RESOLVED/ NOT APPLICABLE/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (268)/ 20[redacted] (295)	Infections and infestations/ Sepsis/ Sepsis	SEVERE	RECOVERED/RESOLVED/ DRUG WITHDRAWN/ DOSE INCREASED	Yes/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (277)/ 20[redacted] (279)	Metabolism and nutrition disorders/ Hypomagnesaemia/ Hypomagnesemia	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (277)/ 20[redacted] (283)	Metabolism and nutrition disorders/ Hyponatraemia/ Hyponatremia	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (278)/ 20[redacted] (362)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Diffuse large B-cell lymphoma/ Diffuse Large B-Cell Lymphoma	SEVERE	RECOVERED/RESOLVED/ DRUG WITHDRAWN/ DOSE INCREASED	Yes/ Yes/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (282)/ 20[redacted] (283)	Metabolism and nutrition disorders/ Hypophosphataemia/ Hypophosphatemia	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (282)/ 20[redacted] (288)	Metabolism and nutrition disorders/ Hypomagnesaemia/ Hypomagnesemia	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted], 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

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Listing 17.13
Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (285)/ 20[redacted] (291)	Vascular disorders/ Deep vein thrombosis/ Deep Vein Thrombosis	SEVERE	RECOVERED/RESOLVED/ NOT APPLICABLE/ NOT APPLICABLE	Yes/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (288)/ Ongoing	Skin and subcutaneous tissue disorders/ Rash papular/ Neck erytematous perifollicular papules	MILD	RECOVERING/RESOLVING/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (290)/ 20[redacted] (291)	Metabolism and nutrition disorders/ Hypophosphataemia/ Hypophosphatemia	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Protocol APL2-302
Adhoc Analysis for EMA Type II Variation

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (217)/ 20[redacted] (223)	Infections and infestations/ Respiratory tract infection/ worsening of respiratory infection	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (253)/ 20[redacted] (254)	Infections and infestations/ Nasopharyngitis/ cold	MILD	RECOVERED/RESOLVED/ NOT APPLICABLE/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (276)/ 20[redacted] (281)	Infections and infestations/ Upper respiratory tract infection/ upper respiratory tract infection	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
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Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (324)/ 20[redacted] (331)	Musculoskeletal and connective tissue disorders/ Joint effusion/ hip joint effusion	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted], 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (149)/ 20[redacted] (149)	Vascular disorders/ Circulatory collapse/ Circulatory collapse	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (149)/ 20[redacted] (156)	Blood and lymphatic system disorders/ Anaemia/ worsened anemia	SEVERE	RECOVERED/RESOLVED/ DOSE INCREASED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (149)/ 20[redacted] (156)	Blood and lymphatic system disorders/ Intravascular haemolysis/ Acute intravascular hemolisis	SEVERE	RECOVERED/RESOLVED/ DOSE INCREASED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (149)/ 20[redacted] (156)	Respiratory, thoracic and mediastinal disorders/ Acute respiratory failure/ Acute Respiratory Failure	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (149)/ 20[redacted] (159)	Infections and infestations/ Post procedural sepsis/ Sepsis post-surgery	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	Yes/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (149)/ 20[redacted] (204)	Injury, poisoning and procedural complications/ Chemical peritonitis/ biliary peritonitis	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (154)/ 20[redacted] (196)	Renal and urinary disorders/ Renal failure/ Acute anuric renal failure	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted], 20[redacted] were used.
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (154)/ 20[redacted] (259)	Vascular disorders/ Hypertension/ hypertention	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (157)/ 20[redacted] (157)	Gastrointestinal disorders/ Haematochezia/ Hematochezia	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (157)/ 20[redacted] (157)	Renal and urinary disorders/ Haematuria/ Hematuria	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (159)/ 20[redacted] (182)	Infections and infestations/ Candida infection/ Candida tropicalis infection	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (159)/ 20[redacted] (182)	Infections and infestations/ Enterococcal infection/ E. Faecium infection	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (159)/ 20[redacted] (182)	Infections and infestations/ Pneumonia/ alveolar pneumonia	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Possibly Related/ Not Applicable/ Not Related
20[redacted] (163)/ 20[redacted] (167)	General disorders and administration site conditions/ Oedema/ Edemas	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted], 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (163)/ 20[redacted] (167)	Respiratory, thoracic and mediastinal disorders/ Pulmonary oedema/ Nephrogenic Pulmonary Edema	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (169)/ 20[redacted] (169)	Vascular disorders/ Jugular vein thrombosis/ bilateral jugular vein thrombosis	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (185)/ 20[redacted] (245)	Blood and lymphatic system disorders/ Haemolysis/ hemolysis	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (191)/ 20[redacted] (259)	Metabolism and nutrition disorders/ Hypoalbuminaemia/ hypoalbuminemia	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (191)/ 20[redacted] (302)	Investigations/ Weight decreased/ weight loss	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (191)/ 20[redacted] (302)	Metabolism and nutrition disorders/ Decreased appetite/ anorexia	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted], 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (220)/ 20[redacted] (233)	Gastrointestinal disorders/ Intestinal ischaemia/ Mesenteric ischemia	SEVERE	RECOVERED/RESOLVED/ DRUG WITHDRAWN/ DOSE NOT CHANGED	Yes/ Yes/ No/ (-)	Possibly Related/ Not Related/ Not Related
20[redacted] (222)/ 20[redacted] (223)	Skin and subcutaneous tissue disorders/ Urticaria/ urticaria	MODERATE	RECOVERED/RESOLVED/ NOT APPLICABLE/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Related/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted], 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (168)/ Ongoing	Blood and lymphatic system disorders/ Haemolysis/ hemolysis	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE INCREASED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (168)/ Ongoing	General disorders and administration site conditions/ Asthenia/ asthenia	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (168)/ Ongoing	Respiratory, thoracic and mediastinal disorders/ Dyspnoea/ Stress dyspnea	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (169)/ 20[redacted] (218)	Blood and lymphatic system disorders/ Immune thrombocytopenia/ Immune thrombocytopenic Purpura	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (217)/ 20[redacted] (217)	General disorders and administration site conditions/ Hyperthermia/ Hyperthermia	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (217)/ 20[redacted] (218)	Immune system disorders/ Allergy to immunoglobulin therapy/ Reaction to intravenous immunoglobulin treatment for the matching duration	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	Yes/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (218)/ 20[redacted] (220)	Respiratory, thoracic and mediastinal disorders/ Epistaxis/ Epistaxis	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (308)/ 20[redacted] (313)	Infections and infestations/ Oral herpes/ Herpes labialisis	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (308)/ 20[redacted] (335)	Nervous system disorders/ Sciatica/ cruralgia	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (336)/ Ongoing	Nervous system disorders/ Sciatica/ cruralgia	MILD	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (56)/ 20[redacted] (224)	Blood and lymphatic system disorders/ Haemolysis/ worsening of hemolisis	MODERATE	RECOVERED/RESOLVED/ DOSE INCREASED/ DOSE INCREASED	No/ No/ No/ (-)	Not Related/ Not Related/ Not Related
20[redacted] (119)/ 20[redacted] (224)	Hepatobiliary disorders/ Ocular icterus/ jaundice conjunctival	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE INCREASED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (127)/ 20[redacted] (224)	General disorders and administration site conditions/ Asthenia/ asthenia	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE INCREASED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (140)/ 20[redacted] (224)	Respiratory, thoracic and mediastinal disorders/ Dyspnoea/ Dyspnia	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE INCREASED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (154)/ 20[redacted] (168)	Infections and infestations/ Cystitis/ cystitis	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (154)/ 20[redacted] (336)	Gastrointestinal disorders/ Abdominal wall cyst/ Periumbilical cyst	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (196)/ 20[redacted] (224)	Infections and infestations/ Oral herpes/ herpes labiale	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Protocol APL2-302
Adhoc Analysis for EMA Type II Variation

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (259)/ 20[redacted] (262)	Cardiac disorders/ Angina pectoris/ Angina*	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Related/ Not Related
20[redacted] (336)/ Ongoing	Skin and subcutaneous tissue disorders/ Erythema/ erythema*	MILD	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Related/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted], Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (306)/ Ongoing	Skin and subcutaneous tissue disorders/ Night sweats/ night sweats	MILD	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted] (188)/ 20[redacted] (221)	Respiratory, thoracic and mediastinal disorders/ Hiccups/ hiccups	MODERATE	RECOVERED/RESOLVED/ DOSE INCREASED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (197)/ 20[redacted] (197)	Respiratory, thoracic and mediastinal disorders/ Acute respiratory failure/ acute respiratory failure	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (197)/ 20[redacted] (221)	Renal and urinary disorders/ Acute kidney injury/ Acute Kidney failure	MODERATE	RECOVERED/RESOLVED/ DOSE INCREASED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (197)/ 20[redacted] (226)	Gastrointestinal disorders/ Constipation/ Constipation	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (197)/ 20[redacted] (226)	Investigations/ Blood creatinine increased/ creatinine increase	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE INCREASED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (197)/ 20[redacted] (251)	Metabolism and nutrition disorders/ Hypoalbuminaemia/ hypoalbuminemia	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted] (197)/ 20[redacted] (251)	Metabolism and nutrition disorders/ Malnutrition/ Denutrition	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

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Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted](197)/ Ongoing	General disorders and administration site conditions/ Asthenia/ worsening of Asthenia	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted](209)/ 20[redacted](210)	Musculoskeletal and connective tissue disorders/ Arthralgia/ right hip pain	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted](210)/ 20[redacted](210)	Gastrointestinal disorders/ Vomiting/ vomitting	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Possibly Related/ Not Applicable/ Not Related
20[redacted](210)/ 20[redacted](212)	Musculoskeletal and connective tissue disorders/ Haematoma muscle/ psoas hematoma	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
20[redacted](210)/ 20[redacted](213)	Gastrointestinal disorders/ Abdominal pain/ abdominal pain	MODERATE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Possibly Related/ Not Applicable/ Not Related
20[redacted](210)/ 20[redacted](214)	General disorders and administration site conditions/ Pyrexia/ fever	MILD	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	No/ No/ No/ (-)	Possibly Related/ Not Applicable/ Not Related
20[redacted](212)/ 20[redacted](252)	Infections and infestations/ Urinary tract infection/ urinary infection	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Possibly Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
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Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

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Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = APL-2, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
20[redacted](213)/ 20[redacted](356)	Musculoskeletal and connective tissue disorders/ Haematoma muscle/ psoas hematoma*	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ NOT APPLICABLE	Yes/ No/ No/ (-)	Not Related/ Not Related/ Not Related
20[redacted](213)/ Ongoing	Respiratory, thoracic and mediastinal disorders/ Pulmonary mass/ lung nodules*	MILD	NOT RECOVERED/NOT RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Possibly Related/ Not Related/ Not Related
20[redacted](226)/ 20[redacted](226)	Respiratory, thoracic and mediastinal disorders/ Acute respiratory failure/ acute respiratory failure*	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Possibly Related/ Possibly Related/ Not Related
20[redacted](253)/ 20[redacted](253)	Respiratory, thoracic and mediastinal disorders/ Acute respiratory failure/ acute respiratory failure*	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Possibly Related/ Possibly Related/ Not Related
20[redacted](282)/ 20[redacted](282)	Respiratory, thoracic and mediastinal disorders/ Acute respiratory failure/ acute respiratory failure*	SEVERE	RECOVERED/RESOLVED/ DOSE NOT CHANGED/ DOSE NOT CHANGED	No/ No/ No/ (-)	Possibly Related/ Possibly Related/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] 20[redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted] whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
A treatment-emergent adverse event (TEAE) is an adverse event that started on or after the first APL-2 dose or that increased in severity from pre-treatment.
Adverse events were coded to System Organ Class and Preferred Term using MedDRA Version 23.0.

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Listing 17.13

Listing of Treatment-Emergent Adverse Events (TEAE) During or After First APL-2 Dosing Escalation of the Randomized Controlled and Open-label Periods (Safety Set)

Subject ID = [redacted] Treatment Group = Eculizumab, First APL-2 Dosing Escalation Date = [redacted]

Onset DateTime (Study Day[1])/ End DateTime (Study Day[1]) or Ongoing	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Outcome/ Action Taken with Pegcetacoplan/ Eculizumab	Serious AE/ AE Led to Discont/ Inject Site Reaction/ (Location)	Relationship to Pegcetacoplan/ Eculizumab/ Infusion
[redacted](189)/ [redacted](210)	Gastrointestinal disorders/ Oedematous pancreatitis/ Acute Pancreatitis Edematous Form	SEVERE	RECOVERED/RESOLVED/ DOSE INCREASED/ NOT APPLICABLE	Yes/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
[redacted](191)/ [redacted](218)	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough hemolysis	MODERATE	RECOVERED/RESOLVED/ DOSE INCREASED/ NOT APPLICABLE	No/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
[redacted](211)/ [redacted]09:00 (211)	Hepatobiliary disorders/ Cholelithiasis/ Gallstone disease	MODERATE	RECOVERED/RESOLVED/ NOT APPLICABLE/ NOT APPLICABLE	Yes/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related
[redacted](310)/ Ongoing	Blood and lymphatic system disorders/ Haemolysis/ Breakthrough hemolysis	MODERATE	NOT RECOVERED/NOT RESOLVED/ DOSE INCREASED/ NOT APPLICABLE	Yes/ No/ No/ (-)	Not Related/ Not Applicable/ Not Related

[1] Study Day is the number of days relative to the date of randomization.
Data locked as of [redacted] were used.
15 subjects were considered to have APL-2 dosing escalation, which is defined as having had at least 5 consecutive APL-2 doses that were <= 3 days apart. However, Subject [redacted], whose dosing was escalated and who discontinued treatment after receiving 4 consecutive APL-2 doses <= 3 days apart, is also counted as having had dosing escalation. Only 13 subjects were included in the listing because 2 subjects did not have any adverse events during or after escalation.
AE = adverse event
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