

MEDIA RELEASE

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BREAKTHROUGH RESEARCH EXTENDS HOPE FOR GASTRIC CANCER PATIENTS WITH PERITONEAL METASTASIS

New study and promising results from the first clinical trial in patients provide novel insights and new hope for one of Singapore's deadliest cancers

SINGAPORE — Gastric cancer remains a formidable adversary, ranking as the fifth most common cancer and the third-leading cause of cancer-related deaths worldwide, with over 1,000,000 new cases and close to 770,000 deaths each year. In Singapore, gastric cancer ranks among the top 10 causes of cancer-related deaths and claims about 300 lives¹ each year.

The peritoneum, the lining of the abdominal cavity, is frequently involved in advanced-stage cancers, including gastric, colon, pancreatic, and ovarian cancers. For gastric cancer, the peritoneum is, in fact, the most common site of metastasis, both before and after treatments. Patients with gastric cancer peritoneal metastases (GCPM) often face an exceptionally grim prognosis, with severe symptoms and rapid disease progression. Median survival rates range from just three to six months, and five-year survival rates are usually below five per cent. Therapeutic options are currently limited.

In a major breakthrough, clinicians and scientists from Singapore have shed light on the intricate mechanisms behind the spread of gastric cancer to the peritoneum. This landmark research, published in the prestigious journal *Gastroenterology*, offers renewed hope for patients battling this aggressive form of cancer. The scientists also conducted a clinical trial, published in another journal *ESMO Open*, demonstrating the safety and potential of a novel treatment approach for the disease.

The research study, spearheaded by a team of clinicians and scientists from the National University Hospital (NUH), the National University Cancer Institute, Singapore (NCIS), the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), the National Cancer Centre Singapore (NCCS) and Duke-NUS Medical School, utilised cutting-edge genomic and transcriptomic technologies to analyse a vast collection of patient samples.

This in-depth analysis has provided an unparalleled understanding of the molecular underpinnings of gastric cancer peritoneal spread.

Dr Raghav Sundar, Senior Consultant in the Department of Haematology-Oncology at NCIS, who led the study published in *Gastroenterology*, emphasised: "Our research

¹ [Singapore Medical Association - For Doctors, For Patients \(sma.org.sg\)](https://www.sma.org.sg)

has pulled back the curtain on the complex biological processes that drive the spread of gastric cancer to the peritoneum. These findings provide a crucial roadmap for developing more effective and targeted treatments for this devastating disease.” Dr Sundar is also Associate Professor of Medicine at NUS Medicine.

Understanding the difficult terrain of peritoneal spread

The new findings not only shed light on why gastric cancer cells tend to metastasise to the peritoneum, but also pave the way for the development of innovative therapies that target the cells and molecules surrounding the tumour – also known as the tumour microenvironment (TME), potentially disrupting the cancer’s ability to thrive in the peritoneum.

Key findings from the research include: -

- **Unravelling the peritoneal connection:** The research pinpointed specific genetic alterations and characteristics within the TME that contribute to the spread, or metastasis, of gastric cancer to the peritoneum. The TME is the complex network of cells and molecules surrounding a tumour. This discovery explains why gastric cancer cells have a tendency to spread to the peritoneum.
- **The tumour microenvironment's pivotal role:** The study underscores the crucial role of the TME in facilitating the establishment and growth of peritoneal metastases. This newfound understanding paves the way for the development of innovative therapies that target the TME, potentially disrupting the cancer's ability to thrive in the peritoneum.
- **Identifying biomarkers and therapeutic targets:** The researchers successfully identified potential biomarkers that could predict the risk of peritoneal metastasis, enabling earlier detection and intervention. Furthermore, they uncovered novel therapeutic targets that could be leveraged to develop more effective treatments specifically for GCPM.

“Prior to our study, there was limited understanding of the tumour microenvironment that contributes to the spread of gastric cancer to the peritoneum. Yet, most cancer patients do not die from their primary tumour but from its metastases to other organs. 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,” said Professor Patrick Tan, Senior Vice-Dean for Research at Duke-NUS and one of the senior authors of the study.

Promising clinical trial

In a parallel development, the same research team conducted a clinical trial that showcased the safety and potential efficacy of a groundbreaking treatment approach for GCPM. The Phase I PIANO trial, published in *ESMO Open*, combined a minimally invasive surgical technique called Pressurised Intra-Peritoneal Aerosol Chemotherapy (PIPAC) with systemic immunotherapy. PIPAC delivers chemotherapy directly to the peritoneal cavity as a fine mist, while immunotherapy helps the body's immune system recognise and attack cancer cells.

This innovative approach aims to bolster the immune system's capacity to combat cancer within the peritoneal cavity. The trial results were promising, demonstrating that the combination therapy was well-tolerated by patients and resulted in a reduction in tumour burden for some. Importantly, molecular profiling of tumour samples revealed an increase in T-cell infiltration, a sign of a positive immune response against the cancer.

The trial was conducted from June 2020 to November 2022 with 18 patients recruited across three cancer centres—two centres in Singapore and one in Belgium.

“The PIANO trial results are incredibly encouraging, demonstrating the potential of combining targeted therapy like PIPAC with immunotherapy to improve outcomes for patients,” said Professor Jimmy So, Senior Consultant and Head of the Division of General Surgery (Upper Gastrointestinal Surgery) at NUH, who led the PIANO trial. “This approach could revolutionise the treatment landscape for this challenging condition.” Professor So is also Head & Senior Consultant, Division of Surgical Oncology, at NCIS, and Professor of Surgery at NUS Medicine.

Paving the way forward

The combined research endeavours mark a significant leap forward in the fight against GCPM. The identification of predictive biomarkers and therapeutic targets could lead to the development of personalised treatment strategies, tailoring treatments to the unique molecular profile of each patient's tumour. The success of the PIANO trial heralds a new era of combination therapies that leverage the power of the immune system to combat peritoneal metastases.

“Our research brought together leaders from multiple institutions who treat and diagnose gastric cancer and clinician-scientists who study the disease,” said Associate Professor Johnny Ong, Senior Consultant in the Department of Sarcoma, Peritoneal and Rare Tumours, Division of Surgery and Surgical Oncology, in Singapore General Hospital and NCCS who is co-author of the *Gastroenterology* study and co-investigator of the PIANO trial. “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 studies are supported by the Singapore Gastric Cancer Consortium, a national translational research group comprising clinicians and scientists working in gastric cancer research from academic medical centres, universities, hospitals and research institutes across Singapore. It receives funding from the National Research Foundation Singapore under its Open Fund-Large Collaborative Grant, administered by the Singapore Ministry of Health's National Medical Research Council.

References:

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Chinese Glossary

National University Health System (NUHS)	国立大学医学组织（国大医学组织）
National University Cancer Institute, Singapore (NCIS)	新加坡国立大学癌症中心
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Annex

Profile: Against the Odds of Gastric Cancer

In November last year, a straightforward surgery at the National University Hospital (NUH) to remove a ruptured appendix revealed something far more sinister for Mdm Hau Chan Kim – a diagnosis of Stage 4 gastric cancer with metastasis to the peritoneum. The discovery came as a shock, as she had only experienced occasional stomach pains and bloating that she had dismissed as indigestion.

Mdm Hau, a homemaker in her 60s, had successfully battled breast cancer some 20 years ago, but now faced another daunting challenge. Gastric cancer with peritoneal metastases is notoriously aggressive, with a poor prognosis for most patients. An overwhelming majority of those who do not receive timely treatment pass on within three to six months.

Determined to fight, Mdm Hau immediately began a rigorous treatment regimen that included both systemic and oral chemotherapy. Under the expert care of Professor Jimmy So, Head & Senior Consultant, Division of Surgical Oncology, NCIS, Mdm Hau experienced remarkable progress.

Recent biopsies have shown no cancer cells in her peritoneum and a reduction in the primary tumour, giving her a renewed sense of hope.

Advances in treatment over the years have resulted in more targeted therapies with fewer side effects – a significant improvement from the harsh chemotherapy Mdm Hau endured during her breast cancer treatment two decades ago. “When I received chemotherapy for breast cancer years ago, it was terrible. I lost all my hair and had many painful mouth ulcers,” she recalled. “Now, I am only undergoing intraperitoneal chemotherapy, which is a lot less uncomfortable.”

Despite the challenges, Mdm Hau has maintained an admirable quality of life. Her positive response to treatment has enabled her to live life on her own terms. “I can still prepare homecooked meals for my family, and meet my friends occasionally. For me, it is very important that I remain independent and stay active,” she shared.

Mdm Hau is now a strong advocate for early treatment and believes in the power of research to improve survival chances for others. Her tissue samples collected during biopsy contributed to the significant research study published in *Gastroenterology*, conducted by Professor So and team, which analysed the tumour microenvironment’s role in gastric cancer spread.

For Mdm Hau, it is heartening news to learn of research that can improve the chances of survival for other patients facing the same battle. “Research is very important, so that doctors know what is going on in the body and can help others like me,” she said.

About Duke-NUS Medical School

Duke-NUS is Singapore’s flagship graduate entry medical school, established in 2005 with a strategic, government-led partnership between two world-class institutions: Duke University School of Medicine and the National University of Singapore (NUS).

Through an innovative curriculum, students at Duke-NUS are nurtured to become multi-faceted ‘Clinicians Plus’ poised to steer the healthcare and biomedical ecosystem in Singapore and beyond. A leader in ground-breaking research and translational innovation, Duke-NUS has gained international renown through its five Signature Research Programmes and ten Centres. The enduring impact of its discoveries is amplified by its successful Academic Medicine partnership with Singapore Health Services (SingHealth), Singapore’s largest healthcare group. This strategic alliance has spawned 15 Academic Clinical Programmes, which harness multi-disciplinary research and education to transform medicine and improve lives.

For more information, please visit www.duke-nus.edu.sg

About the National Cancer Centre Singapore

The National Cancer Centre Singapore (NCCS) is a leading national and regional tertiary cancer centre with specialists who are experts in treating cancer. In addition to offering holistic and multidisciplinary oncology care, our clinicians and scientists collaborate with local and international partners to conduct robust, cutting-edge clinical and translational research. To achieve its vision of being a global leading cancer centre, NCCS offers world-class care and shares its depth of experience and expertise by training local and overseas medical professionals.

To meet growing healthcare needs, the new NCCS building opened in 2023 with increased capacity and expanded facilities dedicated to cancer care, rehabilitation, research and education. To give patients the best treatment outcomes, advanced and innovative treatment such as proton therapy is offered at the new Goh Cheng Liang Proton Therapy Centre at NCCS.

In 2024, NCCS celebrates its silver anniversary, celebrating 25 years of advancing cancer care from breakthroughs to healing.

For more information, please visit www.nccs.com.sg

About the National University Cancer Institute, Singapore

The National University Cancer Institute, Singapore (NCIS) is an academic, national specialist centre for cancer under the National University Health System (NUHS), and is the only public cancer centre in Singapore that treats both paediatric and adult cancers in one facility.

As one of two national cancer centres in Singapore, NCIS (pronounced as “n-sis”) offers a broad spectrum of cancer care and management from screening, diagnosis and treatment to rehabilitation and survivorship, as well as palliative and long-term care. NCIS’ strength lies in the multi-disciplinary approach taken by our clinician scientists and clinician-investigators to develop a comprehensive and personalised plan for each cancer patient

NCIS provides the full suite of specialised oncology and haematology services at the NUH Medical Centre at Kent Ridge, Singapore, including those by the NCIS Chemotherapy Centre, NCIS Radiotherapy Centre and NCIS Cellular Therapy Centre.

NCIS also offers cancer services at other hospitals in Singapore:

- NCIS Cancer & Blood Clinic @ Ng Teng Fong General Hospital
- NCIS Radiotherapy Centre @ Tan Tock Seng Hospital
- NCIS Radiotherapy Clinic @ Khoo Teck Puat Hospital

To bring cancer care even closer to our patients, our NCIS on the Go programme delivers a range of cancer services at clinics within the community for their convenience.

For more information, please visit www.ncis.com.sg.

About the National University Hospital (NUH)

The National University Hospital (NUH) is Singapore's leading university hospital. While the hospital at Kent Ridge first received its patients on 24 June 1985, our legacy started from 1905, the date of the founding of what is today the NUS Yong Loo Lin School of Medicine. NUH is the principal teaching hospital of the medical school.

Our unique identity as a university hospital is a key attraction for healthcare professionals who aspire to do more than practise tertiary medical care. We offer an environment where research and teaching are an integral part of medicine, and continue to shape medicine and transform care for the community we care for.

We are an academic medical centre with over 1,200 beds, serving more than one million patients a year with over 50 medical, surgical and dental specialties. NUH is the only public and not-for-profit hospital in Singapore to provide trusted care for adults, women and children under one roof, including the only paediatric kidney and liver transplant programme in the country.

The NUH is a key member of the National University Health System (NUHS), one of three public healthcare clusters in Singapore.

For more information, please visit: www.nuh.com.sg

About the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine)

The NUS Yong Loo Lin School of Medicine is Singapore's first and largest medical school. Our enduring mission centres on nurturing highly competent, values-driven and inspired healthcare professionals to transform the practice of medicine and improve health around the world.

Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience

that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through our doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is one of the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2024 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2023).

For more information about NUS Medicine, please visit <https://medicine.nus.edu.sg/>