

**Table 1S.I Adverse Events up to Day 28 by Treatment, System Organ Class and Preferred Term (Safety Population)**

System Organ Class Preferred Term	Statistic	Cohort 1 F3 (N = 3)	Cohort 1 F4 (N = 3)	Cohort 2 F3 (N = 3)	Cohort 2 F4 (N = 3)	Cohort 3 F3 (N = 3)	Cohort 3 F4 (N = 4)	Cohort 4 F3 (N = 2)	Cohort 4 F4 (N = 2)	Total (N = 23)
Blood and lymphatic system disorders	n (%) E	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Anaemia	n (%) E	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Gastrointestinal disorders	n (%) E	0 (0.00) 0	0 (0.00) 0	1 (33.33) 2	2 (66.67) 2	0 (0.00) 0	2 (50.00) 2	1 (50.00) 1	1 (50.00) 1	7 (30.43) 8
Abdominal Discomfort	n (%) E	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Abdominal Distension	n (%) E	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	2 (66.67) 2	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	3 (13.04) 3
Diarrhoea	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	1 (50.00) 1	2 (8.70) 2
Gastritis	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	0 (0.00) 0	1 (4.35) 1
Gastrointestinal Disorder	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
General disorders and administration site conditions	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	2 (66.67) 3	0 (0.00) 0	1 (50.00) 1	2 (100.00) 2	5 (21.74) 6
Injection Site Inflammation	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Pyrexia	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (33.33) 2	0 (0.00) 0	1 (50.00) 1	2 (100.00) 2	4 (17.39) 5
Infections and infestations	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
Bacteriuria	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
Investigations	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	2 (50.00) 3	0 (0.00) 0	1 (50.00) 1	3 (13.04) 4
Blood Pressure Increased	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Fibrin D Dimer Increased	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	1 (50.00) 1	2 (8.70) 2
Transaminases Increased	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Nervous system disorders	n (%) E	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	1 (50.00) 1	2 (100.00) 3	5 (21.74) 6
Headache	n (%) E	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	1 (50.00) 1	0 (0.00) 0	3 (13.04) 3
Ischaemic Stroke	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
Paraesthesia	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
Tremor	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
Respiratory, thoracic and mediastinal disorders	n (%) E	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Hypoventilation	n (%) E	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Skin and subcutaneous tissue disorders	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Rash Maculo-Papular	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1

E: Number of events; MedDRA: Medical Dictionary for Regulatory Activities; N: The number of patients in the Safety population within the respective cohort and arm; n: Number of patients with adverse event; %: Calculated using N as the denominator (n/N\*100).

F3: F3 compensated. F4: F4 compensated. There are no patients in F4 early decompensated.

All adverse events are coded using MedDRA version 21.1.

Any missing or inconsistent data from individual visits is due to the incompleteness of the database.

[illegible]

System Organ Class Preferred Term	Causality	Statistic	Cohort 1 F3 (N = 3)	Cohort 1 F4 (N = 3)	Cohort 2 F3 (N = 3)	Cohort 2 F4 (N = 3)	Cohort 3 F3 (N = 3)	Cohort 3 F4 (N = 4)	Cohort 4 F3 (N = 2)	Cohort 4 F4 (N = 2)	Total (N = 23)
Fibrin D Dimer Increased	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	1 (50.00) 1	2 (8.70) 2
	NOT RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Transaminases Increased	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
	NOT RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Nervous system disorders	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 2	1 (4.35) 2
	NOT RELATED	n (%) E	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	1 (50.00) 1	1 (50.00) 1	4 (17.39) 4
Headache	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	NOT RELATED	n (%) E	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	1 (50.00) 1	0 (0.00) 0	3 (13.04) 3
Ischaemic Stroke	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
	NOT RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Paraesthesia	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	NOT RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
Tremor	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
	NOT RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Respiratory, thoracic and mediastinal disorders	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	NOT RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Hypoventilation	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	NOT RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Skin and subcutaneous tissue disorders	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
	NOT RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Rash Maculo-Papular	RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
	NOT RELATED	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0

E: Number of events; MedDRA: Medical Dictionary for Regulatory Activities; N: The number of patients in the Safety population within the respective cohort and arm; n: Number of patients with adverse event; %: Calculated using N as the denominator (n/N\*100).

F3: F3 compensated. F4: F4 compensated. There are no patients in F4 early decompensated.

All adverse events are coded using MedDRA version 21.1.

Any missing or inconsistent data from individual visits is due to the incompleteness of the database.



System Organ Class Preferred Term	Severity	Statistic	Cohort 1 F3 (N = 3)	Cohort 1 F4 (N = 3)	Cohort 2 F3 (N = 3)	Cohort 2 F4 (N = 3)	Cohort 3 F3 (N = 3)	Cohort 3 F4 (N = 4)	Cohort 4 F3 (N = 2)	Cohort 4 F4 (N = 2)	Total (N = 23)
Gastritis	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	0 (0.00) 0	1 (4.35) 1
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Gastrointestinal Disorder	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
General disorders and administration site conditions	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	2 (66.67) 3	0 (0.00) 0	1 (50.00) 1	2 (100.00) 2	5 (21.74) 6
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Injection Site Inflammation	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Pyrexia	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (33.33) 2	0 (0.00) 0	1 (50.00) 1	2 (100.00) 2	4 (17.39) 5
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Infections and infestations	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Bacteriuria	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0

System Organ Class Preferred Term	Severity	Statistic	Cohort 1 F3 (N = 3)	Cohort 1 F4 (N = 3)	Cohort 2 F3 (N = 3)	Cohort 2 F4 (N = 3)	Cohort 3 F3 (N = 3)	Cohort 3 F4 (N = 4)	Cohort 4 F3 (N = 2)	Cohort 4 F4 (N = 2)	Total (N = 23)
Investigations	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	2 (50.00) 3	0 (0.00) 0	0 (0.00) 0	2 (8.70) 3
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Blood Pressure Increased	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Fibrin D Dimer Increased	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Transaminases Increased	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Nervous system disorders	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	1 (50.00) 1	2 (100.00) 3	5 (21.74) 6
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Headache	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	1 (50.00) 1	0 (0.00) 0	3 (13.04) 3
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
Ischaemic Stroke	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1

System Organ Class Preferred Term			Severity	Statistic	Cohort 1 F3 (N = 3)	Cohort 1 F4 (N = 3)	Cohort 2 F3 (N = 3)	Cohort 2 F4 (N = 3)	Cohort 3 F3 (N = 3)	Cohort 3 F4 (N = 4)	Cohort 4 F3 (N = 2)	Cohort 4 F4 (N = 2)	Total (N = 23)
Paraesthesia	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
Tremor	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (50.00) 1	1 (4.35) 1
Respiratory, thoracic and mediastinal disorders	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Hypoventilation	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	1 (33.33) 1	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Skin and subcutaneous tissue disorders	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
Rash Maculo-Papular	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 1	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	1 (25.00) 1	0 (0.00) 0	0 (0.00) 0	1 (4.35) 1
	Grade 2	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 3	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 4	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0

System Organ Class Preferred Term	Severity	Statistic	Cohort 1 F3 (N = 3)	Cohort 1 F4 (N = 3)	Cohort 2 F3 (N = 3)	Cohort 2 F4 (N = 3)	Cohort 3 F3 (N = 3)	Cohort 3 F4 (N = 4)	Cohort 4 F3 (N = 2)	Cohort 4 F4 (N = 2)	Total (N = 23)
	Grade 5	n (%) E	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0	0 (0.00) 0

E: Number of events; MedDRA: Medical Dictionary for Regulatory Activities; N: The number of patients in the Safety population within the respective cohort and arm; n: Number of patients with adverse event; %: Calculated using N as the denominator (n/N\*100).

F3: F3 compensated. F4: F4 compensated. There are no patients in F4 early decompensated.

All adverse events are coded using MedDRA version 21.1.

Any missing or inconsistent data from individual visits is due to the incompleteness of the database.