

THE GREATS TIMES

The Seoul National University Hospital Clinical Trials Center

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Professor Hyoung-Jin Kang Presents on The Lancet Oncology



Professor Hyoung Jin Kang (Division of Hematology and Oncology, Department of Pediatrics, Cancer Research Institute) has performed study with an international research team. His research and findings were published in leading journals such as Wall Street Journal, Lancet Oncology, OncLive and others. The results were also presented at the annual meeting of MASCC (Multinational Association of Supportive Care in Cancer) on June 30th, 2014. The research was about the applicability and the efficacy

of Emend (MSD, Antiemetic) on 302 pediatric cancer patients, aged between 6 months and 17 years (randomized, double-blind, phase 3). One-hundred-fifty-two patients took Emend and Ondansetron, as the reference group, while the rest of them took Ondansetron only as the control group. Consequently, chemotherapy-induced nausea and vomiting prevention rate was 51% in the reference group, which is considerably higher than the control group (26%). Many expect to be extricated from nausea and vomiting, since this research has proved that Aprepitant can be used on

pediatric patients. "I expect this research would affect other high quality pediatric clinical trials in the future. Also, I appreciate professor Kang and his team for their dedication," said Professor Richard Gralla (Albert Einstein College). Professor Kang also said, "This is the first time that the result of pediatric clinical trials led by Korea eventually released in high impact international journals." SNUH CTC has a pediatric clinical trials unit to support investigators in various ways so that research trials can be done more efficiently.



GREEN CROSS

R&D Forum with Green Cross for the New Collaboration



Since 2014, the Seoul National University Hospital Clinical Trials Center (hereafter, SNUH CTC) has regularly held R&D forums with local pharmaceutical companies to exchange farsighted views from the researchers of companies and investigators of SNUH. On 24th April, approximately 30 people participated and shared ideas about Antibody therapeutics of GREEN CROSS. Professor Yung Jue Bang (Director, SNUH CTC) said, "This is the starting point of new stage of development and future cooperation with GREEN CROSS. SNUH CTC expects to share in-depth opinions through this forum that would lead to breakthrough research projects." 13 people from GREEN CROSS, including Mr. DuHong Park (Vice president), attend the forum to present their latest research results for Hemophilia and Chronic Hepatitis B.

Global Focuses GREATS more&more



Sanofi held a meeting with representatives from the Sanofi Investigator Network in Bridgewater, NJ, U.S. on June 11th-12th, 2015. Dr. Howard Lee was at the meeting as a representative of SNUH. The diversity of the sessions, from operational aspects to portfolio reviews, allowed better integration of network site feedback from different angles. This will improve the way clinical trials are conducted in collaboration with the sites, ultimately for the benefit of the patients. Site Quality was one of the topics discussed during the meeting. Following a presentation on sponsor's perspective on audits and inspections, 3 site participants, including Dr. Lee, detailed their perspective on how the sites are organized with

regard to quality and inspection readiness. Sharing best practices from sites of different set-up and size benefited all those present, and it was a great opportunity to share the experience of SNUH, that it is continuously developing ways to more improve the trial quality.

The Sanofi Investigator Network is a global group of expert clinical trial sites. It was successfully initiated three years ago as a new approach to research and development while keeping the investigator sites and patients as the main focus. SNUH is one of Sanofi's network sites and has been demonstrating its value by participating in Sanofi's global studies with excellent site-set up and recruitment metrics.

Next Step to become Global Leader



SNUH CTC obliged a basic education training program for CRC (Clinical Research Coordinator) to elevate the standards of clinical trials performed at snuh. Every CRC will need to take the advanced training course regularly (1 course per year). Basic course provides ways to efficiently manage the process of re-

search and clinical trial-related material.

Through the advanced course, the CRC can learn more detailed instructions such as regulation of IIT (Investigator Initiated Trials) and methods of coping with various situations during trials by the HRPP (Human Research Protection Program) team. Those who would not complete the whole required course, cannot register themselves as CRCs for research from now on. The center expects to elevate the reliability of CRCs' traits and qualities by providing a professional training system.

UPCOMING EVENTS!

- ◆ **Round-table Conference for Local Sponsors**
Date: July 15th, 2015
Place: CMI Conference room #2
- ◆ **The 20th Anniversary of SNUH CTC**
Date: September 17th, 2015
Place: BRI Auditorium
- ◆ **Microdosing Symposium (with Chungnam Nat'l Univ.)**
Date: September 18th, 2015
Place: BRI Auditorium

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GREATS Network is Continuously Expanding!

#1 Chungnam National University, College of Pharmacy



On 17th April, SNUH CTC had a signing ceremony for MoU (Memorandum of Understanding) with College of Pharmacy, Chungnam National University (CNU). Four professors from CNU attended this ceremony, including Professor Chang-Sun Myung, the Dean of College of Pharmacy, CNU. The purpose of this MoU is to cooperate and carry forward a plan for exchange of ideas and trained manpower through a written agreement.

#2 LSK Global Pharma Services



SNUH CTC has signed an MoU with LSK Global Pharma Services (LSK) on 2nd April at the BRI (Biomedical Research Institute), SNUH. The MoU seals a strategic partnership between the two parties, especially on phase 1 clinical trials, which would remain valid for 3 years. Through this agreement, both parties will strive to actively attract and perform global phase 1 studies. Dr. YoungJae Lee (President, LSK) said, "I am pleased to have a partnership with the highly respected investigators of SNUH CTC and this opportunity will be a new stepping stone for new drug development in Korea."

#3 CLIPS Clinical Professional Services



SNUH CTC's network is continuously expanding by signing agreements with local and global companies involved in medical research that will eventually contribute to better human health and welfare. This time, CLIPS (Local CRO) partnered with SNUH CTC for collaboration on key strengths of both sides. The two parties agreed to utilize their own core capabilities and apply them to various sectors.

#4 AstraZeneca-New future of cancer patients <Oncology Alliance Center>

SNUH CTC was assigned as an 'Oncology Alliance Center' by AstraZeneca, along with Samsung Hospital and Asan Medical Center. All centers agreed to a specific cooperation plan by signing a Memorandum of Understanding (MoU). This MoU pertains to collaboration for 3 years on preclinical trials of anti-cancer drugs and pipeline development. There are still many unfulfilled needs in the anti-cancer research and trials sector even though the number of cancer patients are continuously in-

creasing worldwide. AstraZeneca expects this collaboration to raise cancer patients' accessibility to new drugs that would change the quality of their lives.

Five people from AstraZeneca, including Dr. Susan Galbraith (Vice President of Oncology and head of the Oncology Innovative Medicine unit), JoonOh Park (Samsung Hospital), TaeWon Kim (Asan Medical Center) and Yung-Jue Bang (SNUH CTC) attended this ceremony.



Precious True Stories are Shared

Clinical trials are always considered an essential process that contribute to world health and welfare services. The treatment for current patients and potential benefits for the future patients were made by new drug development through clinical trials. To remind everyone of the significance and the value of clinical trials, KoNECT (Korea National Enterprise for Clinical Trials) shared essays by patients, their family members and



investigators.

KoNECT held the 1st Essay Contest about research experiences. And two people who participated in clinical trials at SNUH CTC won the contest – one the grand prize and the other, a runner-up prize. The grand prize winner wrote an essay named 'Endless Moments of Decision' and the runner-up's title was 'The timesaving people'.

The New Takeoff of Medical Device Clinical Trials Center

Medical Device Clinical Trials Center (hereafter MDCTC) successfully obtained and launched 'Medical Device Usability Testing Center' project offered by KHIDI (Korea Health Industry Development Institute). Currently, medical device manufacturing companies individually test and get results, since Korea is yet to establish a chartered institute for function testing. Therefore, SNUH MDCTC was granted permission (announced on March 30th, 2015)



to abolish the licensing barrier between KMFDS (Korea Ministry of Food and Drug Safety), CE and FDA through this

project. MDCTC will focus on building infrastructure at the early stage and will strive to better itself during the project. (2 years and 10 months) Thanks to this project, SNUH MDCTC expects to become a reputable institute that elevates the level of public awareness of medical devices in Korea. MDCTC is making steady progress, including signing an MoU with well experienced usability testing companies and holding business fairs.

Opening Ceremony of CMI (Center for Medical Innovation) with Acclamation



16th July was one of the thrilling day of SNUH due to the opening ceremony of CMI (Center for Medical Innovation).

The center welcomed 200 people including benefactors and members of the National Assembly.

"CMI will be new foundation of HT (health technology) cluster building.", said Prof. Bang. (Director, SNUH CTC)

*More detail would be on next issue.



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Introducing Seoul National University Bundang Hospital CTC!

[Director's Corner] Prof. JongSuk Lee

Professor JongSuk Lee, Director of Seoul National University Bundang Hospital Clinical Trials Center (SNUHBH) recently contributed to successful research on pembrolizumab of MSD, a new possible treatment option for progressive NSCLC, by participating as a local investigator. This research was presented in the prestigious medical magazine, the New England Journal Of Medicine, in May, 2015. (N Engl J Med 2015;

372:2018-2028 May 21, 2015) Pembrolizumab has a 45% treatment reaction rate on

patients who had been treated before, while they have more than 50% of PD-L1 tumor manifestation (expression).



Department of Clinical Pharmacology & Therapeutics of SNUBH

A paper was published online in Antimicrobial Agent and Chemotherapy on May 2015 about a study performed at the Seoul National University Bundang Hospital Clinical Trial Center in 2013. This study for therapeutic drug monitoring (TDM) of second-line anti-tuberculosis (TB) drugs was conducted using ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS), which allows for simultaneous measurement of the blood concentrations of nine second-line anti-TB drugs.

In order to evaluate the pharmacokinetic (PK) characteristics of the second-line anti-TB drugs and to improve the viability of TDM, the author conducted an open-label, multiple-dosing study on 16 healthy subjects divide into two groups. Cycloserine 250 mg, p-aminosalicylic acid (PAS) 5.28 g, prothionamide 250 mg

twice daily and pyrazinamide 1500 mg once daily were administered to both groups. Additionally, levofloxacin 750 mg and streptomycin 1 g once daily were administered to group 1, and moxifloxacin 400 mg and kana-



Antimicrobial Agents
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Pharmacokinetics of Second-line Anti-Tuberculosis Drugs after Multiple Administrations in Healthy Volunteers

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ABSTRACT

Therapeutic drug monitoring (TDM) of second-line anti-tuberculosis (TB) drugs would allow for optimal individualized dosage adjustments and improve drug safety and therapeutic outcomes. To evaluate the pharmacokinetic (PK) characteristics of clinically relevant, multi-drug treatment regimens and improve the viability of TDM, we conducted an open-label, multiple-dosing study on 16 healthy subjects who were divided into two groups. Cycloserine 250 mg, p-aminosalicylic acid (PAS) 5.28 g, prothionamide 250 mg twice daily and pyrazinamide 1500 mg once daily were administered to both groups.

mycin 1 g once daily to group 2.

According to the results, the PK characteristics of the tested second-line anti-TB drugs after concomitant administration were consistent with those reported for separate administration. In addition, the result suggests that sampling at 1, 2.5, and 6 hours post-dose is needed for TDM when all of the seven studied drugs are administered concomitantly.

This study provides valuable information concerning the PK characteristics of second-line anti-TB drugs in commonly used multiple dosing regimens for multidrug-resistant (MDR) TB. Possible drug interactions were observed when co-administering fluoroquinolones with cycloserine, PAS, and prothionamide, and this may warrant further study in MDR TB patients.



SNUH

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Introducing Chonbuk University Hospital Global Center of Excellence!



Chonbuk National University Clinical Trials Center (JBCTC) recently performed a total of 16 research projects, including 11 phase 1 trials, and 5 phase 2 trials. Our center proceeded with drug-drug interaction study between OATP2B1 and OATP1B1, with Konkuk University

Hospital. Also, the Journal of Ginseng Research published a study called 'Changes in the ginsenoside content during the fermentation process using microbial strains', that will be used as a foundation source in future trials related to the botanical drugs. JBCTC has been striving to elevate the overall quality of performance. We have engaged the services of specialists in law to systematically manage regulations and guidelines. We are also pushing forward to acquire an electronic data capture (EDC) system by a company called 'Medidata Rave' to correspond to global standards of clinical trials such as CDISC.

In November 2012, Chonbuk University Hospital Clinical Trials Center (CUH CTC) was designated as the Global Center of Excellence in clinical trials based on early natural medicine with the purpose of strengthening the capacity of national clinical research and creating a globally relevant business model. The designation came with a five-year project which is to conclude in March 2017. Natural medicine is an emerging field of study in drug development, and the number and size of clinical trials within this area is gradually increasing.

Domestic non-clinical/clinical trials involving natural medicine in terms of technology, size and revenue generation have not been competitive in the global market, and the Korea Good Manufacturing Practice (KGMP) has lower standards compared to those of other developed nations. As a result, domestic Contract Research Organizations (CROs) and Contract Manufacturing Organizations (CMOs) have not been attractive in the global market. Consequently, this is "the" time to standardize production processes and set up quality control standards for the development of natural medicine by expanding clinical trials support centers.

CUH CTC strives to build infrastructure and facilities that match global standards of quality and train professionals for the future. The center also contributes to the competitiveness of clinical trials conducted by the country in the global market by exploring the use of technology in natural medicine.

Research Infrastructure



By establishing a new Clinical Research Support Center, CUH CTC has created a sophisticated clinical trial system that comprises of 60 clinical beds, 8 outpatient clinics, and 8 monitoring rooms fully dedicated to clinical research.

Service

CUH CTC boasts a vast experience in conducting many clinical trials not only with domestic, but also with global pharmaceutical companies. Its expertise in clinical research has been proved through numerous audits and inspections. For example, it is the first center in Korea to have been inspected under a pre-qualification program by the World Health Organization (WHO). CUH CTC provides a wide range of services including management of clinical trials electronic records, Statistical Analysis Plan (SAP) and statistics, pharmacokinetic and statistic reporting (WinNonlin®, SAS®, SPSS®), modeling & simulation (Phoenix WinNonlin Software, NONMEN® with PDx-POP, NLME™, e-CRF system, Data Entry, Validation.