

# Singapore team finds drug cocktail effective against Delta

Clinical trials next for combination of drugs found suitable for treating Covid-19 patients with mild to moderate disease

Cheryl Tan

Researchers here have found a combination of drugs which can be used to treat Covid-19 patients with mild to moderate disease.

The drug cocktail has also shown promising results in terms of effectiveness against the Beta and Delta variants of the virus.

A team led by Professor Dean Ho, director of the National University of Singapore's Institute for Digital Medicine, had used an artificial intelligence (AI) platform and live virus testing to derive an optimal combination of drugs with the cor-

rect dosages to treat Covid-19.

The team had collaborated with DSO National Laboratories to set up the platform in April last year.

Prof Ho said drug dosing requires a level of precision that cannot be arbitrarily derived – an issue which AI seeks to address.

The platform, named IDentif.AI, had identified antiviral drug remdesivir, together with lopinavir and ritonavir, which are drugs used to treat patients with the human immunodeficiency virus (HIV).

However, despite being effective, not all of the drugs were readily available or could be easily administered at home.

For instance, remdesivir has to

be administered via intravenous (IV) drip in hospitals, making it challenging to use in a community setting, said Prof Ho, who also heads the NUS' department of biomedical engineering.

Therefore, the study focused on locally available or obtainable drugs which can be taken orally, he added.

One of the resulting combinations was a dynamic duo consisting of Merck and Ridgeback Biotherapeutic's novel antiviral drug, molnupiravir, combined with baricitinib, an anti-inflammatory drug.

Prof Ho said the combination could strongly inhibit the Sars-CoV-2 virus in laboratory tests, making it suitable for further clinical evaluation.

He added: "This is especially timely as Singapore moves towards an endemic Covid-19 situation, so we are looking for combination therapies that can eventually be given to patients with mild illness who are recovering at home, or in community care facilities."

Some combinations will also be suitable for hospitalised patients, he added, noting that this will help shift treatments out of hospitals to general practitioners and polyclinics.

The drugs were chosen in consultation with infectious diseases experts and oncologists from the National Centre for Infectious Diseases, NUS Medicine and the National University Hospital (NUH).

A total of 12 drugs – which included a range of antivirals and cancer drugs – were tested and ranked according to their efficacy in inhibiting the Sars-CoV-2 virus.

Within three weeks, the team had identified the molnupiravir-

baricitinib combination for possible treatment.

Dr Louis Chai, a senior consultant at the division of infectious diseases at NUH, cautioned, however, that there is no data yet from clinical trials that shows the drug combination is effective in all phases of Covid-19 disease. He noted that some drugs could reduce the Sars-CoV-2 viral load in patients, but they may not slow down disease progression or prevent death.

Dr Conrad Chan, laboratory director (applied molecular technology laboratory) at DSO's Defence Medical and Environmental Research Institute, said molnupiravir on its own was effective against the Sars-CoV-2 virus as well as its Beta and Delta variants.

It is thus a strong "backbone" drug candidate from which multiple combinations can be derived, he added. "This is because the drug interferes with a part of the virus that is conserved across different variants – specifically, the enzyme that it uses to copy its genetic material for replication."

Prof Ho said his team is now looking to conduct clinical trials for molnupiravir and its drug combinations on Covid-19 patients. Vaccinated individuals with mild to moderate disease could be considered as part of the study cohort.

Having established a database of drug combinations for Covid-19, the team will continue working with clinicians to look out for novel drugs that can be added to its arsenal.

This can help expand the range of drugs available to treat Covid-19 patients in the future, said Prof Ho.

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THINKING AHEAD

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**PROFESSOR DEAN HO** (above), director of the National University of Singapore's Institute for Digital Medicine.

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