

Cardiac Adverse Events and Remdesivir in Hospitalized Patients with Coronavirus Disease 2019 (COVID-19): A Post Hoc Safety Analysis of the Randomized DisCoVeRy Trial

Supplementary Appendix

Content

DisCoVeRy study group members 2

Supplemental Tables 4

Table S1. Cardiac and Serious Adverse Events in the mITT Population between Remdesivir and Control Groups..... 4

Table S2. Cumulative Cardiac Adverse Events Reported in the DisCoVeRy trial from the mITT Population in the Remdesivir and Control Groups..... 5

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Supplemental Tables

Table S1. Cardiac and Serious Adverse Events in the mITT Population between Remdesivir and Control Groups

	Remdesivir (n=410)		Control (n=423)		Hazard Ratio ^a (95% CI) [p-value]	Hazard Ratio ^b (95% CI) [p-value]
	N patients (%)	Event rate (95% CI)	N patients (%)	Event rate (95% CI)		
Any cardiac adverse events	46 (11.2)	0.076 (0.062-0.089)	48 (11.3)	0.075 (0.061-0.089)	1.0 (0.7 - 1.5) [0.98]	0.9 (0.6 - 1.4) [0.64]
Any serious cardiac adverse events^c	27 (6.6)	0.043 (0.036-0.050)	21 (5.0)	0.042 (0.034-0.049)	1.3 (0.8 - 2.4) [0.32]	0.8 (0.5 - 1.4) [0.59]
Any non-serious cardiac adverse events^d	23 (5.6)	0.039 (0.031-0.049)	30 (7.1)	0.040 (0.031-0.049)	0.7 (0.4 - 1.4) [0.39]	0.9 (0.6 - 1.4) [0.66]
Grades 1-2	14 (3.4)	0.031 (0.025-0.039)	25 (5.9)	0.032 (0.025-0.039)	0.6 (0.3 - 1.1) [0.10]	0.9 (0.6 - 1.4) [0.69]
Grades 3-4	8 (2.0)	0.010 (0.007-0.013)	6 (1.4)	0.009 (0.007-0.013)	1.9 (0.6 - 5.6) [0.25]	0.8 (0.5 - 1.3) [0.59]
Subclasses of cardiac events:						
Any arrhythmic events	39 (9.5)	0.062 (0.050-0.075)	40 (9.5)	0.062 (0.049-0.074)	1.1 (0.7 - 1.7) [0.68]	0.9 (0.5 - 1.4) [0.58]
Any serious arrhythmic events	23 (5.6)	0.033 (0.026-0.041)	14 (3.3)	0.032 (0.024-0.039)	1.7 (0.9 - 3.3) [0.11]	0.8 (0.5 - 1.3) [0.57]
Atrial fibrillation	9 (2.2)		6 (1.4)			
Bradycardia	3 (0.7)		2 (0.5)			
Tachycardia	4 (1.0)		2 (0.5)			
Ventricular tachycardia	0 (0.0)		2 (0.5)			
Arrhythmia not specified	7 (1.7)		2 (0.5)			
Any non-serious arrhythmic events						
Grades 1-2	13 (3.2)	0.027 (0.022-0.033)	24 (5.7)	0.028 (0.022-0.034)	0.6 (0.3 - 1.2) [0.17]	0.9 (0.6 - 1.4) [0.67]
Grades 3-4	7 (1.7)	0.009 (0.007-0.012)	5 (1.2)	0.009 (0.007-0.012)	1.5 (0.5 - 4.6) [0.51]	0.8 (0.5 - 1.4) [0.58]
Any non-arrhythmic events	10 (2.4)	0.018 (0.014-0.021)	12 (2.8)	0.018 (0.014-0.021)	0.9 (0.4 - 2.0) [0.71]	0.9 (0.6 - 1.4) [0.66]
Any serious adverse events	154 (37.6)	0.380 (0.342-0.408)	145 (34.3)	0.372 (0.339-0.405)	1.2 (0.9 - 1.5) [0.21]	0.9 (0.5 - 1.4) [0.64]

Abbreviations: mITT, modified Intention-to-treat; CI, confidence interval.

^aHazard ratios adjusted for the severity of COVID-19 at baseline based on the Cox model.

^bAdjusted hazard ratios based on the Fine and Gray model with death as a competing risk.

^cAs per protocol, a serious adverse event was defined as an adverse event that results in death, is life-threatening, requires prolongation of existing hospitalization, results in persistent or significant disability or incapacity, consists of a congenital anomaly/birth defect or is an important medical event.

^dAs per protocol, the severity (intensity) of all adverse events was graded using the Division of AIDS (DAIDS) table, corrected version 2.1 (July 2017). Some patients experienced different grades of adverse events.

Table S2. Cumulative Cardiac Adverse Events Reported in the DisCoVeRy trial from the mITT Population in the Remdesivir and Control Groups

	Remdesivir (N=410)				Control (N=423)			
	n of events			Total N of patients (%N)	n of events			Total N of patients (%N)
	serious	non-serious	total		serious	non-serious	total	
All cardiac adverse events*	35	23	58	46 (11.2%)	25	42	67	48 (11.3%)
All arrhythmic events	28	20	48	39 (6.1%)	16	36	52	40 (9.5%)
Conduction disorders	1	0	1	1	0	0	0	0
<i>Atrioventricular block</i>	1	0	1	1	0	0	0	0
Rate/rhythm disorders	14	13	27	25	7	21	28	25
<i>Arrhythmia</i>	6	1	7	6	3	4	7	7
<i>Bradycardia</i>	3	5	8	8	2	7	9	9
<i>Tachycardia</i>	4	7	11	11	2	10	12	11
<i>Heart rate irregular</i>	1	0	1	1	0	0	0	0
Supraventricular arrhythmias	13	7	20	15	6	14	20	16
<i>Atrial fibrillation</i>	9	7	16	15	6	14	20	16
<i>Atrial flutter</i>	4	0	4	2	0	0	0	0
Ventricular arrhythmias and Cardiac arrest	0	0	0	0	3	1	4	4
<i>Cardiac arrest</i>	0	0	0	0	1	0	1	1
<i>Ventricular tachycardia</i>	0	0	0	0	2	1	3	3
All non-arrhythmic events	7	3	10	8 (2.0%)	9	6	15	12 (2.8%)
Coronary Artery Disease	2	0	2	2	1	3	4	3
<i>(Acute) Myocardial infarction / ischaemia</i>	1	0	1	1	0	1	1	1
<i>Chest pain / discomfort</i>	1	0	1	1	0	0	0	0
<i>Acute coronary syndrome</i>	0	0	0	0	1	2	3	3
Heart Failure	2	2	4	0	6	3	9	8
Left ventricular failures	0	0	0	0	1	1	2	2
<i>Acute Pulmonary edema (Cardiogenic, Hypertensive)</i>	0	0	0	0	1	1	2	2
Other heart failures	2	2	4	4	5	2	7	7
<i>Cardiac failure</i>	0	2	2	2	3	1	4	4
<i>Cardiac failure congestive</i>	1	0	1	1	1	0	1	1
<i>Cardiogenic shock</i>	1	0	1	1	1	1	2	2
Pericardial Disease	1	0	1	1	0	0	0	0
<i>Noninfectious pericarditis</i>	1	0	1	1	0	0	0	0
Myocardial Disease	0	1	1	1	2	0	2	2
Cardiomyopathy	0	1	1	1	1	0	1	1
<i>Congestive cardiomyopathy</i>	0	0	0	0	1	0	1	1
<i>Stress cardiomyopathy</i>	0	1	1	1	0	0	0	0
Noninfectious myocarditis	0	0	0	0	1	0	1	1
<i>Myocarditis</i>	0	0	0	0	1	0	1	1
Other Cardiac events	2	0	2	2	0	0	0	0
<i>Dyspnea (in a cardiac context)</i>	2	0	2	2	0	0	0	0

*Cumulative data presented in Table S2 are not censored as they were not used in the risk evaluation model (Cox model) that takes into account time-to-event data, *i.e.* only the first adverse event that occurred. Cumulative data were not tested due to small sample size of patients with more than 1 cardiac AE (remdesivir, n=8; control, n=10). In addition, most of the cumulative cardiac AEs correspond to episodes rather than new cardiac events (for instance, one patient with history of atrial flutter experienced 3 atrial flutter episodes out of the 4 reported in the study).