idw - Informationsdienst Wissenschaft
Nachrichten, Termine, Experten

Pressemitteilung

Universität zu Köln
Anna Euteneuer

14.11.2024
http://idw-online.de/de/news842888

Forschungsergebnisse, Wissenschaftliche Publikationen
Biologie, Medizin
überregional

New therapeutic approach for severe COVID-19: faster recovery and reduction in mortality

An international research consortium from Cologne, London, Vienna, Heidelberg, Zaragoza and Madrid have tested a novel therapeutic concept to treat virus-induced lung failure in patients with severe COVID-19 in a phase 2 clinical trial. The approach may also be applicable to other infections / publication in eClinicalMedicine

A new clinical study shows that an inhibitor of Fas ligand (FasL), also called CD95 ligand (CD95L), led to a faster recovery of COVID-19 patients and reduced mortality. On average, it took eight days to recover for patients who received asunercept, a biotherapeutic FasL inhibitor, compared to 13 days in the control group. In addition, mortality was decreased by about 20 per cent. The study 'Efficacy and safety of asunercept, a CD95L-selective inhibitor, in hospitalised patients with moderate-to-severe COVID-19: ASUNCTIS, a multicentre, randomised, open-label, controlled, phase 2 trial' has been published in eClinicalMedicine.

The physiological role of FasL is to keep cells of the immune system, so called T lymphocytes, short T cells, under control by killing them once they have fulfilled their function. In patients with severe COVID-19, however, the immune system is hyper-activated causing an over-production of FasL. As a result, FasL does two things: it kills way too many T cells and it also attacks normal lung cells. This aberrant increase in cell death causes lymphopenia, that is the loss of lymphocytes, and severe lung inflammation, two hallmark characteristics of severe COVID-19. The new therapeutic concept is based on blocking FasL and to thereby prevent the untoward death of T cells and lung epithelial cells and the inflammation resulting therefrom.

The academic members of the research team that conducted the clinical trial recently demonstrated in a preclinical model that therapeutic inhibition of FasL significantly increased survival of mice with severe COVID-19. The phase II dose-finding study with the FasL inhibitor asunercept was initiated as an academic-industrial collaboration by Professor Henning Walczak and his team at the University of Cologne and University College London (UCL) as well as Professor Michael Bergmann at the Medical University of Vienna and Dr Thomas Hoeger at Apogenix GmbH1, a biotech company from Heidelberg, Germany. The clinical trial was conducted at ten study centres in Spain and Russia between October 2020 and December 2021.

"It is important that the inhibition of FasL targets the overreaction of the host's immune system rather than the virus itself. I am therefore confident that our approach should be effective not only during future outbreaks of SARS-CoV-2 variants of concern, but possibly also for other respiratory RNA viruses that may emerge in the human population in the future. Especially before vaccines against such viruses become available, it would be crucial to have such drugs at our disposal from the very beginning should another pandemic situation arise," said Henning Walczak, Alexander von Humboldt Professor of Biochemistry at the Faculty of Medicine and the CECAD Cluster of Excellence for Aging Research at the University of Cologne and Professor of Tumour Biology at the UCL Cancer Institute.

A total of 438 patients took part in the study, which was led by Dr Maria Pilar Ruiz Seco (Infanta Sofía University Hospital, Madrid), Dr Jose Ramon Paño Pardo (University of Zaragoza/IIS Aragón/CIBERINFEC) and Dr Christian Schörgenhofer (Medical University of Vienna) and supervised by the Deputy Head of Clinical Pharmacology at Medical University of Vienna, Professor Bernd Jilma. The participants were divided into four groups. All patients received standard of care treatment. In addition, different doses of the FasL inhibitor asunercept were administered in three of the four groups (25 milligrams, 100 milligrams and 400 milligrams per week) and compared with the control group.

The 100 and 400 mg doses had the most beneficial tendency for early recovery after an average of eight days, and the 25 mg dose after nine days. Patients in the standard-of-care control group achieved clinical improvement after an average of 13 days. While statistical significance was narrowly missed in each of the individual dose groups, a post-hoc analysis combining the three asunercept dose groups showed a significant therapeutic effect of the FasL inhibitor in terms of an earlier recovery of eight days on average instead of 13 days in the control group. The 100 and 400 milligram doses were also associated with a reduction in mortality of approximately 20 per cent. Overall, this study thus showed that the FasL inhibitor was safe and well tolerated by the patients and achieved very promising results for the efficacy of this drug in patients with severe COVID-19.

These results render the inhibition of FasL among the few concepts identified during the COVID-19 pandemic as potentially therapeutically valuable. “Even though further clinical trials are required to confirm the efficacy, our study shows that the administration of the FasL inhibitor has a positive effect on patients. In future pandemics, the shorter recovery time could reduce the burden on the healthcare system on the one hand and the restrictions for the population on the other,” said Michael Bergmann, surgeon and researcher at the Medical University of Vienna. In addition, increased levels of FasL are also found in samples from the lower respiratory tract of patients who are severely ill following infection with a pandemic version of the influenza A virus, which could extend the field of application in the future.

wissenschaftliche Ansprechpartner:

Professor Dr Henning Walczak
Director of the Institute of Biochemistry 1, Faculty of Medicine
+49 221 478 84076
h.walczak@uni-koeln.de

Originalpublikation:

https://doi.org/10.1016/j.eclinm.2024.102879