

## FOR IMMEDIATE RELEASE

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### **Large-scale Malaysia-Singapore 2003 study shows that new personalized treatment regimen improves cure rate for children with leukemia**

Led by specialists at the Department of Paediatrics at the National University Hospital (Singapore), doctors from Singapore and Malaysia have developed a personalised cancer treatment protocol which improves cure rate and decreases mortality by reducing the side effects of chemotherapy. As a result, patients suffer lesser damage to their organs and improve their quality of life.

<sup>1</sup>Childhood Acute Lymphoblastic Leukaemia (ALL) is the most common form of cancer in children and affects three out of every 10 youngsters who are diagnosed in Singapore annually. It is a highly curable disease with intensive chemotherapy and the current cure rates in the developed world surpass 80%. However, one of the significant side effects of the treatment is damage to organs like the heart, skin and brain, which may lead to long-term complications, including <sup>2</sup>secondary cancers. In fact, the costs related to treating the side effects of chemotherapy often exceed those of treating leukemia.

Conventional chemotherapy treatment for childhood ALL uses four drugs to achieve remission from cancer. This results in prolonged hospital stays, usually up to one month. The increased complications add to the cost of therapy, and most importantly, put the young patients at a high risk of long-term side effects, which can be life threatening and significantly reduce quality of life.

The team at the National University Hospital (NUH) postulated that patients who responded well to the initial phase of treatment might be curable with less intensive chemotherapy. Thus, they developed a cost-effective method to accurately measure the patient's response to treatment. This allowed the majority of patients to avoid the most toxic therapy, which is reserved only for those who responded poorly and had the highest risk of having their leukemia return.

A total of 556 children under 18 years were recruited over a period of six years from 2003 to 2009 in this study, which is named Malaysia-Singapore (Ma-Spore) ALL 2003. The trial spanned four centres in Singapore and Malaysia: NUH, KK Women's and Children's Hospital (Singapore), University of Malaya Medical Centre (UMMC) and Sime Darby Medical Centre (SDMC) in Subang Jaya.

The new protocol, which starts with a three-drug remission-induction therapy, reduced the intensity of the treatment by 25%, compared to the conventional therapy given in most developed countries. The NUH doctors were able to develop a simplified yet accurate method to measure the amounts of leukaemia cells remaining in the body after therapy. By using this to guide treatment decisions, the doctors found that in up to 86% of children enrolled in the study, a significantly lower dose of chemotherapy could be given without comprising their long-term cure rate.

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<sup>1</sup> ALL - is a cancer of the blood and bone marrow. This type of cancer gets worse quickly if it is not treated properly. It is the most common type of cancer in children. (source: <http://www.stjude.org>)

<sup>2</sup> A cancer that results from the toxic effect of chemotherapy or radiation is called 'secondary cancer' (source: <http://cancerhelp.cancerresearchuk.org>)

Unlike previous trials where patients typically stayed in the hospital for the first month of treatment, most patients in this study could be discharged and managed as outpatients within five days of diagnosis.

Associate Professor Allen Yeoh, Principal Investigator of the study and Senior Consultant, Division of Paediatrics Haematology-Oncology, NUH said, "Leukaemia treatment creates a conundrum. On one hand, leukaemia is a rapidly fatal cancer if not treated correctly. On the other hand, chemotherapy drugs cause significant side effects that worry both doctors and parents. By personalising the dose of the chemotherapy drugs, we were able to deliver the optimal doses to maximise each child's potential for cure." Associate Professor Yeoh is also a Senior Consultant at the National University Cancer Institute, Singapore.

As a result, 81% of the patients were cured. For patients treated at the UMMC, this represents a 45% improvement in cure compared to their previous study. The Ma-Spore ALL 2003 study was the largest of its kind in the ASEAN region and findings indicate that the cure rates achieved are among the best in Asia and the rest of the world.

Professor Stephen Hunger, Director of the Center for Cancer and Blood Disorders at the University of Colorado Denver School of Medicine and one of the foremost experts in childhood leukemia shared, "The study by Dr Yeoh and his colleagues provides some very important information for the treatment of children with ALL, the most common form of pediatric cancer. They obtained outstanding results treating children from Singapore and Malaysia with newly diagnosed ALL. The first month of treatment is a very vulnerable time during which there is a significant risk of death from toxicity. This is a major problem in areas with more limited resources. Yeoh and colleagues used less intensive therapy for the first month and then measured the response to treatment using very sensitive techniques that allowed them to identify one leukemia cell in a background of 10,000 normal cells. This approach allowed them to identify patients with an excellent response, who could be treated with lower intensity therapy, and those with a poor response that needed to receive much stronger treatment. Their outstanding results have major implications for treatment of children with ALL worldwide."

This is a unique collaboration that brought together doctors from the National University of Singapore, NUH, KKH, UMMC and SDMC. They worked closely together to plan the study and managed patients so as to achieve the sterling result.

This study has benefited over 350 Malaysian children with ALL who received this state-of-the-art therapy.

Said Professor Hany Ariffin, Senior Consultant, Paediatric Haematology-Oncology Unit, UMMC, "It was a monumental effort to coordinate, recruit, treat and follow-up patients who came from different states in Malaysia. We achieved such good results against great odds. Our problems are unique and not seen in other centres where cost and access are not limiting factors. The UMMC team had to ensure that patients continued their treatment when they returned to their peripheral hospitals all over the country. This required innovative ways to track progress of individual patients including regular telephone conferences and a web-based data repository. These children were from diverse socio-economic backgrounds, many of whom would not have been able to afford such sophisticated treatment. As such, we raised funds from local charities and philanthropists to aid poor patients, thus ensuring treatment compliance."

Said Dr Lin Hai Peng, Consultant Paediatric Haematologist-Oncologist, SDMC, Subang Jaya, Selangor Darul Ehsan, Malaysia, "In Malaysia, this new approach to the treatment of childhood ALL enables children with non-high-risk ALL to be treated less intensively, thereby allowing patients and their families to spend less time and money in hospital. Most patients can be treated on an outpatient basis and may even be sent back to their local hospitals for therapy. The Ma-Spore ALL 2003 study also illustrates well the importance of collaboration in cancer research. ALL is not a common disease.

No single institution has adequate numbers over a short period of time to conduct a good study. Patients need to be pooled on a national, regional or international level. This landmark study is the first and remains, to our knowledge, the only successful collaborative clinical research project in medicine in Malaysia and Singapore."

Associate Professor Tan Ah Moy, Senior Consultant, Haematology-Oncology Service at KKH said, "Many children in Singapore and Malaysia have benefited from this study, getting a good cure with reduced late effects caused by the chemotherapy. Acute Lymphoblastic Leukemia is the commonest childhood cancer, and while science has an important role in administering the appropriate chemotherapy combination and monitoring the disease, we must not forget the significance of a holistic approach with psychosocial support in contributing to improved cure rates and success. Continued collaboration among paediatric oncologists, as undertaken for this study, will continue to contribute to better management and addressing issues of childhood cancer that are unique to this part of the world."

The results of the study were published in July 2012, in the Journal of Clinical Oncology, regarded as one of the most prestigious cancer journals in the world.

The doctors have now started a new study, Ma-Spore ALL 2010 that will further explore tailoring the treatment to optimise the treatment outcome of every child.

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## **About the National University Hospital**

The NUH is a tertiary specialist hospital and major referral centre for over 35 medical and surgical specialty services. These include Cardiology, Gastroenterology and Hepatology, Obstetrics and Gynaecology, Oncology, Ophthalmology, Paediatrics, Orthopaedic Surgery and Hand and Reconstructive Microsurgery.

Staffed by a team of healthcare professionals who rank among the best in the field, the NUH offers quality patient care by embracing innovations and advances in medical treatment.

In 2004, the NUH became the first Singapore hospital to receive the Joint Commission International (JCI) accreditation, an international stamp for excellent clinical practices in patient care and safety. Today, patient safety and good clinical outcomes remain the focus of the hospital as it continues to play a key role in the training of doctors, nurses and allied health professionals, and in translational research which paves the way for new cures and treatment, offering patients hope and a new lease of life.

A member of the National University Health System, it is the principal teaching hospital of the NUS Yong Loo Lin School of Medicine and the NUS Faculty of Dentistry.

For more information, please visit [www.nuh.com.sg](http://www.nuh.com.sg)