TABLE S1 Details of included studies for randomised controlled trials of medications in patients with severe COVID-19

Author name (references)	Publication year	Country/ Countries of origin	Study design	Method of COVID-19 testing	Numbers of participants	Gender	Age (years)	Interventions	Treatment medication dose	Controls	Control medication dose	Follow-up time (days)	Primary outcomes
Avendano Sola C et al [17]	2020	Spain	MRCTs	RT-PCR	81	Males (n = 44); Females (n = 37)	≥ 18	Convalescent plasma (n= 38)	Receive one dose (250-300 mL) of convalescent plasma	SOC (n = 43)	Not specified	97	ACM; ratio of TEAEs
Cao B et al [18]	2020	China	RCTs	RT-PCR	199	Males (n = 120); Females (n = 79)	≥ 18	Lopinavir/ ritonavir (n= 99)	Lopinavir–ritonavir (400 mg and 100 mg: respectively) twice a day for 14 days	SOC (n= 100)	Not specified	28	ACM; ratio of TEAEs
Davoudi-Monfared E et al [19]	2020	Iran	RCTs	RT-PCR	81	Males (n = 44); Females (n = 37)	≥ 18	Interferon-beta-1a/SOC (n = 42)	44 mg/ml (12 million IU/ml) dose of interferon-beta-1a three times weekly for two consecutive weeks	SOC (n =39)	Hydroxychloroquine (400 mg twice a day [BID] on the first day and then 200 mg BD) plus lopinavir/ritonavir (400 and 100 mg: respectively: BD) or atazanavir-ritonavir (300 and 100 mg: respectively: daily) for 7–10 days	28	ACM; ratio of TEAEs
Edalatifard M et al [20]	2020	Iran	RCTs	RT-PCR	62	Males (n = 39); Females (n = 23)	≥ 18	Methylprednisolone/SOC (n = 34)	Intravenous injection: 250 mg per day for 3 days	SOC (n = 28)	Hydroxychloroquine sulfate: lopinavir and naproxen	48	ACM

Furtado RHM et al [21]	2020	Brazil	MDRCTs	RT-PCR	397	Males (n = 262); Females (n = 135)	≥ 18	Azithromycin/ SOC (n = 214)	500 mg azithromycin once daily plus SOC for 10 days	SOC (n = 183)	SOC without macrolides: at the discretion of treating hysicians and according to local guidelines	29	ACM; ratio of TEAEs
Lescure FX et al [22]	2021	Argentina, Brazil, Canada, Chile, France, Germany, Israel, Italy, Japan, Russia, and Spain	MDRPCTs	RT-PCR	416	Males (n = 261); Females (n =155)	≥ 18	Sarilumab 400 mg (n = 173)	Intravenous sarilumab 400 mg	Placebo (n = 84)	Not specified	60	ACM; ratio of TEAEs
Lescure FX et al [22]	2021	Argentina, E	MDRPCT	RT-PCR	416	Males (n = 261); Females (n =155)	≥ 18	Sarilumab 200 mg (n = 159)	Intravenous sarilumab 200 mg	Placebo (n = 84)	Not specified	60	ACM; ratio of TEAEs
Li L et al [23]	2020	China	MRCTs	RT-PCR	103	Males (n = 60); Females (n =43)	≥ 18	Convalescent plasma/SOC (n = 52)	The dose of convalescent plasma was approximately 4 to 13 mL/kg of recipient body weight.	SOC (n = 51)	Not specified	74	ACM

Miller J et al [24]	2020	American	RCTs	RT-PCR	30	Males (n =14); Females (n =16)	≥ 18	Auxora (n = 20)	Auxora was administered on three consecutive days as a 4-h continuous intravenous infusion. The initial dose was 2.0mg/kg (max 250 mg): and subsequent doses were 1.6 mg/kg (max 200 mg) at 24 and 48 h	SOC (n = 10)	Not specified	30	ACM
Olender SA et al [25]	2020	United States	RCTs	RT-PCR	1114	Males (n =672); Females (n = 442)	≥ 18	Remdesivir (n = 298)	Remdesivir 200 mg on day 1: followed by remdesivir 100 mg daily on days 2–5; or SOC plus remdesivir 200 mg on day 1: followed by remdesivir 100 mg daily on days 2–10	SOC (n = 816)	Allowed to receive medications that may potentially treat COVID-19: excluding remdesivir	30	ACM

Rahmani H et al [26]	2020	Iran	RCTs	RT-PCR	66	Males (n =39); Females (n =27)	≥ 18	Interferon-beta-1b (n = 33)	Patients in the interferon group received interferon-beta-1b (250 mcg subcutaneously every other day for two consecutive weeks) along with the national protocol medications	SOC (n = 33)	Patients received only the national protocol medications (lopinavir/ritonavir or atazanavir/ritonavir plus hydroxychloroquine for 7–10 days	28	ACM
Rasheed AM et al [27]	2020	Iraq	RCTs	RT-PCR	49	Not specifed	≥ 18	Convalescent plasma (n = 21)	Not specifed	SOC (n = 28)	Not specified	60	ACM; ratio of TEAEs
Simonovich VA et al [28]	2020	Argentina	RPCTs	RT-PCR	333	Males (n =225); Females (n =108)	≥ 18	Convalescent plasma (n = 228)	Received convalescent plasma	Placebo (n = 105)	Not specified	30	ACM; ratio of TEAEs
Veiga VC et al [29]	2021	Portugal	DRCTs	RT-PCR	129	Males(n=88); Females(n= 41)	≥ 18	Tocilizumab/ SOC (n = 65)	Single intravenous infusion of 8 mg/kg	SOC (n = 64)	Not specifed	15	ACM
Zhong M et al [30]	2020	China	RPCTs	RT-PCR	17	Males (n =13); Females (n = 4)	51 to 91	α-Lipoic acid (n = 8)	1200 mg/d, intravenous infusion	Placebo (n = 9)	Equal volume saline infusion (placebo) for 7 days	30	ACM

Abbreviations: RCTs, randomised controlled trials; COVID-19, coronavirus disease 2019; RPCTs, randomised placebo-controlled trials; MRCTs, multicenter; randomised controlled trials; DRCTs, double-blind; randomised controlled trials; MDRCTs, multicenter; double-blind; randomised controlled trials; MDRPCTs, multicenter; double-blind; randomised placebo-controlled trials; RT-PCR, reverse transcription-polymerase chain reaction; SOC, standard of care; ACM, all-cause mortality; TEAEs, treatment-emergent adverse events.