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Dr Anand Jeyasekharan, a co-author of the study, with topotecan, which was found to reduce the severity and death rates of infection by Sars-CoV-2 in lab animals. PHOTO: NATIONAL UNIVERSITY CANCER INSTITUTE, SINGAPORE

Anti-cancer drug can treat Covid-19: S'pore-US study

A drug used in cancer treatment can treat patients with moderate to severe forms of Covid-19, according to a study by Singapore and United States researchers.

They found that topotecan, which is used in chemotherapy, reduced the severity and death rates of infection by Sars-CoV-2 – the virus causing Covid-19 – by suppressing inflammation in the lungs of laboratory animals.

Patients with moderate to severe forms of Covid-19 suffer from inflammation, a result of an overactive, abnormal immune response. In some patients, an exaggerated immune response – typically occurring in the lungs – can flood the in-

fectured area with white blood cells, resulting in severe inflammation, tissue damage and often death.

Topotecan works by curbing this immune response, reducing the risk of injury to the body. This was achieved at doses lower than that typically used in cancer treatment, hence significantly reducing the likelihood of any side effects from the drug.

The immune response was also not completely eliminated, with the lab animals still able to produce antibodies to overcome the virus.

The study, led by Associate Professor Ivan Marazzi of the microbiology department at the Icahn School of Medicine at Mount Sinai

in the US, involved researchers from the National University Cancer Institute, Singapore (NCIS). The findings were published online in the scientific journal *Cell* on March 30.

A co-author of the study, Dr Anand Jeyasekharan, who is a consultant and assistant director of research in medical oncology at the department of haematology-oncology at NCIS, said: “With the drug used in cancer treatment for over 25 years, it is globally available and inexpensive, with a well understood safety profile in humans. This research is therefore timely given the lack of universal access to vaccines.”

The completion of successful lab studies has led to a phase one clinical trial in India, given the high numbers of moderate to severe Covid-19 cases there.

The team has already secured a research grant for the clinical trial. The research is supported by the Singapore Ministry of Health’s National Medical Research Council and the National Research Foundation.

Around 20 adult patients with moderate forms of Covid-19 and a history of cancer will be recruited. They will be given topotecan in addition to the steroid dexamethasone and the antiviral drug remdesivir – both now used to treat Covid-19.

Cancer patients are recruited because they have a higher risk of severe disease and are also familiar with the concept of chemotherapy treatment, Dr Jeyasekharan said.

“After an appropriate dose has been established in phase one, the aim will be to bring this forward to all moderate Covid-19 cases, not just for cancer patients.”

Patients will be given a single dose in phase one.

The first six patients will be given 0.25mg of the drug. If no adverse effects are observed, a slightly higher dose of 0.5mg will

then be administered to the next six patients. If no adverse effects are observed, the dose will then be increased to 0.75mg for the next six patients. An additional dose level may be added if required, potentially expanding the trial to 24 patients.

These doses are significantly lower than those given to cancer patients, which are about 2mg a day for three to five days.

“The aim of the phase one clinical trial is to establish the lowest dose of topotecan that can safely reduce Covid-19 inflammatory markers in patients. We want to start from the lowest possible dose and then slowly build up from there,” said Dr Jeyasekharan.

Patients will be monitored on three fronts: the use of blood tests to check for inflammation markers; checking of the actual levels of the drug in the blood to ensure that it remains within safe levels; and finally checking the clinical status of the patients – such as if they experience more or less difficulty breathing.

The trial is expected to last between three and six months, depending on how quickly suitable patients are recruited.

If the phase one clinical trial is successful, phase two will start, with a larger pool of patients recruited from different countries. Additional parameters will also be tracked, such as the time taken for the patients to be discharged from the intensive care unit and the patients’ survival rate.

Dr Jeyasekharan added: “Repurposing of existing drugs represents a valuable global strategy for treating Covid-19... Topotecan is an attractive candidate given that it is safe and inexpensive with generic formulations existing throughout the world.”

One vial of topotecan, which contains 4mg of the drug, costs around \$60 in Singapore.

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