Table 2. List of registered, ongoing, clinical trials using mesenchymal stem/stromal cells (MSCs) as a therapy to treat COVID-19 – **Source:** https://clinicaltrials.gov/ct2/home and https://trialstreamer.robotreviewer.net/

Clinical trials number	Participants	MSC source	Outcomes
NCT04371393 (USA)	**Target: N = 300**	MSCs (Remestemcel-L) at 2 x 10^6 cells/kg administered twice during first week (second infusion four days following first) plus standard care versus placebo (Plasma-Lyte) (second infusion four days following first) plus standard care	- All-cause mortality - SAEs - No. of days off mechanical ventilation - Resolution/improvement of ARDS - Length of stay - Clinical improvement scale - Hs-CRP, IL-6, IL-8, TNF-α
NCT03042143 (Northern Ireland) – REALIST trial	**Target: N = 75**	Single infusion of human umbilical cord derived CD362 enriched MSCs at maximum tolerable dose from phase I (dose escalation pilot study) plus standard care versus placebo (Plasma-Lyte) plus standard care	- Oxygenation index - SAEs - SOFA - Respiratory compliance - P/F ratio - Driving pressure - Extubation & reintubation - Ventilation free days - Length of ICU/hospital stay - Mortality
NCT04444271 (Pakistan)	**Target: N = 20**	Bone marrow derived MSCs at 2 x 10^6 cells/kg on day 1 & 7 plus standard care versus saline injection plus standard care	- Survival - No. oxygen support days - Time to negative nCoV test - CT scan - No. days to discharge
NCT04416139 (Mexico)	**Target: N = 10**	Umbilical cord derived MSCs from De bank Laboratory at 1 x 10^6 cells/kg (no control group – data compared to controls treated in a previous trial)	- PaO_2/FiO_2 ratio - HR & RR - Body temperature

			- Leukocyte, lymphocyte & platelet counts - PCT, fibrinogen, D-dimer, ferritin - CRP, TNF-α, IL-1, IL-10, IL-6, IL-17 - VEGF - T-cell analysis ($CD4^+$ & $CD8^+$) - NK and dendritic cells - SAEs - CT scan - nCoV test
NCT04429763 (Colombia) - CELMA	**Target: N = 30**	Umbilical cord derived MSCs at 1 x 10^6 cells/kg plus standard care versus placebo (not stated) plus standard care control	- NEWS scale - Time to hospital discharge - Respiratory function - Inflammatory markers - Haematological and renal assessments
NCT04315987 (Brazil)	**Target: N = 90**	NestaCell MSCs at 2 x 10^7 cells/kg on days 1, 3, 5 & 7 plus standard care versus placebo (not stated) on days 1, 3, 5 & 7 plus standard care	- Change in clinical condition - Mortality - SpO_2 - PaO_2/FiO_2 ratio - T-cell analysis ($CD4^+$ & $CD8^+$) - SAEs - Blood count and cardiac, hepatic & renal profiles
NCT04366323 (Spain)	**Target: N = 26**	Allogenic and expanded adipose tissue derived MSCs at 8 x 10^6 cells x 2 (no control group)	- Safety of administration (SAEs) - Efficacy of administration
NCT04456361 (Mexico)	**Target: N = 9**	Wharton's jelly derived MSCs at 1 x 10^8 cells/kg (no control group)	- SpO_2 - PaO_2/FiO_2 ratio - Ground glass opacity & pneumonia infiltration

			- LDH, CRP, D-dimer & Ferritin
NCT04366271 (Spain)	**Target: N = 106**	Undifferentiated allogenic umbilical cord MSCs (dose not stated) versus standard care	- Mortality due to lung involvement - All-cause mortality - Days without mechanical ventilation - Days without vasopressors - Negative nCoV test - SAEs
NCT04252118 (China)	**Target: N = 20**	MSCs (source not stated) at 3 x 10^7 cells at day 0, 3 & 6 versus standard care	- CT scan - SAEs - Pneumonia evaluation - Mortality - T-cell analysis ($CD4^+$ & $CD8^+$) - AAT, CRP & CK
NCT04313322 (Jordan)	**Target: N = 5**	Wharton's jelly derived MSCs at 1 x 10^6 cells/kg for 3 doses, spaced 3 days apart (No control group)	- Alleviations of symptoms - CT scan - Negative nCoV test
NCT04336254 (China)	**Target: N = 20**	Allogenic human dental pulp MSCs at 3 x 10^7 cells at day 1, 4 & 7 versus saline control at day 1, 4 & 7	- TTCI - CT scan - Immune function markers - Time for negative nCoV test - Blood count and classification - SpO_2 - RR - Body temperature - SAEs - CRP
NCT04346368 (China)	**Target: N = 20**	Bone marrow derived MSCs at 1 x 10^6 cells/kg at day 1 versus standard care	- PaO_2/FiO_2 ratio - SAEs

			- Clinical outcome - No. days in hospital - CT scan - Changes in viral load - T-cell analysis ($CD4^+$ & $CD8^+$) - Mortality - CRP
NCT04288102 (China)	**Target: N = 100**	Umbilical cord derived MSCs at 4 x 10^7 at day 0, 3 & 6 versus saline control at day 0, 3 & 6	- Pneumonia evaluation - Time to clinical improvement - PaO_2/FiO_2 ratio - Days on oxygen therapy - SpO_2 - 6-minute walk test - Lymphocyte counts - Cytokine/chemokine assessment - SAEs - All-course mortality
NCT04273646 (China)	**Target: N = 48**	Umbilical cord derived MSCs at 0.5 x 10^6 cells/kg at day 1, 3, 5 & 7 plus standard care versus saline control at day 1, 3, 5 & 7 plus standard care	- Pneumonia evaluation - SAEs - Survival - Organ failure assessment - CRP & Procalcitonin - Lymphocyte count - T-cell analysis ($CD3^+$, $CD4^+$ & $CD8^+$) - $CD4^+/CD8^+$ ratio
NCT04339660 (China)	**Target: N = 30**	Umbilical cord derived MSCs at 1 x 10^6 cells/kg versus saline control	- TNF-α, IL-1β, IL-6, TGF-β, IL-8, PCT, CRP - SpO_2 - Mortality - CT scan - Blood count recovery time - Duration of respiratory symptoms

			- Negative nCoV test
NCT04382547 (Belarus)	**Target: N = 40**	Allogenic pooled olfactory mucosa derived MSCs (dose not stated) versus standard care control	- nCoV test - SAEs
NCT04457609 (Indonesia)	**Target: N = 40**	Umbilical cord derived MSCs at 1 x 10^6 cells/kg with Oseltamivir & Azithromycin versus standard care with Oseltamivir & Azithromycin	- Clinical improvement markers - General laboratory outcomes - PCT, bilirubin, D-dimer & fibrinogen - Troponin & NT-proBNP - LIF, IL-6, IL-10, ferritin, CXCR3 - T-cell analysis ($CD4^+$, $CD8^+$ & $CD56^+$) - VEGF - CT scan
NCT04352803 (USA)	**Target: N = 20**	Autologous adipose derived MSCs at 0.5 x 10^6 cells/kg versus standard care control	- SAEs - Progression and time to/on mechanical ventilation - Length of hospital stay - All-cause mortality
NCT04490486 (USA)	**Target: N = 21**	Umbilical cord derived MSCs at 1 x 10^8 cells on day 0 & 3 versus 1% human serum albumin in Plasmalyte A on day 0 & 3	- SAEs - Inflammatory markers - COVID-19 viral load - SOFA score - Electrolyte levels - LDH - No. ICU discharges - Vasoactive agent use - Mortality - Immune markers - CT scan

NCT04522986 (Japan)	**Target: N = 6**	Adipose derived MSCs at 1 x 10^8 cells once a week for 4 weeks (no control group)	- SAEs
NCT04461925 (Ukraine)	**Target: N = 30**	Placenta derived MSCs at 1 x 10^6 cells/kg once every 3 days for 3 infusions versus standard care control	- PaO_2/FiO_2 ratio - Length of hospital stay - Mortality - CRP - CT scan - Duration of respiratory symptoms - Blood count recovery time
NCT04362189 (USA)	**Target: N = 100**	Allogenic adipose tissue derived MSCs (Hope Biosciences) at 1 x 10^6 cells/dose at day 0, 3, 7 & 10 versus saline control at day 0, 3, 7 & 10	- IL-6, CRP, TNF-α & IL-10 - Oxygenation - RTRA - ECG assessment - Routine blood assessments - Cardiac, hepatic & renal assessment - Blood count - Platelets, Prothrombin time, D-dimer & INR - Immune markers - SAEs - Chest X-ray - CT scan - Negative nCoV test
NCT04371601 (China)	**Target: N = 60**	Umbilical cord derived MSCs at 1 x 10^6 cells/kg once every 4 days for 4 infusions versus standard care control	- PaO_2/FiO_2 ratio - TNF-α & IL-6 - Immune markers - CRP & calcitonin
NCT04348461 (Spain)	**Target: N = 100**	Allogenic expanded adipose tissue derived MSCs at 1.5 x 10^6 cells/kg versus standard care control	- Efficacy of administration of MSCs

			- SAEs
NCT04452097 (USA)	**Target: N = 9**	Umbilical cord derived MSCs (3 groups): - Low dose: 0.5 x 10^6 cells/kg - Middle dose: 1 x 10^6 cells/kg - High dose: 1.5 x 10^6 cells/kg	- SAEs - TEAEs - Selection of appropriate dose for Phase II trial
NCT04494386 (USA)	**Target: N = 60**	Umbilical cord lining derived MSCs at 1 x 10^6 cells/dose versus saline control – either a single dose or 2 doses separated by 48 hours	- DLT - SAEs - Berlin definition of ARDS - SpO_2 & PaO_2/FiO_2 ratio - No. of VFDs - Blood count - Routine blood assessments - BUN & urinalysis - AAT
NCT04345601 (USA)	**Target: N = 30**	MSCs (source not specified) at 1 x 10^8 cells versus standard care control	- SAEs - Change to clinical status
NCT04377334 (Germany)	**Target: N = 40**	Allogenic bone marrow derived MSCs (dose not stated) versus standard care control	- Lung injury score - D-dimer - Pro-resolving lipid mediators - Phenotype of immune cells - Cytokine & chemokine analysis - Survival - Extubation - Lymphocyte subpopulation - Complement molecules - SARS-CoV-2 specific antibody
NCT04390139 (Spain)	**Target: N = 30**	Wharton's jelly derived MSCs at 1 x 10^6 cells/kg on day 1 & 3 versus placebo (not stated) on day 1 & 3	- All-cause mortality - SAEs - Need for mechanical ventilation

			- No. of VFDs - PaO_2/FiO_2 ratio - SOFA index - APACHE II score - Duration of hospitalisation - Immune response - Feasibility of MSCs - nCoV test - LDH, D-dimer & ferritin - Subpopulations of lymphocytes & immunoglobins - *In vitro* response of receptor lymphocytes
NCT04392778 (Turkey)	**Target: N = 30**	MSCs (source not stated) at 3 x 10^6 cells/kg on day 0, 3 & 6 to COVID-19 patients with a ventilator versus saline control on day 0, 3 & 6 to COVID-19 patients with a ventilator versus standard care control to COVID-19 patients without a ventilator	- Clinical improvement - CT scan - Negative nCoV test - Blood tests
NCT04467047 (Brazil)	**Target: N = 10**	MSCs (source not stated) at 1 x 10^6 cells/kg (safety and feasibility study)	- Survival - CRP - Length of hospital stay - PaO_2/FiO_2 ratio - Liao's score (2020) - CT scan - Negative nCoV test
NCT04398303 (USA)	**Target: N = 70**	Allogenic umbilical cord derived MSCs at 1 x 10^6 cells/kg versus MSC conditioned media at 100 ml versus placebo (MEM-α) at 100 ml	- Mortality - No. of VFDs - No. of days on O_2 therapy - No. of ICU-free days - Pulmonary function - Berlin criteria score

NCT04437823 (USA)	**Target: N = 20**	Umbilical cord derived MSCs at 0.5 x 10^6 cells/kg on day 1, 3 & 5 versus standard care control	- SAEs - CT scan - Negative nCoV test - SOFA score - Mortality - Clinical respiratory changes
NCT04269525 (China)	**Target: N = 16**	Umbilical cord derived MSCs at 3.3 x 10^7 cells on day 1, 3, 5 & 7	- PaO_2/FiO_2 ratio - Mortality - Length of hospital stay - nCoV PCR & antibody test - Lung imaging - WBC & lymphocyte count - PCT - IL-2, IL-4, IL-4, IL-6, IL-10, TNF-α, γ-IFN & CRP - NK cells - T-cell analysis ($CD4^+$, $CD8^+$)
NCT04447833 (Sweden)	**Target: N = 9**	Allogenic bone marrow derived MSCs at 1 x 10^6 cells/kg (n = 3) & 2 x 10^6 cells/kg (n = 6)	- SAEs - All-cause mortality - Leucocytes & thrombocytes - CRP - Prothrombin - Creatinine - AST & AAT - NT-proBNP - Blood pressure - Body temperature - Efficacy for MSC use - Lung function - 6-minute walk test - Quality of life assessment - Blood biomarkers - Sensitisation test

NCT04491240 (Russia)	**Target: N = 90**	Inhalation of MSC exosomes at 0.5-2 x 10^{10} nanoparticles for COVID-19 patients (n = 30) & SARS-CoV-2 pneumonia patients (n = 30) versus inhalation of solution free placebo (n = 30) – inhalation twice a day for 10 days	- SAEs - TTCI - Blood gases - SpO_2 - Chest imaging
NCT04333368 (France)	**Target: N = 40**	Umbilical cord Wharton's jelly derived MSCs at 1 x 10^6 cells/kg at day 1, 3 & 5 versus placebo (NaCl) control at day 1, 3 & 5	- PaO_2/FiO_2 ratio - Lung injury score - Mortality - No. of VFDs - Use of sedatives - Use of neuromuscular blocking agent - ICU-acquired weakness - SAEs - Quality of life at 1 year - Cytokine analysis - Anti-HLA antibodies
NCT04466098 (USA)	**Target: N = 30**	Thawed product containing MSCs (source not stated) at 300 x 10^6 cells 3 times separated by 48 hours versus placebo (dextran & human serum albumin) control 3 times separated by 48 hours	- SAEs - Inflammatory markers - PaO_2/FiO_2 ratio - Mean airway, peak & plateau pressure - PEEP - Mortality - No. of ICU free days - No. of VFDs - Acute lung injury score - No. of days off O_2 therapy
NCT04445220 (USA)	**Target: N = 22**	Allogenic human MSCs at 2.5 x 10^6 cells (low dose) and 7.5 x 10^6 cells (high dose) versus standard care control – patients with COVID-19 and acute kidney injury	- Safety and tolerability - SAEs

NCT04276987 (China)	**Target: N = 30**	Allogenic adipose tissue derived MSC exosomes inhaled at 2 x 10^8 nano-vesicles on 5 consecutive days	- SAEs - TTCI - No. of patients weaning from mechanical ventilation - Vasoactive agent use - No. of days on mechanical ventilation - Mortality - SOFA score - Lymphocyte count - CRP, LDH & D-dimer - NT-proBNP - IL-1β, IL-2R, IL-6 & IL-8 - Chest imaging - Negative nCoV test
IRCT20140528017891N8 (Iran)	**Target: N = 10**	Umbilical cord derived MSCs at 0.5-1 million cells/kg at 1^{st}, 3^{rd} & 6^{th} day versus saline injection at 1^{st}, 3^{rd} & 6^{th} day plus standard care	- Mortality - Pneumonia severity index & CT scan - SpO_2 supply - CRP & PCT - Lymphocyte count - T-cell analysis ($CD3^+$, $CD4^+$ & $CD8^+$
NCT04355728 (USA)	**Target: N = 24**	Umbilical cord derived versus standard care control	- Adverse events - 90 day survival post infusion - No. of VFDs - Change in oxygenation index and plat-PEEP - SOFA and SIT scores - TnI, CRP & D-dimer - WBC and platelet count - AA/EPA ratio - 25-Hydroxyl Vitamin D

			- Alloantibody levels
CHICTR2000030224 (China)	**Target: N = NA**	MSCs (source unknown): critical and severe group injected with MSCs versus critical and severe control group injected with saline	- SpO_2 - CT scan - Temperature - Routine blood markers - Inflammatory markers - Hepatic and renal function
ChiCTR2000030173 (China)	**Target: N = NA**	Umbilical cord derived versus standard care control	- Pulmonary function - nCoV pneumonic nucleic acid test - Pulmonary CT and chest radiography
CHICTR2000030138 (China)	**Target: N = NA**	Umbilical cord derived versus standard care plus saline injection control	- Clinical index
ChiCTR2000030088 (China)	**Target: N = NA**	Umbilical cord Wharton's jelly derived MSCs at 1 x 10^6 cells/kg versus standard care and saline injection control	- nCoV pneumonic nucleic acid test - CT scan of ground glass shadow
CHICTR2000029990; TARGET N = NA (China)	**Target: N = NA**	MSCs (source unknown) versus standard care and saline injection control	- Respiratory system function (O_2 saturation) recovery time
ChiCTR2000029817 (NA)	**Target: N = NA**	Umbilical cord derived MSCs and NK cells:	- Time to disease recovery and time to negative nCoV test

		- High dose group: NK cells and MSCs at > 5 x 10^9; Once every two days, five times - Conventional dose group: NK cells and MSCs at > 3 x 10^9; once every two days, three times - Preventive dose group: NK cells and MSCs at > 3 x 10^9; one infusion	- Clearance rate and time of main symptoms - Transfer to ICU time - Routine blood tests - Biochemical indicators - Immune indices
CHICTR2000029816 (NA)	**Target: N = NA**	Umbilical cord derived MSCs (dose not stated) versus standard care control	- Time to disease recovery and time to negative nCoV test - Clearance rate and time of main symptoms - Transfer to ICU time - Routine blood tests - Biochemical indicators - Immune indices
ChiCTR2000029580 (China)	**Target: N = NA**	Ruxolitinib and MSCs (source and dose not stated) versus standard care control	- Safety
CHICTR2000029569 (China)	**Target: N = NA**	Umbilical cord derived blood mononuclear cells conditioned medium versus standard care control	- PSI, CT & X-Ray - Arterial blood gas - Assisted breathing time - Mortality - Disease evolution - Hospitalisation days - Safety outcome index
EUCTR2020-001450-22-ES (Spain)	**Target: N = NA**	Allogenic umbilical cord derived MSCs (dose not stated)	- Mortality - Mechanical ventilation incidence - Need for vasopressors - Safety profile of MSCs - Neutrophils, monocytes & NK cells - PCT, ferritin, D-dimer & hs-troponin

			- PCR test - B & T lymphocytes - Interleukins, Th1,2&17, NLRP3 & HMGB1
IRCT20200421047150N1 (Iran)	**Target: N = NA**	Umbilical card Wharton's jelly derived: three injections at 0.5-1 million cells/kg at 1st, 3rd & 6th day. Control receiving standard care plus saline injection at 1st, 3rd & 6th day	- Not stated
ACTRN12620000612910 (Australia)	**Target: N = NA**	Mesenchymoangioblast derived MSCs (CYP-001) at 2 x 10^6 cells/kg twice versus ICU standard care control	- Not stated
NCT04361942 (Spain)	**Target: N = 24**	Allogenic MSCs (source unknown) versus placebo (not stated)	- Withdrawal of invasive mechanical ventilation - Mortality - Patients achieving a clinical response - Patients achieving a radiological response
EUCTR2020-001266-11-ES (Spain)	**Target: N = 100**	Allogenic adipose tissue MSCs	- Efficacy and safety of administration of MSCs - Survival - Temperature - Withdrawal of mechanical ventilation - Patients transitioning to O_2 therapy from mechanical ventilation - O_2 therapy duration - Days in ICU - Duration of hospitalisation - PaO_2/FiO_2 - Chest radiology - Routine blood markers

		- Inflammatory markers - Coagulation markers - Immune markers

Note: hs-CRP = high sensitivity C-reactive protein; IL- = Interleukin-; TNF-α = Tumor necrosis factor-α; SAE = Serious adverse event; HR = Heart rate; RR = Respiratory rate; PCT = Procalcitonin; VEGF = Vascular endothelial growth factor; RTRA = Return to room air; INR = International normalised ratio of blood coagulation; TEAE = treatment emergent serious adverse events; DLT = Dose limiting toxicity; VFD = Ventilator free days; BUN = Blood urea nitrogen; APACHE = Acute physiology and chronic health disease classification; AST = Aspartate aminotransferase; NEWS = National early warning score; LDH = Lactate dehydrogenase; AAT = Alanine aminotransferase; CK = Creatine kinase; TTCI = Time to clinical improvement; LIF = Leukaemia inhibiting factor; PEEP = Positive end-expiratory pressure; SOFA = Sequential organ failure assessment; SIT = Small identification test; TnI = Troponin I; AA = Arachidonic acid; EPA = Eicosapentaenoic acid; nCoV = novel coronavirus; Polymerase chain reaction; NK = Natural killer; Th = T helper; NLRP3 = NLR Family Pyrin Domain Containing 3; HMGB1 = High mobility group box 1