



Do effective drugs against COVID-19 (already in use or under clinical development) exist?

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In recent months, much has been said about people who have recovered from the new coronavirus infection. While many of these patients have spontaneously recovered, other ones received pharmacological treatments. So the question is: do drugs able to counteract the proliferation of the virus in infected patients exist? Or drugs active on the symptoms were used and the healing was spontaneous as for the other patients? The Italian Society of Pharmacology (SIF) has decided to intervene in an attempt to clarify, providing hypotheses, strategies, tests and some certainties to understand how the scientific community is moving forward with Covid-19.

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Are there any medicines useful to fight Covid-19 infection?

The answer to this question requires important preliminary remarks. Drugs need to have a specific target, a molecular structure that, once modified by the drug, produces the pharmacological effect and promotes the recovery. Since Covid-19 is a new virus, in order to identify a drug able to counteract it, the identification of the virus structures to be targeted by the drug is necessary. For instance, after the identification in 1983 of the virus responsible for AIDS, the first drug able to control the disease, Zidovudine, was recognized only in 1987, because it took time to understand the mechanism by which the virus reproduced in infected cells. The introduction of Zidovudine changed the clinical history of the HIV infection and created the conditions for the identification of further useful targets and drugs that are effectively and extensively used in patients with AIDS.

What can we learn from the HIV infection experience?

Today we are going through an emergency that is very similar to the one that struck humanity in 1983. Even today we are faced with a virus of which little is known. We know that it is a virus with an RNA genetic code (like that of influenza viruses, HIV, SARS and Ebola), we know that it has a high degree of infection (it passes very easily from a sick individual to a healthy one) but we still need to know how the infection evolves, because it is so different from one individual to another (some individuals do not manifest the disease while others face very serious, often lethal, pneumonia). Therefore, we must quickly answer to these questions in order to find something that will allow us to stem the infection.

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Are vaccines useful to treat patients with Covid-19?

Vaccines certainly represent the best solution for the treatment of viral outbreaks, because they are able to reduce the spread of the infection and reduce the number of infected people. But no vaccines for the prevention of Covid-19 today exist. As for drugs, vaccines also take time to be developed. Even though for some of them the authorization for clinical development on humans has already been requested, vaccines do not represent the correct strategy for patients who have already the disease; indeed, for these patients drugs able to modify the infective process are necessary.

Are there drugs on the horizon for the treatment of Covid-19, yes or no?

Considering that a drug approval procedure required at least 10-12 years, we are trying to use those already existing as we did in the case of HIV. We are trying that on the base of assumptions and hypotheses (not a certainty) led by the knowledge on the virus biology that we are acquiring every day. So, analogously to what happened with the HIV, for which the first drug used (AZT previously cited) was the recycling of a drug used in 1964 as anticancer, we are nowadays facing the attempt of using medicines already marketed for which there is scientific evidence suggesting a possible activity against Covid-19.

During the first phases of the infection, in China, it was authorized the use of interferon-alfa, ritonavir, and lopinavir. This combination therapy showed its efficacy also in the treatment of AIDS. Moreover, just the combination of ritonavir and lopinavir, used against the SARS, seems to be effective in the treatment of Covid-19.

Analogously, the combined therapy with ribavirin (an inhibitor of RNA synthesis) and inhibitors of the reverse transcriptase (the enzyme that allows the virus of transforming its RNA in DNA) like emtricitabine and tenofovir alafenamide fumarate was authorized.

However, the opinions are conflicting in the scientific community. Some researchers believe that the use of medicines demonstrated effective on other viruses, but whose targets have a low relevance in Covid-19 should be avoided. They highlight that coronavirus tends not to use the reverse transcriptase for its viral cycle. Nevertheless, there are clinical trials involving other medicines (baloxavir marboxil, oseltamivir, and umifenovir), which results will be available on May.

More promising are the results expected for remdesivir, a medicine already used with success against the Ebola, as this virus shares some biological aspects with Covid-19. Results on the efficacy of remdesivir will be expected for the end of April.

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An opinion shared by different researchers is to use medicines with a wide spectrum of activity and a good safety profile since little is known on Covid-19. In this way, we have more possibilities of finding some important biological components of Covid-19. For this reason, the medicine favipiravir, normally used to treat Influenza A and B, the antimalarial drug chloroquine, the new anti-HIV medicines like camostat mesylate, baricitinib and ruxolitinib, the antivirals saquinavir, indinavir, lopinavir, and ritonavir, the proteasome inhibitor carfilzomib, or medicines for the treatment of respiratory syncytial viruses or schizophrenia, and immunosuppressant agents were also tested.

Among medicines able to modulate the inflammatory response, there is tocilizumab, a monoclonal antibody authorized for the treatment of some form of arthritis. This medicine has been donated by the marketing authorization holder to China to manage patients infected by Covid-19. This medicine doesn't act directly against the virus but improves the control of the inflammatory process.

In conclusion, we still are in a research phase, but many initiatives and investors are showing a worldwide scientific coalition in finding rapid and adequate solutions to be used in hospitalized patients, especially those in more critical conditions.

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