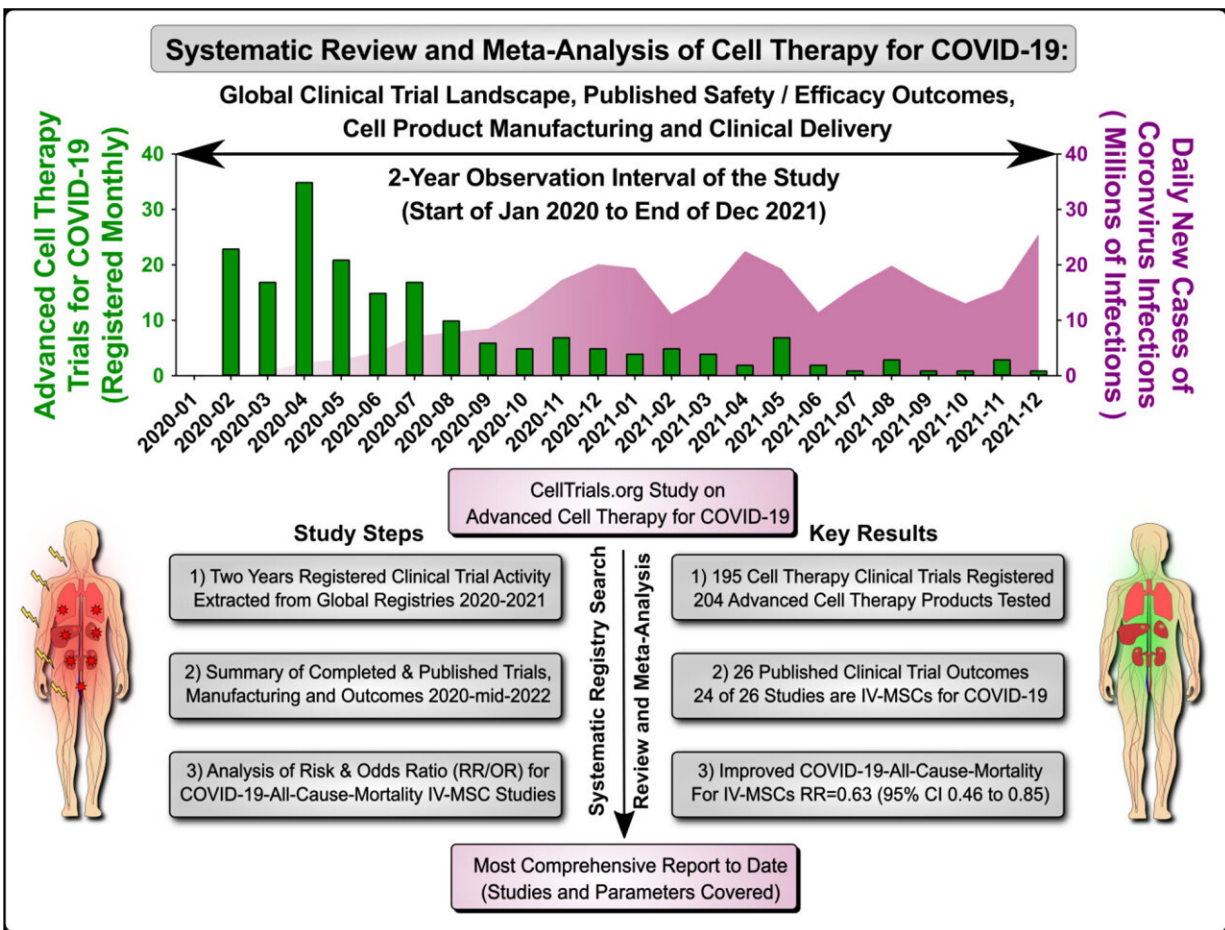


Cell therapy can reduce risk of death from COVID-19 by 60%, study finds

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Systematic review and meta-analysis of cell therapy for COVID-19. Credit: *Frontiers in Immunology* (2023). DOI: 10.3389/fimmu.2023.1200180

The use of cell therapy to treat COVID-19 patients can reduce the risk of death from the disease by 60%, according to a systematic review and meta-analysis conducted by researchers at the University of São Paulo (USP) in Brazil, in partnership with colleagues in Germany and the United States.

Their findings are reported in an article [published](#) in the journal *Frontiers in Immunology*.

The review covers 195 clinical trials of advanced cell therapies targeting COVID-19 that were conducted in 30 countries between January 2020 and December 2021, as well as 26 trials with outcomes published by July 2022.

Cell therapy has come into increasingly frequent use in recent years to treat several diseases, especially cancer. It consists basically of introducing [healthy cells](#) into the patient's organism in order to restore or alter certain sets of cells, carry a therapy through the body, or modulate the function of diseased cells.

The technique uses [stem cells](#) and derivatives from the patient (autologous) or from a donor (allogenic). The cells are cultured or modified in the laboratory before being administered. According to the article, the cell types most frequently used in clinical trials relating to treatment of COVID-19 in the period were multipotent mesenchymal stem (stromal) cells from [connective tissue](#), used in 72% of the studies reviewed; [natural killer cells](#) from lymphoblasts, used in 9%; and mononuclear cells from blood, used in 6%.

"Cell therapy has advanced significantly in recent years and has been used to treat cancer and auto-immune, heart and infectious diseases. During the pandemic, it was used to treat COVID-19 in several clinical trials," said Otávio Cabral-Marques, a professor at USP's Medical School

and coordinator of the study.

"Our study is the first to review all the information on these experiences scattered around the world and to verify by means of a meta-analysis [[a statistical method](#) of aggregating data from many independent studies] how cell therapy functions when used to treat COVID-19 and related complications," he continued.

Stem cell therapy and models involving organoids derived from stem cells drew a great deal of attention as novel methods for treating and studying COVID-19 during the pandemic, he noted, given the significant immune regulatory power and tissue repair functions of stem cells, especially the mesenchymal variety. In the case of the lungs, for example, clinical trials have shown to a greater or lesser extent that advanced cell therapy can limit the severity of the inflammatory response in COVID-19 patients, reduce pulmonary damage, improve lung function and help combat fibrosis.

Despite the attention paid to cell therapy, the real protection assured by vaccination should be stressed, according to Cabral-Marques. "Although all these studies have shown that advanced cell therapy could become established soon as an important adjunct treatment for these patients, prevention of the disease by vaccination remains the best protection," he said.

Data standardization

The [clinical trials](#) involving advanced cell therapy for COVID-19 analyzed by the authors of the review article were conducted in 30 countries, mainly the United States, China, Iran and Spain. They were highly heterogeneous, however, with widely varying numbers of participants, designs and methodologies, so for meta-analysis purposes the researchers created a specially curated COVID-19 trials database at

CellTrials.org with several quality refinements, such as inclusion of trials from all national registries, exclusion of false positives on keywords, and exclusion of double counting of the same trials.

The authors also note differences in terms of the phases of trials. In many countries, especially in Europe, strict regulation limits the number of human cell therapy products with established safety profiles that can be trialed, and 56% of the trials did not reach phase 2, which typically focuses on determining safety, efficacy and dose-response in a few hundred volunteers with the disease. Another limitation was that 31% of the trials analyzed did not have a control group.

"To arrive at such a large reduction in the risk of death, we had to take into account the findings and characteristics of the different studies, as well as making a certain number of corrections and estimates," said Igor Salerno Filgueiras, a Ph.D. candidate and co-author of the article.

"There are techniques to standardize the data, eliminate biases and produce an impartial result, enabling analysts to reach conclusions that often go unnoticed in a specific study but add up to relevant scientific evidence when they are reinforced by other data," said Dennyson Leandro M. Fonseca, another co-author.

Fabrication and clinical delivery methods in studies involving mesenchymal stem cells were "remarkably heterogeneous," according to the article. "The results highlight the important role these cells can play in adjuvant therapies for COVID-19 and the associated complications. However, they also point to a need for better control of key parameters relating to the way the [cell therapy](#) products are made if we are to assure comparability between studies," Cabral-Marques said.

More information: Pedro S. Couto et al, Systematic review and meta-analysis of cell therapy for COVID-19: global clinical trial landscape,

published safety/efficacy outcomes, cell product manufacturing and clinical delivery, *Frontiers in Immunology* (2023). [DOI: 10.3389/fimmu.2023.1200180](#)

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