Supplemental Online Content

Spyropoulos AC, Goldin M, Giannis D, et al; for the HEP-COVID Investigators. Efficacy and safety of therapeutic-dose heparin vs standard prophylactic or intermediate-dose heparins for thromboprophylaxis in high-risk hospitalized patients with COVID-19: the HEP-COVID randomized clinical trial. *JAMA Intern Med*. Published online October 7, 2021. doi:10.1001/jamainternmed.2021.6203

This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Characteristics of the Patients at Baseline in the Per-Protocol Population		
Characteristic	**Therapeutic Dose (N=113)**	**Standard Dose (N=102)**
Mean age – yr	65.7 ± 14.0	68.4 ± 14.1
Male sex - no. (%)	60 (53.1)	55 (53.9)
Mean BMI – kg/m^2 *	31.0±9.5	29.6±14.6
Race - no. (%)†		
Asian	9/113 (8.0)	13/102 (12.8)
Black	30/113 (26.6)	28/102 (27.5)
White	47/113 (41.6)	36/102 (35.3)
ICU - no. (%)	39/113 (34.5)	33/102 (32.4)
Comorbidities - no./total no. (%)		
Hypertension	70/113 (62.0)	57/101 (56.4)
Heart failure	0/113 (0.0)	1/102 (1.0)
Diabetes mellitus	44/112 (39.3)	35/102 (34.3)
Dyslipidemia	43/113 (38.1)	35/102 (34.3)
Coronary artery disease	6/113 (5.3)	9/102 (8.8)
Valvular heart disease	1/113 (0.9)	3/102 (2.9)
History of ischemic stroke	5/113 (4.4)	3/102 (2.9)
History of carotid occlusive disease	0/113 (0.0)	0/102 (0.0)
Peripheral arterial disease	4/113 (3.5)	1/102 (1.0)
Chronic renal disease	4/113 (3.5)	3/102 (2.9)
Chronic lung disease	8/113 (7.1)	8/102 (7.8)
Chronic liver disease/Cirrhosis	0/113 (0.0)	1/102 (1.0)
Pulmonary hypertension	1/111 (0.9)	1/102 (1.0)
VTE Risk factors - no./total no. (%)		
Personal history of VTE	5/113 (4.4)	2/102 (2.0)
History of Cancer	12/113 (10.6)	7/102 (6.9)
Active cancer	1/113 (0.9)	2/102 (2.0)
Autoimmune disease	1/112 (0.9)	1/102 (1.0)
Hormonal therapy/oral contraceptives	0/113 (0.0)	1/102 (1.0)
Known thrombophilia	0/113 (0.0)	0/102 (0.0)
History of recent stroke with paresis	1/113 (0.9)	1/102 (1.0)
Clinical scores – mean ± SD		
IMPROVE-DD VTE Risk Score	4.31±1.45	4.38±1.37
Sepsis-induced coagulopathy (SIC) Score	2.39±0.72	2.33±0.92
Laboratory parameters – mean ± SD		
White blood cell count – 10^3/uL	9.7± 5.8	10.3±8.9
Platelets - 10^3/uL	288.4±117.8	276.7±110.2
Serum creatinine – mg/dL	0.95±0.46	0.99±0.52
Prothrombin time - sec	13.5±1.7	13.5±1.9
D-Dimer - ng/ml	4184±6510 Lower quartile 1068 Median 1652 Upper quartile 3775	3301±5834 Lower quartile 1067 Median 1728.5 Upper quartile 2918
Medications prior to randomization – no./total no. (%)		
Low molecular weight heparin	93/112 (83.0)	83/102 (81.4)
Unfractionated heparin	16/112 (14.3)	18/100 (18.0)
Remdesivir	82/113 (72.6)	72/102 (70.6)
Glucocorticoids	95/11 (85.6)	77/101 (76.2)
Antiplatelets	35/113 (31.0)	20/102 (19.6)

Oxygen therapy - no./total no. (%)		
Nasal cannula	70/113 (62.0)	65/102 (63.7)
Non-rebreather mask	11/113 (9.7)	11/102 (10.8)
Ventilation mask	4/113 (3.5)	1/102 (1.0)
High-flow or non-invasive positive pressure ventilation	17/113 (15.0)	16/102 (15.7)
Invasive mechanical ventilation	7/113 (6.2)	5/102 (4.9)
Length of hospital stay (LOS) - mean ± SD		
Mean LOS - days	12.4±9.3	11.9±7.8

* The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.

† Race was reported by the patient.

‡ ICU denotes intensive care unit, VTE venous thromboembolism.

eTable 2. Clinical Outcomes During the 30-Day Post-Randomization Phase in the Per-Protocol Population				
Outcome	**Therapeutic Dose (N=113)**	**Standard Dose (N=102)**	**RR (95% CI)**	**P Value**
	Number (percent)			
Primary efficacy outcome				
VTE, ATE, or death	34/113 (30.1)	49/102 (48.0)	0.63 (0.44-0.89)	0.007
Non-ICU Stratum	13/74 (17.6)	29/69 (42.0)	0.42 (0.24-0.74)	0.001
ICU Stratum	21/39 (53.9)	20/33 (60.6)	0.89 (0.60-1.33)	0.56
VTE+ATE	12/113 (10.6)	34/102 (33.3)	0.32 (0.17-0.58)	<0.001
Death	24/113 (21.2)	29/102 (28.4)	0.75 (0.47-1.20)	0.22
Secondary efficacy outcomes				
Primary Efficacy Outcome at Day 14	27/113 (23.9)	43/102 (42.2)	0.57 (0.38-0.85)	0.004
Progression to ARDS	9/111 (8.1)	5/99 (5.1)	1.61 (0.56-4.63)	0.38
Rehospitalization	0/113 (0.0)	3/102 (2.9)	0.13 (0.01-2.47)	0.11
Need for intubation	16/107 (15.0)	20/99 (20.2)	0.74 (0.41-1.35)	0.32
Need for ECMO	1/113 (0.9)	1/102 (1.0)	0.90 (0.06-14.25)	1.00
Non-fatal cardiac arrest	0/113 (0.0)	2/102 (2.0)	0.18 (0.01-3.72)	0.22
Acute Kidney Injury	14/113 (12.4)	9/102 (8.8)	1.40 (0.64-3.10)	0.40
New Onset Atrial Fibrillation	4/113 (3.5)	5/102 (4.9)	0.72 (0.20-2.62)	0.74
Principal Safety Outcome				
Major Bleeding	6/113 (5.3)	2/102 (2.0)	2.71 (0.56-13.12)	0.29
Non-ICU Stratum	2/74 (2.7)	2/69 (2.9)	0.93 (0.14-6.44)	1.00
ICU Stratum	4/39 (10.3)	0/33 (0.0)	7.63 (0.43-136.69)	0.12

*VTE denotes venous thromboembolism, ATE arterial thromboembolism, ICU intensive care unit, ARDS Acute respiratory distress syndrome, ECMO extracorporeal membrane oxygenation, RR relative risk, CI confidence interval