Press Release

For Immediate Release

26 June 2015

NEW DRUG SHOWS PROMISE FOR HARD-TO-TREAT CANCERS

More than half of the patients with advanced or metastatic cancers in a Phase I clinical trial for selinexor, a new first-in-class cancer drug candidate, see their tumours either shrink or grow more slowly.

A new drug candidate currently being tested has shown promising results in treating cancers in a Phase I clinical trial conducted at the Developmental Therapeutics Unit of the National University Cancer Institute, Singapore (NCIS).

Out of the 28 patients who participated in the clinical trial of selinexor, 19 patients have been evaluated for response so far. Two patients with previously treatment refractory lymphoma have shown partial response – more than 30% shrinkage in their tumours, while 12 patients with other types of tumours have displayed stable disease, defined as tumour shrinkage of less than 30% or tumour growth of less than 20%.

Selinexor is a first-in-class (i.e. using a new and unique mechanism in treating a medical condition[1]) cancer drug being developed by Karyopharm Therapeutics. It works by preventing proteins that can stop cancer development and growth (i.e. tumour suppressor proteins) from being exported out of the cancer cell nucleus. Tumour suppressor proteins are usually only effective when they are in the cell nucleus and tumours have been shown to push these proteins out from the cell nucleus into the cell cytoplasm using a transport protein known as Exportin 1 (XPO1), rendering them ineffective in stopping abnormal cell growth. Selinexor blocks the XPO1 transport protein and forces the tumour suppressor proteins to stay in the cell nucleus. Selinexor is taken orally.

While the primary objective of this Phase I study is to assess the tolerability of selinexor in Asian patients and determine the safe dosage level, the results shown are significant, said Dr David Tan, the principal investigator of the study and a consultant at the Department of Haematology-Oncology, NCIS as well as an assistant professor at the Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore. “Shrinkage

[1] http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM337830.pdf

Press Release

of the tumour is good news. Stable disease is still a positive sign as all the patients in the clinical trial have advanced or metastatic cancers that have been treated with multiple previous therapies, so our results indicate that this is a drug that is able to slow the growth rate of, and in some cases, shrink these highly treatment resistant cancers."

Especially encouraging are the results for a patient with thymoma – a cancer that affects thymus gland, an area in the middle of the chest between the lungs. This cancer is rare and resistant to standard cancer treatment when it recurs and metastasizes. After five cycles of treatment, the size of the patient's tumour has decreased by about 17%.

Also heartening is the prolonged disease control seen in patients with advanced colorectal cancers featuring mutation in a particular gene, known as *KRAS*, that usually renders the tumours resistant to conventional chemotherapeutic agents. One such patient is Mdm S. C. Theng, who has advanced KRAS-mutant colorectal cancer and has been on treatment since 9 February 2015. She is currently on cycle 7 of selinexor. Said Mdm Theng, "I feel generally okay although I do have some side effects such as a slight headache on the day I take the medication, some fatigue and nausea, and occasional bitterness in my tastebuds."

Encouraged by the results seen so far, Dr Tan and the research team are expanding the study. "We are currently still looking at the best way of scheduling the drug to ensure maximum drug effectiveness with minimal toxicity, but in the next phase, we will look at specific cancers in Asian patients such as lymphoma, nasopharyngeal, gynaecological and gastrointestinal cancers, and find out how each cancer responds to selinexor." For the expanded clinical trial, the Developmental Therapeutics Unit at the NCIS will be working with the Phase I unit at the National Cancer Centre Singapore to recruit a total of 60 patients. The study has just received additional funding from the National Medical Research Council.

Findings from Phase I study of the selinexor clinical trial in Asian patients were presented at the recent American Society of Clinical Oncology conference in Chicago. Selinexor clinical trials are also on-going in North America and Europe.

Importance of Phase I clinical trials

In cancer therapeutics, the scientific research landscape is rapidly evolving. The pace of research has increased tremendously – clinical trials are now completed in much shorter

Press Release

periods than before. Said Adjunct Associate Professor Goh Boon Cher, Head and Senior Consultant of the Department of Haematology-Oncology, NCIS, “Phase I of clinical trials is becoming increasingly important and crucial in novel drug development. In fact, drugs have been approved in an accelerated programme after Phase I/II trials based on very promising results shown while the study continues with Phase III to confirm the results.”

Added Dr Tan, “Phase I trials are the key drug development interface between laboratory findings and our patients in the clinic. However, the safety and quality of the early phase clinical trials cannot be compromised even as they help accelerate the pace of drug development.”

The Developmental Therapeutics Unit of the Haematology Oncology Research Group at the NCIS is one of the most active Phase I clinical trial centres for cancer in Asia. The Haematology Oncology Research Group at the NCIS has as many as 100 cancer trials currently on-going, including multiple collaborative early phase clinical studies with Astra Zeneca, Roche and Bayer Pharmaceuticals.

Patients interested in participating in the selinexor clinical trials can contact the Haemotology Oncology Research Group at the NCIS - please refer to www.horg.org.sg, email horg@nuhs.edu.sg or call 6772 4619.

– End –

For more information, contact:

Sharon Aw
Senior Assistant Manager, Communications
Tel: 6772 3987
Email: sharon_aw@nuhs.edu.sg

Press Release

About the National University Cancer Institute, Singapore

The National University Cancer Institute, Singapore (NCIS) offers a broad spectrum of cancer care and management covering both paediatric and adult cancers, with expertise in prevention, screening, diagnosis, treatment, rehabilitation and palliative care. The Institute's strength lies in the multi-disciplinary approach taken to develop a comprehensive and personalised plan for each cancer patient and his or her family. NCIS draws on the expertise of its specialists in the fields of haematology-oncology, radiation oncology, gynaecologic oncology, paediatric oncology, surgical oncology, oncology nursing, oncology pharmacy, palliative care, pathology, radiology, medical specialties including gastroenterology and hepatology, infectious diseases, pulmonary and critical care, psychiatry, epidemiology and public health as well as other allied health sciences. NCIS's strength in research allows patients to access drugs and devices before they are commercially available. NCIS is also closely affiliated with the Cancer Science Institute of Singapore, National University of Singapore.

For more information about the NCIS, please visit www.ncis.com.sg

About the National University Health System (NUHS)

The National University Health System (NUHS) groups the National University Hospital, the NUS Yong Loo Lin School of Medicine, the NUS Faculty of Dentistry and the NUS Saw Swee Hock School of Public Health under a common governance structure to create synergies for the advancement of health by integrating clinical care, research and education.

The enhanced capabilities and capacity enable the NUHS to deliver better patient care, train future generations of doctors more effectively and bring innovative treatments to patients through groundbreaking research.

Visit www.nuhs.edu.sg