

Cell-based therapies for COVID-19: A living, systematic review

doi:10.5867/medwave.2020.11.8078

Appendix 1: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2, N/A
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5-6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6

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Section/topic	#	Checklist item	Reported on page #
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5,8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8

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Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9,11
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	11
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	11
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	11
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	12, Appendix

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Section/topic	#	Checklist item	Reported on page #
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	N/A
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A

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Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	N/A
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	N/A
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

APPENDIX 2 - Search strategies - Cell-based therapies for COVID-19: A living systematic review

L·OVE platform strategies

Search strategies used in the L·OVE platform for the following question:

[Cell-based therapies for Coronavirus infection](#)

The components below are combined by the system with the boolean operator AND

Population component: Coronavirus

This is the population component of the search strategy used by L·OVE platform to automatically retrieve potentially eligible articles from Epistemonikos Database (see [special COVID-19 methods](#))

Date: 16 April, 2020 (this strategy is continuously improved any time a relevant article is missed)

coronavir* OR coronavirus* OR "corona virus" OR "virus corona" OR "corono virus" OR "virus corono" OR hcov* OR "covid-19" OR covid19* OR "covid 19" OR "2019-nCoV" OR cv19* OR "cv-19" OR "cv 19" OR "n-

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cov" OR ncov* OR "sars-cov-2" OR "sars-cov2" OR "SARS-Coronavirus-2" OR "SARS-Coronavirus2" OR (wuhan* AND (virus OR viruses OR viral)) OR (covid* AND (virus OR viruses OR viral)) OR "sars-cov" OR "sars cov" OR "sars-coronavirus" OR "severe acute respiratory syndrome" OR "mers-cov" OR "mers cov" OR "middle east respiratory syndrome" OR "middle-east respiratory syndrome" OR "covid-19-related" OR "SARS-CoV-2-related" OR "SARS-CoV2-related" OR "2019-nCoV-related" OR "cv-19-related" OR "n-cov-related"

Intervention component: Cell-based therapies

This is the intervention component of the strategy used by L·OVE platform to automatically retrieve potentially eligible articles from Epistemonikos Database

The terms below are combined by the system with the boolean operator OR

Date: 13 April, 2020 (this strategy is continuously improved any time a relevant article is missed)

Relevant terms in L·OVE taxonomy	Search strategy
Cell-based therapies	"cell therapy" OR "cell therapies" OR "cell-therapy" OR "cell-therapies"
Stem-cell therapy	"stem-cell" OR "stem-cells" OR "stem cell" OR "stem cells" OR "cell therapy" OR "cell-therapy" OR "cell therapies" OR "cell-therapies"
Hematopoietic stem cells	((stem* OR "bone marrow" OR "bone-marrow") AND (transplant* OR rescue)) OR BMT OR HSC*
Mesenchymal stem cells	MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR nestcell* OR ((mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*)) OR (medicinal* AND signalling* AND (cell OR cells)) OR (stromal* AND (stem OR multipotent*)) OR ("tissue-derived" AND mesenchymal*)
Bone marrow mesenchymal stromal cells	"bm-msc" OR "bm msc" OR bmmsc* OR "bm-mscs" OR "bm mscs" OR "bm-scs" OR "bm scs" OR bmssc* OR "bm-sc" OR "bm sc" OR hbmmsc* OR "hbm-msc" OR "hbm msc" OR hbmmsc* OR "hbm-mscs" OR "hbm mscs" OR "hbm-scs" OR "hbm scs" OR hbmmsc* OR "hbm-sc" OR "hbm sc" OR ((marrow OR "bone-marrow-derived") AND (MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR nestcell* OR ((mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*)) OR (medicinal* AND signalling* AND (cell OR cells)) OR (stromal* AND (stem OR multipotent*)) OR ("tissue-derived" AND mesenchymal*))
Adipose mesenchymal stromal cells	"ad-msc" OR "ad msc" OR admsc* OR "ad-mscs" OR "ad mscs" OR "ad-sc" OR "ad sc" OR adsc* OR "ad-scs" OR "ad scs" OR "ha-sc" OR "ha sc" OR hasc* OR "ha-scs" OR "ha scs" OR "am-sc" OR "am sc" OR amsc* OR "am-scs" OR "am scs" OR (adipose* AND (MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR nestcell* OR ((mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*)) OR (medicinal* AND signalling* AND (cell OR cells)) OR (stromal* AND (stem OR multipotent*)) OR ("tissue-derived" AND mesenchymal*))
Amniotic fluid mesenchymal stromal cells	"af-msc" OR "af msc" OR "af-mscs" OR "af mscs" OR afmsc* OR "af-sc" OR "af sc" OR "af-scs" OR "af scs" OR afsc* OR "haf-msc" OR "haf msc" OR "haf-mscs" OR "haf mscs" OR hafmsc* OR "haf-sc" OR "haf sc" OR "haf-scs" OR "haf scs" OR hafsc* OR ((amniotic* OR fluid*) AND (MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR nestcell* OR ((mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND

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	(stromal* OR stem OR multipotent* OR progenitor*) OR (medicinal* AND signalling* AND (cell OR cells)) OR (stromal* AND (stem OR multipotent*)) OR ("tissue-derived" AND mesenchymal*))
Umbilical cord mesenchymal stromal cells	"huc-msc" OR "huc msc" OR "huc-mscs" OR "huc mscs" OR hucmsc* OR "uc-msc" OR "uc msc" OR "uc-mscs" OR "uc mscs" OR ucmsc* OR "wj-msc" OR "wj msc" OR "wj-mscs" OR "wj mscs" OR wjmsc* OR ((umbilical* OR cord OR cord-derived OR wharton* OR jelly*) AND (MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR nestcell* OR ((mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*)) OR (medicinal* AND signalling* AND (cell OR cells)) OR (stromal* AND (stem OR multipotent*)) OR ("tissue-derived" AND mesenchymal*))
Peripheral blood mesenchymal stromal cells	"b-msc" OR "b msc" OR "b-mscs" OR "b mscs" OR bmsc* OR "bd-sc" OR "bd sc" OR "bd-scs" OR "bd scs" OR bdsc* OR (menstrual* AND (stem* OR stromal*)) OR ((blood* OR menstrual*) AND (MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR nestcell* OR ((mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*)) OR (medicinal* AND signalling* AND (cell OR cells)) OR (stromal* AND (stem OR multipotent*)) OR ("tissue-derived" AND mesenchymal*))
Dental pulp mesenchymal stromal cells	"dp-msc" OR "dp msc" OR "dp-mscs" OR "dp mscs" OR dpmsc* OR "hdp-msc" OR "hdp msc" OR "hdp-mscs" OR "hdp mscs" OR hdpmsc* OR ((dental* OR pulp OR molar OR teeth) AND (MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR nestcell* OR ((mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*)) OR (medicinal* AND signalling* AND (cell OR cells)) OR (stromal* AND (stem OR multipotent*)) OR ("tissue-derived" AND mesenchymal*))
Synovial mesenchymal stromal cells	synov* AND (MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR nestcell* OR ((mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*)) OR (medicinal* AND signalling* AND (cell OR cells)) OR (stromal* AND (stem OR multipotent*)) OR ("tissue-derived" AND mesenchymal*))
Human embryonic stem cells	"e-sc" OR "e sc" OR esc OR "e-scs" OR "e scs" OR escs* OR "he-sc" OR "he sc" OR hesc OR "he-scs" OR "he scs" OR hescs* OR "e-msc" OR "e msc" OR emsc* OR "e-mscs" OR "e mscs" OR emscs* OR "he-msc" OR "he msc" OR hemsc* OR "he-mscs" OR "he mscs" OR hemscs* OR "es cells" OR "es cell" OR ((embryo OR embryonic* OR "embryo-derived") AND (MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR mesenchymal* OR stromal* OR stem OR multipotent* OR progenitor*))
Cell-based immunotherapies	"cell-based" OR (cell* AND immunotherap*)
Natural Killer cell therapy	nk* OR (natural* AND killer*) OR "natural-killer"

Single-block search strategy in L·OVE platform for the question: mesenchymal stromal cells for COVID-19 (adapted for simplicity)

Date: April 13, 2020

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((coronavir* OR coronavirus* OR "corona virus" OR "virus corona" OR "corono virus" OR "virus corono" OR hcov* OR "covid-19" OR covid19* OR "covid 19" OR "2019-nCoV" OR cv19* OR "cv-19" OR "cv 19" OR "n-cov" OR ncov* OR "sars-cov-2" OR "sars-cov2" OR "SARS-Coronavirus-2" OR "SARS-Coronavirus2" OR (wuhan* AND (virus OR viruses OR viral)) OR (covid* AND (virus OR viruses OR viral)) OR "sars-cov" OR "sars cov" OR "sars-coronavirus" OR "severe acute respiratory syndrome" OR "mers-cov" OR "mers cov" OR "middle east respiratory syndrome" OR "middle-east respiratory syndrome" OR "covid-19-related" OR "SARS-CoV-2-related" OR "SARS-CoV2-related" OR "2019-nCoV-related" OR "cv-19-related" OR "n-cov-related")) AND ("cell therapy" OR "cell therapies" OR "cell-therapy" OR "cell-therapies" OR "mesenchymal cell" OR "mesenchymal cells" OR MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR nestcell* OR ((mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*)) OR (medicinal* AND signalling* AND (cell OR cells)) OR (stromal* AND (stem OR multipotent*)) OR ("tissue-derived" AND mesenchymal*))

Additional searches in electronic databases

Search strategy for Pubmed/MEDLINE

Search date: 24.04.2020

- #1 coronavir*
- #2 coronavirus*
- #3 "corona virus"
- #4 "virus corona"
- #5 "corono virus"
- #6 "virus corono"
- #7 hcov*
- #8 "covid-19"
- #9 covid19*
- #10 "covid 19"
- #11 "2019-nCoV"
- #12 cv19*
- #13 "cv-19"
- #14 "cv 19"
- #15 "n-cov"
- #16 ncov*
- #17 "sars-cov-2"
- #18 wuhan*[Tiab] AND (virus OR viruses OR viral)
- #19 covid* AND (virus OR viruses OR viral)
- #20 "sars-cov"
- #21 "sars cov"
- #22 "sars-coronavirus"
- #23 "severe acute respiratory syndrome"
- #24 "mers-cov"
- #25 "mers cov"

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- #26 "middle east respiratory syndrome"
- #27 "middle-east respiratory syndrome"
- #28 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27
- #29 "cell therapy" OR "cell therapies" OR "cell-therapy" OR "cell-therapies"
- #30 MSC OR MSCs OR "mesenchymal cell" OR "mesenchymal cells"
- #31 HMSC*
- #32 stemstromal*
- #33 stromalstem*
- #34 nestcell*
- #35 (mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*)
- #36 (medicinal* AND signalling* AND (cell OR cells))
- #37 stromal* AND (stem OR multipotent*)
- #38 "tissue-derived" AND mesenchymal*
- #39 #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38
- #40 #28 AND #39

Search strategy for EMBASE (Elsevier)

Search date: 24.04.2020

- #1. coronavirus*
- #2. coronavir*
- #3. 'corona virus'
- #4. 'virus corona'
- #5. 'corono virus'
- #6. 'virus corono'
- #7. hcov*
- #8. 'covid-19'
- #9. covid19*
- #10. 'covid 19'
- #11. '2019-ncov'
- #12. cv19*
- #13. 'cv-19'
- #14. 'cv 19'
- #15. 'n-cov'
- #16. ncov*
- #17. 'sars-cov-2'

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- #18. wuhan*:ti,ab AND (virus OR viruses OR viral)
- #19. covid* AND (virus OR viruses OR viral)
- #20. 'sars-cov'
- #21. 'sars cov'
- #22. 'sars-coronavirus'
- #23. 'severe acute respiratory syndrome'
- #24. 'mers-cov'
- #25. 'mers cov'
- #26. 'middle east respiratory syndrome'
- #27. 'middle-east respiratory syndrome'
- #28. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27
- #29. 'cell therapy' OR 'cell therapies' OR 'cell-therapy' OR 'cell-therapies'
- #30. msc OR mscs OR 'mesenchymal cell' OR 'mesenchymal cells'
- #31. hmsc*
- #32. stemstromal*
- #33. stromalstem*
- #34. nestcell*
- #35. (mesenchymal* OR 'tissue-derived' OR 'derived-mesenchymal') AND (stromal* OR stem OR multipotent* OR progenitor*)
- #36. medicinal* AND signalling* AND (cell OR cells)
- #37. stromal* AND (stem OR multipotent*)
- #38. 'tissue-derived' AND mesenchymal*
- #39. #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38
- #40. #28 AND #39

Search strategy for CENTRAL (The Cochrane Library Issue 1, 2019)

Search date:24.04.2020

- #1 coronavir*:ti,ab,kw
- #2 coronavirus*:ti,ab,kw
- #3 "corona virus":ti,ab,kw
- #4 "virus corona":ti,ab,kw
- #5 "corono virus":ti,ab,kw
- #6 "virus corono":ti,ab,kw
- #7 hcov*:ti,ab,kw
- #8 "covid-19":ti,ab,kw
- #9 covid19*:ti,ab,kw

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- #10 "covid 19":ti,ab,kw
- #11 "2019-nCoV":ti,ab,kw
- #12 cv19* :ti,ab,kw
- #13 "cv-19":ti,ab,kw
- #14 "cv 19":ti,ab,kw
- #15 "n-cov":ti,ab,kw
- #16 ncov*:ti,ab,kw
- #17 "sars-cov-2"
- #18 (wuhan* AND (virus OR viruses OR viral):ti,ab,kw
- #19 covid* AND (virus OR viruses OR viral):ti,ab,kw
- #20 "sars-cov":ti,ab,kw
- #21 "sars cov" :ti,ab,kw
- #22 "sars-coronavirus":ti,ab,kw
- #23 "severe acute respiratory syndrome":ti,ab,kw
- #24 "mers-cov":ti,ab,kw
- #25 "mers cov":ti,ab,kw
- #26 "middle east respiratory syndrome":ti,ab,kw
- #27 "middle-east respiratory syndrome":ti,ab,kw
- #28 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27
- #29 ("cell therapy" OR "cell therapies" OR "cell-therapy" OR "cell-therapies"):ti,ab,kw
- #30 (MSC OR MSCs OR "mesenchymal cell" OR "mesenchymal cells"):ti,ab,kw
- #31 HMSC*:ti,ab,kw
- #32 stemstromal*:ti,ab,kw
- #33 stromalstem*:ti,ab,kw
- #34 nestcell*:ti,ab,kw
- #35 (mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*):ti,ab,kw
- #36 (medicinal* AND signalling* AND (cell OR cells)):ti,ab,kw
- #37 (stromal* AND (stem OR multipotent*)):ti,ab,kw
- #38 ("tissue-derived" AND mesenchymal*):ti,ab,kw
- #39 #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38
- #40 #28 AND #39

Databases and registries automatically screened by Epistemonikos Database for COVID-19 ('COVID-19 repository')

Updated daily or more than daily

PubMed

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<https://www.ncbi.nlm.nih.gov/pubmed/>

coronavir* OR coronavirus* OR "corona virus" OR "virus corona" OR "corono virus" OR "virus corono" OR hcov* OR "covid-19" OR covid19* OR "covid 19" OR 2019-nCoV OR cv19* OR "cv-19" OR "cv 19" OR "n-cov" OR ncov* OR "sars-cov-2" OR (wuhan*[tiab] AND (virus OR viruses OR viral OR coronav*)) OR (covid* AND (virus OR viruses OR viral)) OR "sars-cov" OR "sars cov" OR "sars-coronavirus" OR "severe acute respiratory syndrome" OR "mers-cov" OR "mers cov" OR "middle east respiratory syndrome" OR "middle-east respiratory syndrome"

COVID-19 SARS-CoV-2 preprints from medRxiv and bioRxiv

<https://connect.medrxiv.org/relate/content/181>

* All the articles in this list are uploaded

Clinicaltrials.gov

<https://clinicaltrials.gov/>

Search date: 23.04.2020

"SARS-COV-2" OR "Sars-CoV2" OR nCoV OR COVID OR Coronavirus OR Corona OR "covid-19" OR covid19 OR "covid 19" OR "2019-nCoV" OR cv19 OR "cv-19" OR "cv 19" OR "n-cov" OR coronavirus

ISRCTN registry

<https://www.isrctn.com/>

Search date: 23.04.2020

MSC OR MSCs OR HMSC OR stem OR stromal OR mesenchymal OR multipotent OR progenitor

Chinese Clinical Trial Registry

<http://www.chictr.org.cn/>

Search date: 23.04.2020

Separate searches for the following terms:

coronavirus; coronavirus; corona virus; virus corona; corono virus; virus corono; hcov; covid-19; covid19; covid 19; 2019-nCoV; cv19; cv-19; cv 19; n-cov; ncov; sars-cov-2; sars-cov2; SARS-Coronavirus-2; SARS-Coronavirus2

Iranian Registry of Clinical Trials

<https://www.irct.ir/>

Search date: 23.04.2020

((coronavir* OR coronavirus* OR "corona virus" OR "virus corona" OR "corono virus" OR "virus corono" OR hcov* OR "covid-19" OR covid19* OR "covid 19" OR "2019-nCoV" OR cv19* OR "cv-19" OR "cv 19" OR "n-cov" OR ncov* OR "sars-cov-2" OR "sars-cov2" OR "SARS-Coronavirus-2" OR "SARS-Coronavirus2" OR (wuhan* AND (virus OR viruses OR viral)) OR (covid* AND (virus OR viruses OR viral)) OR "sars-cov" OR "sars cov" OR "sars-coronavirus" OR "severe acute respiratory syndrome" OR "mers-cov" OR "mers cov" OR "middle east respiratory syndrome" OR "middle-east respiratory syndrome" OR "covid-19-related" OR "SARS-CoV-2-related" OR "SARS-CoV2-related" OR "2019-nCoV-related" OR "cv-19-related" OR "n-cov-related")) AND (MSC OR MSCs OR HMSC* OR stemstromal* OR stromalstem* OR nestcell* OR ((mesenchymal* OR "tissue-derived" OR "derived-mesenchymal") AND (stromal* OR stem OR multipotent* OR progenitor*)) OR (medicinal* AND signalling* AND (cell OR cells)) OR (stromal* AND (stem OR multipotent*)) OR ("tissue-derived" AND mesenchymal*))

Other databases and websites specialised in COVID-19 manually searched for this review

Google Scholar

<https://scholar.google.com/>

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Search date: 23.04.2020

allintitle:"COVID-19" | COVID19 | 2019nCoV | "Corona Virus" | Coronavirus | "CoV
2" | CoV2 | COVID | nCoV | SARS2 | SARSCoV | "SARS-CoV"

EU Clinical Trials Register: Clinical trials for covid-19

Search date: 23.04.2020

<https://www.clinicaltrialsregister.eu/ctr-search/search?query=covid-19>

* All the references in this list were screened

NIPH Clinical Trials Search (Japan)

Search date: 23.04.2020

<https://rctportal.niph.go.jp/en/>

Separate searches for the following terms:

coronavirus; coronavirus; corona virus; virus corona; corono virus; virus corono; hcov; covid-19; covid19; covid
19; 2019-nCoV; cv19; cv-19; cv 19; n-cov; ncov; sars-cov-2; sars-cov2; SARS-Coronavirus-2; SARS-Coronavirus2

Clinical Research Information System (Korea)

Search date: 23.04.2020

<https://cris.nih.go.kr/cris/en/>

Separate searches for the following terms:

coronavirus; coronavirus; corona virus; virus corona; corono virus; virus corono; hcov; covid-19; covid19; covid
19; 2019-nCoV; cv19; cv-19; cv 19; n-cov; ncov; sars-cov-2; sars-cov2; SARS-Coronavirus-2; SARS-Coronavirus2

ICTRP Search Portal

Search date: 10.04.2020 (resource was not available on 23 April, 2020)

<http://apps.who.int/trialsearch>

MSC OR MSCs OR HMSC OR stem OR stromal OR mesenchymal OR multipotent OR progenitor

Cochrane COVID-19 Study Register

Search date: 23.04.2020

<https://covid-19.cochrane.org/>

MSC OR MSCs OR HMSC OR stem OR stromal OR mesenchymal OR multipotent OR progenitor

Resources scanned without using a search strategy

COVID-19: Global literature on coronavirus disease (<https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/>)

NIHR: Innovation observatory: COVID-19 Updates (<http://www.io.nihr.ac.uk/covid-19-updates/>)

COVID-19: a living systematic map of the evidence (http://eppi.ioe.ac.uk/COVID19_MAP/covid_map_v8.html)

COVID-evidence website (<https://covid-evidence.org/database>)

Live map of COVID-19 evidence (<https://www.fhi.no/en/qk/systematic-reviews-hta/map/>)

LitCovid (<https://www.ncbi.nlm.nih.gov/research/coronavirus/>)

COVID-19 Special Collection (JBI) (<https://jbi.global/ebp/covid-19>)

Coronavirus disease (COVID-2019) R&D (<https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/>)

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Coronavirus (COVID-19) Resource Hub (<https://pharmacist.therapeuticresearch.com/Content/Topic/all/covid-19-Resource-Hub>)

Coronavirus Research Repository (Elsevier Connect) (<https://www.cdc.gov/coronavirus/2019-ncov/publications.html>)

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Orientación sobre la COVID-19 y últimas investigaciones en las Américas (PAHO) (<https://covid19-evidence.paho.org/>)

COVID-19. Información confiable para la toma de decisiones (<https://www.iecs.org.ar/covid/>)

New England Journal of Medicine: Coronavirus (Covid-19) (<https://www.nejm.org/coronavirus>)

BMJ: Coronavirus (covid-19): Latest news and resources (<http://bmj.com/coronavirus>)

Lancet: COVID-19 Resource Centre (<https://www.thelancet.com/coronavirus>)

JAMA: Coronavirus Disease 2019 (COVID-19) (<https://jamanetwork.com/journals/jama/pages/coronavirus-alert>)

Cochrane Resources on Coronavirus (COVID-19) (<https://www.cochranelibrary.com/covid-19>)

Oxford COVID-19 Evidence Service (<https://www.cebm.net/covid-19/>)

NICE Rapid Guideline and Summaries on COVID-19 (<https://www.nice.org.uk/covid-19>)

Coronavirus disease (COVID-19) - European Medicines Agency (EMA) (<https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19>)

Coronavirus Disease 2019 (COVID-19) - U.S. Food & Drug Administration (FDA) (<https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19>)

APPENDIX 3 - Description of relevant studies - Cell-based therapies for COVID-19: A living systematic review

INCLUDED STUDIES

No studies were found

EXCLUDED STUDIES

Study name	Reason for exclusion
Liang et al	Not a comparative study (case report)
Leng et al	Not a comparative study (case series)

References to excluded studies

Liang B, Chen J, Li T, Wu H, Yang W, Li Y, Li J, Yu C, Nie F, Ma Z, Yang M, Nie P, Gao Y. Clinical remission of a critically ill COVID-19 patient treated by human umbilical cord mesenchymal stem cells. chinaXiv. 2020; [Epistemonikos](#)

Leng et al, Zikuan, Zhu, Rongjia, Hou, Wei, Feng, Yingmei, Yang, Yanlei, Han, Qin, Shan, Guangliang, Meng, Fanyan, Du, Dongshu, Wang, Shihua. Transplantation of ACE2-mesenchymal stem cells improves the outcome of patients with COVID-19 pneumonia. Aging and disease. 2020;11(2):216-228. [Epistemonikos](#)

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ONGOING STUDIES

References to ongoing randomised trials

Puren Hospital Affiliated to Wuhan University of Science and Technology. Clinical Research of Human Mesenchymal Stem Cells in the Treatment of COVID-19 Pneumonia. clinicaltrials.gov. 2020;

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Safety and effectiveness of human umbilical cord mesenchymal stem cells in the treatment of acute respiratory distress syndrome of severe novel coronavirus pneumonia (COVID-19). Chinese Clinical Trial Registry. 2020;

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Safety and efficacy of umbilical cord blood mononuclear cells conditioned medium in the treatment of severe and critically novel coronavirus pneumonia (COVID-19): a randomized controlled trial. Chinese Clinical Trial Registry. 2020;

Severe novel coronavirus pneumonia (COVID-19) patients treated with ruxolitinib in combination with mesenchymal stem cells: a prospective, single blind, randomized controlled clinical trial. Chinese Clinical Trial Registry. 2020;

Tianhe Stem Cell Biotechnologies Inc. Stem Cell Educator Therapy Treat the Viral Inflammation Caused by Severe Acute Respiratory Syndrome Coronavirus 2. clinicaltrials.gov. 2020;

Feng Ganzhu. Clinical study for stem cells in the treatment of severe novel coronavirus pneumonia (COVID-19). Chinese Clinical Trial Registry. 2020;

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Beijing 302 Hospital. Treatment With Mesenchymal Stem Cells for Severe Corona Virus Disease 2019(COVID-19). clinicaltrials.gov. 2020;

Renmin Hospital of Wuhan University. Safety and Efficacy Study of Allogeneic Human Dental Pulp Mesenchymal Stem Cells to Treat Severe COVID-19 Patients. clinicaltrials.gov. 2020;

Chongqing Public Health Medical Center. A Phase I/II Study of Universal Off-the-shelf NKG2D-ACE2 CAR-NK Cells for Therapy of COVID-19. clinicaltrials.gov. 2020;

Hope Biosciences. A Randomized, Double-Blind, Single Center, Efficacy and Safety Study of Allogeneic HB-ad-MSCs to Provide Immune Support Against COVID-19. clinicaltrials.gov. 2020;

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Assistance Publique - Hôpitaux de Paris. Cell Therapy Using Umbilical Cord-derived Mesenchymal Stromal Cells in SARS-CoV-2-related ARDS. clinicaltrials.gov. 2020;

Instituto de Investigación Sanitaria de la Fundación Jiménez Díaz. BAAttLe Against COVID-19 Using Mesenchymal Stromal Cells. clinicaltrials.gov. 2020;

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