

MEDIA RELEASE

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NOVEL CAR-T CELL THERAPY DEVELOPED IN SINGAPORE BEGINS CLINICAL TRIAL IN NCIS

Treatment that uses blood from healthy donors offers hope to advanced cancer patients who have failed other types of treatments

Singapore — Cell-based immunotherapy, a growing field of medicine that harnesses immune cells to fight cancer, has been given a boost with a new type of chimeric antigen receptor (CAR) T-cell therapy that will be trialled at the National University Cancer Institute, Singapore (NCIS).

CAR-T cell therapy is currently an individualised treatment that typically involves taking a patient's blood cells and modifying these in the laboratory by grafting an artificial protein, known as a chimeric antigen receptor, on the surface of T cells, a type of white blood cells. The modified T cells are then reinfused to the patient to target and destroy cancer cells.

Unlike chemotherapy which targets all actively dividing cells including healthy ones, CAR-T cells specifically recognise targets present on cancer cells (antigens) to kill them, thus sparing healthy cells.

The new therapy taps on blood drawn from healthy donors, such that it potentially improves the quality of CAR-T cells manufactured, lowers production cost and increases patients' access to therapy.

The therapy is developed by home-grown biotechnology company CytoMed Therapeutics, which was founded in 2018 as a spin-off from the Agency for Science, Technology and Research (A*STAR). The phase 1 clinical trial was approved by the Health Sciences Authority in January.

In the new therapy, CytoMed uses a subtype of immune cells – gamma-delta ($\gamma\delta$) T cells – that can be modified from healthy donors and reinfused into unrelated patients without the need for matching.

Dr Tan Wee Kiat, Chief Operating Officer at CytoMed, said: "Gamma-delta T cells make up a small proportion of T cells in the human body, typically less than 5 per cent, hence the challenge is in expanding harvested gamma-delta T cells into sufficient numbers for cancer therapy, a challenge that CytoMed has met and successfully implemented through proprietary technology developed in Singapore.

"Obtaining immune cells from healthy donors means the starting material would be of high quality and this can potentially improve the quality of modified CAR-T cells. Furthermore, a non-personalised approach can drive down the cost of treatment," he added.

Current established CAR-T cell therapies use alpha-beta ($\alpha\beta$) T cells, a type of immune cells which are largely non-transferable between individual human beings due to the high risk of graft-versus-host disease.

From April, the trial at NCIS will begin in two phases, starting with the recruitment of healthy blood donors at the National University Hospital who are put through stringent tests and screened for infectious diseases. The process will be similar to a regular blood donation.

After blood collection, immune cells will be isolated from the donated blood and further qualified before being used for CAR-T cell manufacturing.

The second phase of the trial will recruit suitable patients who have any of six types of advanced cancers that are resistant to standard cancer therapy regimens. The types of cancers are colorectal, lung, liver, ovarian, lymphoma and multiple myeloma.

These patients, who are at least 21 years old, will receive a course of low-dose chemotherapy prior to weekly infusions of allogeneic CAR-T cells for four consecutive weeks. They will be closely monitored by the clinical trial team of more than 20 doctors and staff during the treatment, as well as during follow-up visits.

Potential side effects of allogeneic CAR-T cell therapy – similar to autologous CAR-T cell therapy – include cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome.

Cytokine release syndrome is a cluster of symptoms that can include fever, nausea, chills, irregular heartbeat, headache, rash and low blood pressure. Immune effector cell-associated neurotoxicity syndrome is a potentially life-threatening neurotoxicity that causes symptoms ranging from confusion, headache and attention deficits, to brain swelling and seizures.

The trial, a collaboration between CytoMed and NCIS, aims to investigate the safety and tolerability of the new CAR-T cell therapy among patients, as well as determine its optimal dose.

The principal investigator of the trial, Dr Raghav Sundar, Consultant, Department of Haematology-Oncology, NCIS, said: “Cellular therapies form a new frontier of immunotherapy approaches to target cancer and its surrounding microenvironment. While inroads have been made with CAR-T cell therapies in blood cancers, those for solid tumours have had fewer successes. Hopefully, this trial will provide us with the information we need to bring this promising treatment strategy to a broader group of patients with cancer.”

For close to a decade, NCIS has been offering cell therapy to adult and paediatric patients through the NCIS cell therapy programme, which translates science from the bench to bedside.

Dr Esther Chan, Senior Consultant, Department of Haematology-Oncology, NCIS, said: “CAR-T cell therapy can be a life-saving treatment for many patients who are given a slim to no chance of survival. We are concurrently doing several trials for autologous CAR-T cell therapies, yet this is the first locally designed trial that uses an allogeneic method to modify cells to fight cancer.”

Dr Tan Lip Kun, Senior Consultant, Department of Haematology-Oncology, NCIS, said: “At NCIS, we have a well-established stem cell transplant and cellular therapy programme. We look forward to participating in the clinical trial using the first locally developed CAR-T cell

therapy that uses cells from healthy donors to treat not just blood cancers, but also solid cancers.”

Professor Tan Sze Wee, Assistant Chief Executive, Innovation and Enterprise Group, A*STAR, said: “We are proud that CytoMed has successfully developed technology licensed from A*STAR that is now entering clinical trials. We will continue to provide strong support to our spin-offs in their research and development efforts to develop innovative healthcare solutions.”

Chinese Glossary

National University Cancer Institute, Singapore (NCIS)	新加坡国立大学癌症中心 (国大癌症中心)
Chimeric antigen receptor (CAR)-T cell therapy	嵌合抗原受体 T 细胞疗法
Dr Raghav Sundar Consultant, Department of Haematology-Oncology, NCIS	Raghav Sundar 顾问医生, 肿瘤血液科, 新加坡国立大学癌症中心
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About National University Cancer Institute, Singapore (NCIS)

The National University Cancer Institute, Singapore (NCIS) is a national specialist centre 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. NCIS (*n-sis*) offers a broad spectrum of cancer care and management from screening, diagnosis and treatment, to rehabilitation, palliative and long-term care. NCIS's strength lies in the multidisciplinary approach taken by our clinician-scientists and clinician-investigators to develop a comprehensive and personalised plan for each cancer patient.

NCIS cancer services span across several acute hospitals: NCIS @ National University Hospital, NCIS @ Ng Teng Fong General Hospital, NCIS @ Alexandra Hospital, and the NCIS Radiation Therapy Centre @ Tan Tock Seng Hospital. We also deliver a range of cancer services for our patients' convenience at satellite clinics in the community, as well as in the comfort of their homes. For more information, please visit www.ncis.com.sg.

About CytoMed Therapeutics

Incorporated in 2018, CytoMed Therapeutics is a biotech company spun off from the Agency for Science, Technology and Research (A*STAR), Singapore's lead public sector R&D agency. CytoMed focuses on translating its proprietary technologies into cell-based immunotherapies for cancers. The development of its novel technologies has been inspired by the clinical success of chimeric antigen receptor-modified T (CAR-T) cells in treating haematological malignancies as well as the clinical limitations and commercial challenges in extrapolating the CAR-T principle into treatment of solid tumours.

CytoMed has established two novel patient blood cell-independent platform technologies to manufacture "off-the-shelf" cell-based cancer immunotherapies, namely CAR- $\gamma\delta$ T-cell technology (CTM-N2D therapy) and iPSC-derived $\gamma\delta$ NKT cell technology (gdNKT therapy). Such therapies exploit the multiple antigen recognition systems of natural killer (NK) cells and $\gamma\delta$ T cells and may be used to recognise and treat a broad range of cancers. To develop its technologies into therapies, CytoMed has established a GMP facility to manufacture cell therapy products to support clinical trials. The facility has been built to the international PIC/S GMP Standards and it has a well-trained team to conduct all essential GMP activities including manufacture, QC, QA and documentation. The team is directly overseeing the manufacture of cell therapy products by themselves in their own GMP facility instead of engaging and relying on a contract manufacturing organisation. Now, they have developed their lead CAR- $\gamma\delta$ T cell technology into a clinical trial-ready product (CTM-N2D therapy) for a phase I trial.

Infographic

