Table 15.4.1.1
Number of AEs through Day 28 by system organ class, preferred term, and severity
Safety analysis set

System Organ Class (SOC) Preferred Term (PT) Severity	Treatment Placebo (N=108) n_{AEs}	 n (%)		 Ilofotase Alfa (N=112) n_{AEs}	 n (%)		 Total (N=220) n_{AEs}	 n (%)	
Any AE through Day 28	244	71	(65.7)	200	69	(61.6)	444	140	(63.6)
Mild	97	51	(47.2)	82	42	(37.5)	179	93	(42.3)
Moderate	107	43	(39.8)	88	47	(42.0)	195	90	(40.9)
Severe	40	26	(24.1)	30	22	(19.6)	70	48	(21.8)
Blood and lymphatic system disorders	16	15	(13.9)	25	17	(15.2)	41	32	(14.5)
Mild	10	10	(9.3)	12	11	(9.8)	22	21	(9.5)
Moderate	5	5	(4.6)	11	9	(8.0)	16	14	(6.4)
Severe	1	1	(0.9)	2	1	(0.9)	3	2	(0.9)
Anaemia	11	11	(10.2)	14	14	(12.5)	25	25	(11.4)
Mild	8	8	(7.4)	7	7	(6.3)	15	15	(6.8)
Moderate	3	3	(2.8)	6	6	(5.4)	9	9	(4.1)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Blood loss anaemia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Coagulopathy	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Hypofibrinogenaemia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Leukopenia	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Thrombocytopenia	3	3	(2.8)	8	8	(7.1)	11	11	(5.0)
Mild	2	2	(1.9)	3	3	(2.7)	5	5	(2.3)
Moderate	0	0	(0.0)	4	4	(3.6)	4	4	(1.8)
Severe	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Thrombocytosis	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)

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Table 15.4.1.1
Number of AEs through Day 28 by system organ class, preferred term, and severity
Safety analysis set

System Organ Class (SOC) Preferred Term (PT) Severity	Treatment Placebo (N=108) n_{AEs}	 n (%)		Ilofotase Alfa (N=112) n_{AEs}	 n (%)		Total (N=220) n_{AEs}	 n (%)	
Cardiac disorders	34	22	(20.4)	34	27	(24.1)	68	49	(22.3)
Mild	9	8	(7.4)	11	8	(7.1)	20	16	(7.3)
Moderate	13	11	(10.2)	9	7	(6.3)	22	18	(8.2)
Severe	12	9	(8.3)	14	13	(11.6)	26	22	(10.0)
Acute coronary syndrome	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Arrhythmia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Arrhythmia supraventricular	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Atrial fibrillation	8	8	(7.4)	10	9	(8.0)	18	17	(7.7)
Mild	1	1	(0.9)	5	4	(3.6)	6	5	(2.3)
Moderate	7	7	(6.5)	3	3	(2.7)	10	10	(4.5)
Severe	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Atrial thrombosis	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Atrioventricular block	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Atrioventricular block complete	5	5	(4.6)	3	3	(2.7)	8	8	(3.6)
Mild	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	3	3	(2.8)	2	2	(1.8)	5	5	(2.3)
Atrioventricular block first degree	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Mild	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Bradycardia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Bundle branch block left	2	1	(0.9)	0	0	(0.0)	2	1	(0.5)
Mild	2	1	(0.9)	0	0	(0.0)	2	1	(0.5)

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Table 15.4.1.1
Number of AEs through Day 28 by system organ class, preferred term, and severity
Safety analysis set

System Organ Class (SOC) Preferred Term (PT) Severity	Treatment Placebo (N=108) n_{AEs}	 n (%)		Ilofotase Alfa (N=112) n_{AEs}	 n (%)		Total (N=220) n_{AEs}	 n (%)	
Bundle branch block right	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Cardiac arrest	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Severe	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Cardiac failure	3	3	(2.8)	0	0	(0.0)	3	3	(1.4)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Cardiac tamponade	2	2	(1.9)	2	2	(1.8)	4	4	(1.8)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Cardiogenic shock	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Severe	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Dressler's syndrome	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Extrasystoles	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Left ventricular failure	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Low cardiac output syndrome	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Myocardial infarction	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Palpitations	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Pericardial effusion	0	0	(0.0)	6	5	(4.5)	6	5	(2.3)
Mild	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Moderate	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)

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Table 15.4.1.1
Number of AEs through Day 28 by system organ class, preferred term, and severity
Safety analysis set

System Organ Class (SOC) Preferred Term (PT) Severity	Treatment Placebo (N=108) n_{AEs}	 n (%)		Ilofotase Alfa (N=112) n_{AEs}	 n (%)		Total (N=220) n_{AEs}	 n (%)	
Severe	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Pericardial haemorrhage	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Pericarditis	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Pulseless electrical activity	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Sinus arrhythmia	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Sinus bradycardia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Tachycardia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Ventricular tachycardia	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Eye disorders	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Optic ischaemic neuropathy	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Vision blurred	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Gastrointestinal disorders	12	9	(8.3)	3	3	(2.7)	15	12	(5.5)
Mild	4	3	(2.8)	1	1	(0.9)	5	4	(1.8)
Moderate	8	8	(7.4)	2	2	(1.8)	10	10	(4.5)

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Constipation	2	2	(1.9)	2	2	(1.8)	4	4	(1.8)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Diarrhoea	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Dysphagia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Nausea	5	4	(3.7)	0	0	(0.0)	5	4	(1.8)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	4	4	(3.7)	0	0	(0.0)	4	4	(1.8)
Pancreatitis chronic	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Toothache	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Vomiting	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
General disorders and administration site conditions	9	7	(6.5)	9	9	(8.0)	18	16	(7.3)
Mild	6	5	(4.6)	4	4	(3.6)	10	9	(4.1)
Moderate	1	1	(0.9)	5	5	(4.5)	6	6	(2.7)
Severe	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Chest pain	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Impaired healing	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Malaise	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)

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Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Multiple organ dysfunction syndrome	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Severe	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Oedema	2	1	(0.9)	0	0	(0.0)	2	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Oedema peripheral	2	2	(1.9)	3	3	(2.7)	5	5	(2.3)
Mild	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Moderate	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Peripheral swelling	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Pyrexia	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Mild	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Systemic inflammatory response syndrome	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Infections and infestations	35	31	(28.7)	30	25	(22.3)	65	56	(25.5)
Mild	7	6	(5.6)	6	6	(5.4)	13	12	(5.5)
Moderate	17	15	(13.9)	23	19	(17.0)	40	34	(15.5)
Severe	11	11	(10.2)	1	1	(0.9)	12	12	(5.5)
Bacteraemia	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
COVID-19	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Mild	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Candida infection	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Cellulitis	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)

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Clostridial infection	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Enterococcal bacteraemia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Erysipelas	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Folliculitis	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Haematoma infection	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Herpes ophthalmic	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Infection	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Lower respiratory tract infection	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Moderate	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Mediastinitis	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Nosocomial infection	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Otitis externa	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Pneumocystis jirovecii pneumonia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Pneumonia	12	12	(11.1)	16	14	(12.5)	28	26	(11.8)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)

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Number of AEs through Day 28 by system organ class, preferred term, and severity
Safety analysis set

System Organ Class (SOC) Preferred Term (PT) Severity	Treatment Placebo (N=108) n_{AEs}	 n (%)		 Ilofotase Alfa (N=112) n_{AEs}	 n (%)		 Total (N=220) n_{AEs}	 n (%)	
Moderate	7	7	(6.5)	16	14	(12.5)	23	21	(9.5)
Severe	4	4	(3.7)	0	0	(0.0)	4	4	(1.8)
Pneumonia aspiration	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Postoperative wound infection	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Mild	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Pulmonary sepsis	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Respiratory tract infection	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Moderate	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Sepsis	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Septic shock	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Upper respiratory tract infection	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Urinary tract infection	4	4	(3.7)	1	1	(0.9)	5	5	(2.3)
Mild	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Moderate	3	3	(2.8)	0	0	(0.0)	3	3	(1.4)
Urosepsis	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Wound infection	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Injury, poisoning and procedural complications	13	8	(7.4)	10	10	(8.9)	23	18	(8.2)
Mild	3	3	(2.8)	2	2	(1.8)	5	5	(2.3)
Moderate	7	4	(3.7)	3	3	(2.7)	10	7	(3.2)
Severe	3	2	(1.9)	5	5	(4.5)	8	7	(3.2)

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Table 15.4.1.1
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Safety analysis set

System Organ Class (SOC) Preferred Term (PT) Severity	Treatment Placebo (N=108) n_{AEs}	 n (%)		 Ilofotase Alfa (N=112) n_{AEs}	 n (%)		 Total (N=220) n_{AEs}	 n (%)	
Anastomotic haemorrhage	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Fall	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Moderate	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Head injury	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Post procedural discharge	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Post procedural haematuria	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Post procedural haemorrhage	3	3	(2.8)	2	2	(1.8)	5	5	(2.3)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Severe	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Post procedural inflammation	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Postoperative delirium	3	3	(2.8)	1	1	(0.9)	4	4	(1.8)
Moderate	3	3	(2.8)	1	1	(0.9)	4	4	(1.8)
Postoperative respiratory failure	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Postoperative thoracic procedure complication	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Severe	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Postpericardiotomy syndrome	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Procedural haemorrhage	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Toxicity to various agents	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)

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Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Vasoplegia syndrome	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Investigations	13	10	(9.3)	15	11	(9.8)	28	21	(9.5)
Mild	6	6	(5.6)	9	7	(6.3)	15	13	(5.9)
Moderate	7	4	(3.7)	6	5	(4.5)	13	9	(4.1)
Alanine aminotransferase increased	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Aspartate aminotransferase increased	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Blood phosphorus decreased	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Blood urea increased	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Breath sounds abnormal	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
C-reactive protein increased	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Cardiac output decreased	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Electrocardiogram ST segment depression	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Electrocardiogram T wave inversion	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Mild	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Haemoglobin decreased	7	6	(5.6)	4	4	(3.6)	11	10	(4.5)
Mild	3	3	(2.8)	2	2	(1.8)	5	5	(2.3)
Moderate	4	3	(2.8)	2	2	(1.8)	6	5	(2.3)

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Safety analysis set

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Platelet count decreased	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Moderate	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
SARS-CoV-2 test positive	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Ultrasound Doppler abnormal	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Urine output decreased	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Mild	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Venous oxygen saturation decreased	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Metabolism and nutrition disorders	12	10	(9.3)	13	12	(10.7)	25	22	(10.0)
Mild	9	8	(7.4)	10	10	(8.9)	19	18	(8.2)
Moderate	2	2	(1.9)	2	2	(1.8)	4	4	(1.8)
Severe	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Dehydration	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Gout	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Hyperglycaemia	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Mild	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Hyperkalaemia	3	3	(2.8)	4	4	(3.6)	7	7	(3.2)
Mild	3	3	(2.8)	3	3	(2.7)	6	6	(2.7)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Hyperlactacidaemia	1	1	(0.9)	3	3	(2.7)	4	4	(1.8)
Mild	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Moderate	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Hypoalbuminaemia	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)

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Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Hypokalaemia	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Mild	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Hyponatraemia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Iron deficiency	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Lactic acidosis	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Metabolic acidosis	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Musculoskeletal and connective tissue disorders	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Myopathy	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Pain in extremity	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Nervous system disorders	10	7	(6.5)	6	5	(4.5)	16	12	(5.5)
Mild	6	5	(4.6)	5	4	(3.6)	11	9	(4.1)
Moderate	3	3	(2.8)	1	1	(0.9)	4	4	(1.8)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Altered state of consciousness	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Cerebral infarction	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)

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Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Disturbance in attention	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Dizziness	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Dysmetria	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Hemiparesis	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Middle cerebral artery stroke	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Nerve compression	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Mild	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Partial seizures	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Presyncope	2	2	(1.9)	2	1	(0.9)	4	3	(1.4)
Mild	2	2	(1.9)	2	1	(0.9)	4	3	(1.4)
Transient ischaemic attack	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Psychiatric disorders	13	9	(8.3)	2	2	(1.8)	15	11	(5.0)
Mild	8	8	(7.4)	2	2	(1.8)	10	10	(4.5)
Moderate	3	2	(1.9)	0	0	(0.0)	3	2	(0.9)
Severe	2	1	(0.9)	0	0	(0.0)	2	1	(0.5)
Aggression	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Confusional state	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)

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Delirium	5	5	(4.6)	2	2	(1.8)	7	7	(3.2)
Mild	3	3	(2.8)	2	2	(1.8)	5	5	(2.3)
Moderate	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Delusion	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Insomnia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Nervousness	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Nightmare	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Sleep disorder	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Renal and urinary disorders	32	28	(25.9)	23	19	(17.0)	55	47	(21.4)
Mild	10	10	(9.3)	8	7	(6.3)	18	17	(7.7)
Moderate	19	17	(15.7)	11	11	(9.8)	30	28	(12.7)
Severe	3	3	(2.8)	4	3	(2.7)	7	6	(2.7)
Acute kidney injury	26	23	(21.3)	18	17	(15.2)	44	40	(18.2)
Mild	7	7	(6.5)	6	6	(5.4)	13	13	(5.9)
Moderate	16	14	(13.0)	9	9	(8.0)	25	23	(10.5)
Severe	3	3	(2.8)	3	3	(2.7)	6	6	(2.7)
Anuria	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Dysuria	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)

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Number of AEs through Day 28 by system organ class, preferred term, and severity
Safety analysis set

System Organ Class (SOC) Preferred Term (PT) Severity	Treatment Placebo (N=108) n_{AEs}	 n (%)		 Ilofotase Alfa (N=112) n_{AEs}	 n (%)		 Total (N=220) n_{AEs}	 n (%)	
Haematuria	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Nocturia	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Oliguria	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Moderate	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Urinary retention	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Reproductive system and breast disorders	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Prostatitis	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Respiratory, thoracic and mediastinal disorders	30	18	(16.7)	16	16	(14.3)	46	34	(15.5)
Mild	10	8	(7.4)	5	5	(4.5)	15	13	(5.9)
Moderate	16	11	(10.2)	9	9	(8.0)	25	20	(9.1)
Severe	4	4	(3.7)	2	2	(1.8)	6	6	(2.7)
Atelectasis	2	2	(1.9)	2	2	(1.8)	4	4	(1.8)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Dyspnoea	3	3	(2.8)	1	1	(0.9)	4	4	(1.8)
Mild	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Epistaxis	4	4	(3.7)	0	0	(0.0)	4	4	(1.8)

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System Organ Class (SOC) Preferred Term (PT) Severity	Treatment: Placebo (N=108) n_{AEs}	Placebo n (%)		Ilofotase Alfa (N=112) n_{AEs}	Ilofotase Alfa n (%)		Total (N=220) n_{AEs}	Total n (%)	
Mild	3	3	(2.8)	0	0	(0.0)	3	3	(1.4)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Hyperventilation	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Hypoventilation	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Hypoxia	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Moderate	0	0	(0.0)	2	2	(1.8)	2	2	(0.9)
Pleural effusion	6	5	(4.6)	6	6	(5.4)	12	11	(5.0)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	5	4	(3.7)	4	4	(3.6)	9	8	(3.6)
Severe	1	1	(0.9)	1	1	(0.9)	2	2	(0.9)
Pneumothorax	3	3	(2.8)	3	3	(2.7)	6	6	(2.7)
Mild	1	1	(0.9)	3	3	(2.7)	4	4	(1.8)
Moderate	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Productive cough	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Pulmonary embolism	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Pulmonary oedema	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Rales	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Respiratory alkalosis	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Respiratory failure	5	5	(4.6)	0	0	(0.0)	5	5	(2.3)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	3	3	(2.8)	0	0	(0.0)	3	3	(1.4)

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Severe	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Wheezing	2	1	(0.9)	0	0	(0.0)	2	1	(0.5)
Mild	2	1	(0.9)	0	0	(0.0)	2	1	(0.5)
Skin and subcutaneous tissue disorders	3	3	(2.8)	1	1	(0.9)	4	4	(1.8)
Mild	3	3	(2.8)	1	1	(0.9)	4	4	(1.8)
Erythema	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Livedo reticularis	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Pruritus	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Rash	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Mild	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Surgical and medical procedures	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Sternotomy	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Vascular disorders	9	7	(6.5)	9	8	(7.1)	18	15	(6.8)
Mild	4	3	(2.8)	6	5	(4.5)	10	8	(3.6)
Moderate	5	5	(4.6)	2	2	(1.8)	7	7	(3.2)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Haematoma	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Moderate	1	1	(0.9)	0	0	(0.0)	1	1	(0.5)
Haemodynamic instability	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)

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Haemodynamic rebound	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Mild	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Haemorrhage	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Moderate	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Hypertension	3	3	(2.8)	2	2	(1.8)	5	5	(2.3)
Mild	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Moderate	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Hypotension	3	3	(2.8)	2	2	(1.8)	5	5	(2.3)
Mild	1	1	(0.9)	2	2	(1.8)	3	3	(1.4)
Moderate	2	2	(1.9)	0	0	(0.0)	2	2	(0.9)
Orthostatic hypotension	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Mild	2	2	(1.9)	1	1	(0.9)	3	3	(1.4)
Thrombosis	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)
Severe	0	0	(0.0)	1	1	(0.9)	1	1	(0.5)

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