

Novel 'spray' gives hope to patients with advanced gastric cancer

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Using a novel "spray" to administer chemotherapy drugs beyond the protective membrane surrounding the abdomen cavity, combined with immunotherapy through the bloodstream, could stop gastric cancer cells from spreading, a new study has shown.

With this ground-breaking treatment, gastric cancer may no longer be a death sentence, with the therapy offering hope of a better chance of survival for patients, especially those whose cancer has spread to the protective membrane or peritoneum.

The trial involving 18 patients took place in Singapore and Belgium from June 2020 to November 2022.

It was carried out concurrently with separate new research that used the latest in genomics to discover how the environment around the primary cancer plays an important part in its spread to the membrane.

The two studies, when taken together, mark a significant leap forward in the fight against gastric cancer peritoneal metastases in

terms of tailoring personalised treatments for each patient's tumour. Metastasis refers to the spread of the cancer to other parts of the body from the primary tumour.

Gastric cancer remains formidable, ranking fifth among the most common cancers and the third-leading cause of cancer-related deaths worldwide, with over a million new cases and close to 770,000 deaths a year.

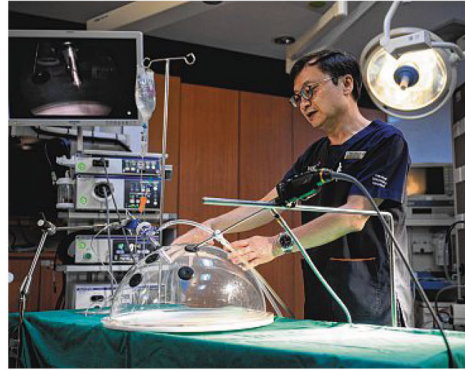
In Singapore, gastric cancer is among the top 10 causes of cancer-related deaths and claims about 300 lives every year.

Patients whose gastric cancer has spread to the peritoneum often face a grim prognosis and rapid disease progression.

The median survival rates range from just three to six months, and five-year survival rates are usually below 5 per cent.

Therapeutic options for them are currently limited. The new research could help such patients whose cancer has reached an advanced stage.

In a major breakthrough, clinicians and scientists from Singapore have discovered the intricate mechanisms behind the spread of gastric cancer to the peritoneum by looking beyond the primary



Professor Jimmy So from the National University Hospital with the equipment used to spray chemotherapy drugs into a cancer patient's abdomen cavity through a keyhole procedure.
ST PHOTO: MARK CHEONG

cancer into the role of its surrounding microenvironment.

Spearheaded by a team from the National University Hospital (NUH), the National University Cancer Institute, Singapore (NCIS), the NUS Yong Loo Lin School of Medicine, the National Cancer Centre Singapore (NCCS) and Duke-NUS Medical School, the study used cutting-edge technology in genomics to analyse a collection of patient samples.

Dr Raghav Sundar, who led the study, which was published in peer-reviewed journal *Gastroenterology* in March, said: "To understand every different component of the tumour in the past, what many people used to do is just take the entire tumour, grind it up, and then put it through a sequencing machine."

Using the MRT system as an analogy, Dr Sundar, a senior consultant in the department of haematology-oncology at NCIS, said that to get from Choa Chu Kang to

Punggol, "you actually need to understand all the different transition points".

"(Similarly), we took tumours from the stomach, we took those that spread through the peritoneum, (and) we try to understand why certain tumours from the stomach spread to the peritoneum..."

"We also studied what happened to the tumours themselves as we apply chemotherapy or something into the peritoneum, and whether they change over time."

The team looked at some 500 samples from about 300 patients using various techniques.

The research pinpointed specific genetic alterations and characteristics within the tumour microenvironment (TME) that contributed to the spread of gastric cancer to the peritoneum.

It also showed the crucial role of the TME in facilitating the establishment and growth of the spread, and helped to identify the bio-

markers and therapeutic targets.

Professor Patrick Tan, senior vice-dean for research at Duke-NUS and a senior author of the study, said that before this study, there was limited understanding of how the TME contributed to the spread of gastric cancer to the peritoneum.

"Most cancer patients do not die from their primary tumour but from its metastases to other organs," he said.

"Our results highlight the complexity of gastric cancer metastases, revealing that gastric tumours can use distinct genetic and molecular mechanisms to spread to different organs."

The team also conducted the phase one clinical trial of the 18 patients, demonstrating the safety and potential of a novel treatment approach for the disease.

A nebuliser – a machine that turns liquid medicine into a mist – is used to spray chemotherapy drugs into a cancer patient's abdomen cavity through a keyhole procedure.

Thirteen of the patients were from NCIS and NCCS in Singapore, and the remaining five from Ghent University Hospital in Belgium.

Professor Jimmy So, head of the division of general surgery (upper

gastrointestinal surgery) at NUH, who led the trial, said the treatment was safely administered for 16 patients. The remaining two had severe complications.

Associate Professor Johnny Ong from the department of sarcoma, peritoneal and rare tumours at the division of surgery and surgical oncology in NCCS, and co-investigator of the trial, said: "Combining bench and bedside research, we have shed new light on the biology of gastric cancer, which will pave the way for the much-needed therapeutics in patients with peritoneal metastases."

The results will be published in *ESMO Open*, an online-only, peer-reviewed oncology journal of the European Society for Medical Oncology, later in September.

The two studies were supported by the Singapore Gastric Cancer Consortium, a national translational research group working in gastric cancer research. It receives funding from the National Research Foundation Singapore.

The teams are now working towards raising funds in both Singapore and overseas to recruit more patients worldwide for phase two of clinical trials.

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