



PRESS RELEASE

NUS Yong Loo Lin School of Medicine students and researchers develop novel algorithm to assess immunotherapy benefit in stomach cancer patients

Findings indicate that a particular group of patients will not benefit from the addition of immunotherapy to their chemotherapy regimen

Singapore, 25 November 2021 — Using a novel algorithm that they devised, a team of medical students and researchers at the National University of Singapore's Yong Loo Lin School of Medicine (NUS Medicine) has identified a group of stomach cancer patients who may not benefit from undergoing joint immunotherapy-chemotherapy treatment. The NUS Medicine team's finding means such patients can potentially be spared unnecessary treatment side effects as well as high treatment costs, even though recent clinical studies indicate that patients with stomach cancer treated with a combination of immunotherapy and chemotherapy have a higher survival rate compared to those who were treated with chemotherapy alone.

In the study published in the *Journal of Clinical Oncology*, fifth-year medical students Joseph Zhao, Teo Chong Boon, Benjamin Tan and third-year medical student Dominic Yap, led by Assistant Professor Raghav Sundar, Consultant from the Department of Haematology-Oncology at the National University Cancer Institute, Singapore, and the Department of Medicine at NUS Medicine, developed KMSubtraction to retrieve unreported subgroup survival data of patients who derived no benefit from adding immunotherapy to their cancer treatment options. Immunotherapy is a new class of drugs that have shown significant benefit in some cancer types. It redirects the body's own immune system to target cancer cells in the body, harnessing the body's innate ability to distinguish between cancer and healthy cells.

The impetus for this algorithm came about when a recently-conducted Phase III randomised controlled trial –CheckMate-649– demonstrated that the addition of immunotherapy to conventional chemotherapy provides patients with advanced gastro-esophageal cancer a significant chance of survival. A protein biomarker, known as PD-L1, has been hypothesised to be an indicator that can identify patients who may respond well to immunotherapy, along with conventional chemotherapy. This protein biomarker is commonly found on the tumour cells and the immune cells around the tumour. Patients with higher indicators of PD-L1 have been observed to derive more benefits from immunotherapy.

The authors of the CheckMate-649 clinical trial reported that patients with the biomarker score of more than 1 or more than 5 showed a high survival rate when treated with a combination of immunotherapy and chemotherapy. This manner of reporting meant that clinicians were unable to tell if patients with the biomarker score between 1 to 4 would truly benefit from immunotherapy-chemotherapy treatment. Based on the trial results from CheckMate-649, the Food and Drug Administration in the United States had given approval to use the

immunotherapy drug nivolumab for all gastric cancer patients, while Europe approval has only been extended to a specific sub-group of patients with PD-L1 score of 5 or more).

KMSubtraction effectively streamlines the process of having to reach out to senior authors of major studies to request for new analysis to be performed. To demonstrate the robustness of the new algorithm and explore its limits of error, the algorithm was validated with over 500,000 simulations. The implementation of KMSubtraction in these trials resulted in new findings confirming that more than 20% of the patient population will not benefit from the addition of immunotherapy into chemotherapy regimen. Instead, they could possibly be enrolled into clinical trials with newer agents, and spared the side effects and high costs of immunotherapy drugs.

The two first authors of the NUS paper, Mr Joseph Zhao and Mr Dominic Yap, said they were grateful for the opportunity to work on this practice-changing study and the mentorship the team has received. Said Mr Yap, "The topic of immunotherapy and its implementation is complex and complicated by different interests." Added Mr Zhao, "As medical students, we learn to treat patients with various diseases, with the focus on helping them at the individual patient level. Conversely, research utilising such biostatistical coding techniques allow us to contribute to patient care on a larger scale."

The team's supervisor, Assistant Professor Raghav Sundar affirms the efforts and enterprising spirit of the medical students in coming up with this new algorithm and says, "The students have demonstrated phenomenal drive, ingenuity, innovativeness and the willingness to learn throughout this project. Eventually, the team hopes that the derived data from KMSubtraction will be fit for use in other fields as well to inform clinical decision-making to benefit patients and improve the overall cost-effectiveness of care."

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About the National University of Singapore (NUS)

The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research and entrepreneurship, with a focus on Asian perspectives and expertise. We have 17 faculties across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established our NUS Overseas Colleges programme in more than 15 cities around the world.

Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, 30 university-level research institutes, research centres of excellence and corporate labs focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

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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 Asia's leading medical school and ranks among the best in the world (Times Higher Education World University Rankings 2020 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2020).

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