

Supplementary Material

Tiprelestat for treatment of hospitalized COVID-19: Results of the double-blind randomized placebo-controlled COMCOVID trial

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Table s1: Previous diseases including surgical procedures (SES)

Medical History	Tiprelestat (N=9)		Placebo (N=8)		Total (N=17)	
System Organ Class (SOC) Preferred Terms (PT)	Events	Patients with at least one Event	Events	Patients with at least one Event	Events	Patients with at least one Event
Overall						
All SOC	13	5 (55.6%)	12	5 (62.5%)	25	10 (58.8%)
Cardiac disorders						
Any	0	0 (0.0%)	2	1 (12.5%)	2	1 (5.9%)
Angina unstable	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Cardiac failure acute	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Gastrointestinal disorders						
Any	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Inguinal hernia	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Infections and infestations						
Any	1	1 (11.1%)	3	2 (25.0%)	4	3 (17.6%)
Coronavirus infection	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Pneumonia bacterial	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Pneumonia viral	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Superinfection bacterial	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Injury, poisoning and procedural complications						
Any	4	1 (11.1%)	0	0 (0.0%)	4	1 (5.9%)
Fractured sacrum	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Lumbar vertebral fracture	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Pelvic fracture	2	1 (11.1%)	0	0 (0.0%)	2	1 (5.9%)
Investigations						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Arthroscopy	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Metabolism and nutrition disorders						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Hypokalaemia	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Musculoskeletal and connective tissue disorders						
Any	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Spinal pain	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Nervous system disorders						
Any	1	1 (11.1%)	1	1 (12.5%)	2	2 (11.8%)
Cerebral ischaemia	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Cerebrovascular accident	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Renal and urinary disorders						
Any	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Acute kidney injury	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Respiratory, thoracic and mediastinal disorders						
Any	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Pulmonary embolism	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Surgical and medical procedures						

Medical History	Tiprelestat (N=9)		Placebo (N=8)		Total (N=17)	
System Organ Class (SOC)		Patients with at least		Patients with at least		Patients with at least
Preferred Terms (PT)	Events	one Event	Events	one Event	Events	one Event
Any	3	3 (33.3%)	4	2 (25.0%)	7	5 (29.4%)
Cardiac resynchronisation therapy	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Cholecystectomy	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Coronary arterial stent insertion	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Internal fixation of spine	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Large intestinal polypectomy	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Sigmoidectomy	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Transurethral prostatectomy	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)

Table s2 Concomitant diseases including surgical procedures (SES)

Medical History	Tiprelestat (N=9)		Placebo (N=8)		Total (N=17)	
System Organ Class (SOC) Preferred Terms (PT)	Events	Patients with at least one Event	Events	Patients with at least one Event	Events	Patients with at least one Event
Overall						
All SOC	60	9 (100%)	63	8 (100%)	123	17 (100%)
Blood and lymphatic system disorders						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Anaemia	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Cardiac disorders						
Any	12	7 (77.8%)	10	5 (62.5%)	22	12 (70.6%)
Atrial fibrillation	5	5 (55.6%)	3	3 (37.5%)	8	8 (47.1%)
Cardiac failure	1	1 (11.1%)	1	1 (12.5%)	2	2 (11.8%)
Cardiac failure chronic	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Coronary artery disease	2	2 (22.2%)	3	3 (37.5%)	5	5 (29.4%)
Hypertensive heart disease	1	1 (11.1%)	1	1 (12.5%)	2	2 (11.8%)
Mitral valve incompetence	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Myocardial infarction	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Sinus node dysfunction	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Tricuspid valve incompetence	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Congenital, familial and genetic disorders						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Phimosis	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Endocrine disorders						
Any	1	1 (11.1%)	2	1 (12.5%)	3	2 (11.8%)
Addison's disease	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Autoimmune thyroiditis	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Hypothyroidism	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Eye disorders						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Cataract	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Gastrointestinal disorders						
Any	1	1 (11.1%)	2	1 (12.5%)	3	2 (11.8%)
Constipation	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Diverticulum intestinal	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Hiatus hernia	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
General disorders and administration site conditions						
Any	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Pain	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Hepatobiliary disorders						
Any	1	1 (11.1%)	2	2 (25.0%)	3	3 (17.6%)
Congestive hepatopathy	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Hepatic steatosis	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Hepatitis	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)

Medical History	Tibrelestat (N=9)		Placebo (N=8)		Total (N=17)	
System Organ Class (SOC) Preferred Terms (PT)	Events	Patients with at least one Event	Events	Patients with at least one Event	Events	Patients with at least one Event
Infections and infestations						
Any	1	1 (11.1%)	2	2 (25.0%)	3	3 (17.6%)
Helicobacter gastritis	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Superinfection	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Urinary tract infection	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Injury, poisoning and procedural complications						
Any	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Post procedural hypothyroidism	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Metabolism and nutrition disorders						
Any	14	7 (77.8%)	13	7 (87.5%)	27	14 (82.4%)
Diabetes mellitus	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Folate deficiency	1	1 (11.1%)	1	1 (12.5%)	2	2 (11.8%)
Gout	2	2 (22.2%)	1	1 (12.5%)	3	3 (17.6%)
Hypercholesterolaemia	3	3 (33.3%)	0	0 (0.0%)	3	3 (17.6%)
Hyperglycaemia	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Hyperkalaemia	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Hyperlipidaemia	2	2 (22.2%)	2	2 (25.0%)	4	4 (23.5%)
Hypertriglyceridaemia	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Hyperuricaemia	2	2 (22.2%)	2	2 (25.0%)	4	4 (23.5%)
Obesity	0	0 (0.0%)	2	2 (25.0%)	2	2 (11.8%)
Type 2 diabetes mellitus	1	1 (11.1%)	2	2 (25.0%)	3	3 (17.6%)
Vitamin B1 deficiency	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Vitamin D deficiency	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Musculoskeletal and connective tissue disorders						
Any	3	1 (11.1%)	4	2 (25.0%)	7	3 (17.6%)
Arthralgia	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Fibromyalgia	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Kyphosis	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Muscular weakness	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Spinal osteoarthritis	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Spondylitis	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Systemic lupus erythematosus	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Any	1	1 (11.1%)	1	1 (12.5%)	2	2 (11.8%)
Chronic lymphocytic leukaemia	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Lipoma	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Nervous system disorders						
Any	1	1 (11.1%)	3	3 (37.5%)	4	4 (23.5%)
Cerebrovascular accident	0	0 (0.0%)	2	2 (25.0%)	2	2 (11.8%)
Seizure	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Tremor	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)

Medical History	Tiprelestat (N=9)		Placebo (N=8)		Total (N=17)	
System Organ Class (SOC) Preferred Terms (PT)	Events	Patients with at least one Event	Events	Patients with at least one Event	Events	Patients with at least one Event
Psychiatric disorders						
Any	1	1 (11.1%)	3	3 (37.5%)	4	4 (23.5%)
Depression	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Panic attack	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Sleep disorder	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Tobacco abuse	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Renal and urinary disorders						
Any	8	7 (77.8%)	4	4 (50.0%)	12	11 (64.7%)
Acute kidney injury	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Chronic kidney disease	2	2 (22.2%)	3	3 (37.5%)	5	5 (29.4%)
Diabetic nephropathy	2	1 (11.1%)	0	0 (0.0%)	2	1 (5.9%)
Incontinence	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Renal failure	2	2 (22.2%)	1	1 (12.5%)	3	3 (17.6%)
Reproductive system and breast disorders						
Any	1	1 (11.1%)	2	2 (25.0%)	3	3 (17.6%)
Benign prostatic hyperplasia	1	1 (11.1%)	1	1 (12.5%)	2	2 (11.8%)
Prostatomegaly	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Respiratory, thoracic and mediastinal disorders						
Any	7	3 (33.3%)	2	2 (25.0%)	9	5 (29.4%)
Asthma	2	2 (22.2%)	1	1 (12.5%)	3	3 (17.6%)
Chronic obstructive pulmonary disease	3	3 (33.3%)	0	0 (0.0%)	3	3 (17.6%)
Interstitial lung disease	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Pulmonary hypertension	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Sleep apnoea syndrome	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Skin and subcutaneous tissue disorders						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Stasis dermatitis	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Social circumstances						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Menopause	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Surgical and medical procedures						
Any	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Cardiac pacemaker insertion	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Vascular disorders						
Any	5	5 (55.6%)	8	8 (100%)	13	13 (76.5%)
Hypertension	5	5 (55.6%)	8	8 (100%)	13	13 (76.5%)

Table s3 Treatment emergent adverse events by SOC and PT

TEAE	Tiprelestat (N=9)		Placebo (N=8)		Total (N=17)	
System Organ Class (SOC) Preferred Terms (PT)	Events	Patients with at least one Event	Events	Patients with at least one Event	Events	Patients with at least one Event
Overall						
All SOC	5	3 (33.3%)	7	4 (50.0%)	12	7 (41.2%)
Blood and lymphatic system disorders						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Anaemia	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Gastrointestinal disorders						
Any	1	1 (11.1%)	1	1 (12.5%)	2	2 (11.8%)
Constipation	1	1 (11.1%)	1	1 (12.5%)	2	2 (11.8%)
General disorders and administration site conditions						
Any	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Pyrexia	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Hepatobiliary disorders						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Congestive hepatopathy	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Infections and infestations						
Any	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Urosepsis	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Injury, poisoning and procedural complications						
Any	2	2 (22.2%)	0	0 (0.0%)	2	2 (11.8%)
Post procedural haematuria	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Thoracic vertebral fracture	1	1 (11.1%)	0	0 (0.0%)	1	1 (5.9%)
Investigations						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
N-terminal prohormone brain natriuretic peptide increased	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Metabolism and nutrition disorders						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Hypokalaemia	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Skin and subcutaneous tissue disorders						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Blister	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Vascular disorders						
Any	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)
Hot flush	0	0 (0.0%)	1	1 (12.5%)	1	1 (5.9%)