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THE GREATS TIMES

The Seoul National University Hospital Clinical Trials Center

Publisher: Yung-Jue Bang, MD, PhD, Director

Exclusive Seminar

On Wednesday, September 17, 2014, executives from major pharmaceutical companies and Contract Research Organizations (CROs) gathered at Lee Kun-Hee Hall of Seoul National University Cancer Research Institute to attend an exclusive meeting sponsored by Innovative Center for Bio-Imaging Guided Drug Discovery and Development (iCBigD[3]) and GREATS. The seminar was initiated to activate the use of novel technology in the field of early clinical trials.

In the beginning of the seminar, all attendees had a chance to introduce themselves briefly to share their interests and find someone who has common views. It was followed by the first speaker, Professor Sang-Eun Kim, the director of iCBigD[3]. He introduced bio-imaging— a latest innovation in early clinical trials—and explained how cost-effective and time-saving the new technology is.

The next three presentations were given by executives from pharmaceutical industry including Dr. Won Choi (Vice President of Clinical Development, LG Life Sciences), Dr. Seong-Choon Choe (Head of Seoul Research Institute, Boryung Pharm), and Ms. Taeyoun Jo (Country Lead of Global Clinical Trial Operations, MSD Korea) under the topic of "*Expectations & Requests to Early Phase Trials Investigators and Regulatory Authorities from Pharmaceutical Industry*." It allowed the audience, especially the investigators present at the seminar, to understand the perspectives of the industry. Dr. Eui Sik Han (Director of Drug Evaluation Department, Ministry of Food and Drug Safety) was invited to give the last presentation under the title of "*Considerations for Early Phase Clinical Trials Investigators*." Through his presentation, he updated the audience on the current approval status of early clinical trials and explained about the considerations to be taken while designing clinical trials. Also, he shared gave his insights on some frequently asked questions by pharmaceutical firms and researchers.

Professor Yung-Jue Bang was the chairperson of free discussion, which was the last program of the exclusive seminar. Attendees had the opportunity to share some advantages and disadvantages they gained by working with GREATS. As the director of SNUH CTC, Professor Yung-Jue Bang promised to make prompt use of the suggestions shared during the free discussion. He also strongly suggested the audience to contact GREATS leaders directly for any difficulties that may arise from conducting the studies at SNUH. Moreover, the GREATS team was assigned to follow up with any problems shared at the seminar.

Revised Notice for Clinical Drug Approval Regulation

MFDS KOREA

[**Regulatory Updates**] The Korean Ministry of Food and Drug Safety (MFDS) issued a revised notice for clinical drug approval regulation, stating that clinical study protocols in English for Phase I trials can be submitted to MFDS for an approval. The revision became effective on September 11, 2014, and was intended to attract global clinical trials in Korea.

The revision has simplified the required documents since earlier, a copy of clinical study protocol translated in Korean was needed to be submitted along with the original version. Due to the Korean version requirement, the approval process often took a longer time than it does in other countries, consequently missing the deadline for the trials. Therefore, Korea was often not selected by global pharmaceutical companies since all global clinical trials must start at the same time. However, a written consent form and explanation of clinical research for study participants are still required to be translated into Korean for submission.

UPCOMING EVENTS!

- **Microdosing Symposium**
  Date: November 27, 2014
  Time: 1:40 pm
  Place: Auditorium
  (Biomedical Research Institute @ SNUH)
  Sponsored by: Sekisui, DCK, GREATS

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Quintiles CEO Visits SNUH CTC

Top executives from Quintiles, one of the leading providers of biopharmaceutical services around the globe, including Mr. Tom Pike (Chief Executive Officer), Dr. Derek Winstanly (Chief Customer & Governance Officer), Dr. Anand Tharmaratnam (Senior Vice President and Head of Asia Market), and Dr. Amar Kureishi (Vice President) visited SNUH Clinical Trials Center on September 24, 2014 to have a brief meeting with Professor Yung-Jue Bang. During the meeting, Professor Bang gave an overview of the capabilities and strengths that SNUH Clinical Trials Center has.

In addition, they had a discussion focusing on some of the areas to be developed further to strengthen the relationship between two parties. After the Q&A session, Ms. Theresa Choi gave a guided tour of the facility which included the research ward, core laboratory, pharmacy, and outpatient units. She also spoke in detail about the future plans to implement a fully automated clinical trial management system, TrialOne, and to expand the facility space. Both plans are expected to be completed by the early 2015. One of the board members said that he was very impressed with facility.

Quintiles is one of the largest global Contract Research Organization (CRO) headquartered in North Carolina, USA, with over 60 offices around the globe. The relationship between SNUH Clinical Trials Center and Quintiles has been cooperative through various researches, and the meeting provided them an opportunity to develop the relationship further.

Seeking Possible Collaboration with Bio-Imaging Technology

Professor Sang-Eun Kim, the director of Innovative Center for Bio-Imaging Guided Drug Discovery and Development (iCBigD^3), was invited to speak at the GREATS mini-seminar on August 8, 2014. The mini-seminar took place in Conference Room 1 of the Biomedical Research Institute at SNUH.

As a closed meeting, professors in the field of early clinical trials interested in bio-imaging were selectively invited. About 20 professors attended the meeting to learn more about the ways bio-imaging technology can contribute to the new drug development and how iCBigD3 could step in to support the possible collaboration. Professor Sang-Eun Kim also spoke about the capabilities and skills developed by his team.

His presentation was followed by a Q&A session in which some ideas for collaboration were shared. The mini-seminar inspired the attendees to a huge extent, providing an opportunity to think about a way to advance in the field of clinical trials with the help of current technology.

Seeking for Collaboration with CNIBR!

SNUH Clinical Trials Center has been collaborating with Novartis Korea, and the business relationship led to potential research collaboration with the China Novartis Institute for Biomedical Research (CINBR).

On September 23, 2014, key leaders including Dr. En Li, Dr. Chris Lu, Dr. Anfan Wu, Dr. Jessi Gu, Dr. Amber Cai, and Dr. Zhijian, from CNIBR visited SNUH Clinical Trials Center to share their interest in research areas. After Professor Yung-Jue Bang gave a brief introduction of SNUH Clinical Trials Center to the visitors, Professor Jeong-Hoon Lee and Professor Yoo-Wook Kwon briefly spoke on the areas of their research—liver disease and cardiology & stem cell study, respectively. Presentations were followed by the Q&A session during which more interest areas were shared and discussed.

The First SNUH R&D Forum

On Thursday October 23, 2014, the First SNUH R&D Forum with Samyang Biopharmaceutical Corporation (Samyang Corp.) was held in Ji Suk Young Hall at the Biomedical Research Institute on Seoul National University Hospital (SNUH) campus. SNUH was designated as a research-oriented hospital by the Korean Ministry of Food and Drug Safety (MFDS) and was chosen to conduct a project of researching and developing technologies to fight cancers and inflammatory diseases under the government support until 2023.

SNUH believes that open innovation based on cooperation is the key to success, and plans to establish platforms to activate and commercialize the research and development. This forum was the first step, and it provided a chance to share knowledge from both academia and industry to more efficiently develop drugs and medical devices. Samyang Corp. has been an active participant in the area of drug/bio business of biopolymers.

The forum started with the Memorandum of Understanding Signing Ceremony followed by several presentations by project coordinators from Samyang Corp. After each presentation, plenty of time was given to discuss over potential collaboration between two institutions.

10th Year Anniversary of SNUH Medical Research Collaborating Center (MRCC)

[**SNUH News**] On September 19, 2014, a symposium celebrating the 10th year anniversary of SNUH Medical Research Collaborating Center (MRCC) was held in the auditorium of Biomedical Research Institute at SNUH.

SNUH MRCC, the first MRCC in Korea, was established in 2004 for the construction of infrastructure that promotes joint medical research between Seoul National University (SNU) and SNUH.

Even though the center started as a small group, it currently has three different departments specializing in epidemiology, statistics, and data management. For the last 10 years, SNUH MRCC has supported over 2,100 cases of clinical research developed by SNU and SNUH. Also, it has been one of main institutions selected by Korea National Enterprise for Clinical Trials (KoNECT) to educate more than a thousand professionals in the fields of Pharmacokinetic research, medical statistics, and data management. As a result, it has contributed significantly to improving the domestic level of medical research.

The anniversary symposium provided an opportunity for the audience to look back at the major events of the center and to discuss some important areas to be improved.

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* Poor clinical trials participation status of the elderly and direction of future improvement—Is there discrimination against the elderly in clinical trials when recruiting subjects?
  Recruiting the elderly should not be an option, but a must.
* Applying clinical trials results based on the study of young population or patients with mild conditions to the elderly could be problematic. Experts in clinical trials pointed out that excluding the elderly from clinical trials recruitment could become an issue. Supports and incentives are needed to activate clinical trials of the elderly.

As advances in science, technology, and medicine continue, new drugs and treatments are being actively developed and numerous clinical trials are underway to prove the efficacy and safety before being sold on the market.

However, if a clinical trial has targeted a specific population, it is hard to apply its result to the general population. For example, if the clinical trial has only targeted young people or patients with mild conditions, the result should not be applied to the elderly with multiple varying health conditions.

Korea is one of the fastest aging countries in the world, and according to the 2012 statistics, 33.3 percent of total medical spending is accounted for the health care of the elderly. Although this age group will benefit the most from the new drug or treatment, it is hard to define how much the old people are involved in clinical trials and what the solutions are, if they are discriminated from the participation.

Interesting results of recent research by SNUBH Clinical Trials Center and Geriatric Center, led by Professor Gwang-Il Kim (Principal Investigator, SNUBH Geriatric Center), on clinical trials specialists have drawn attention.

The research surveys were conducted among 240 people including members of Korean National Enterprise for Clinical Trials (KoNECT), professors of SNUBH, oncologists from Seoul National University Hospital, and clinical practitioners. 166 respondents (69.2%) believe that participation rate of the elderly in clinical trials is low which can become problematic.

Also, 203 respondents (84.6%) insisted that it is inappropriate to apply the results of young people directly on the elderly, and according 188 respondents (78.3%), low participation rate of the elderly in clinical trials could work as a disadvantage to them. Moreover, most respondents pointed out that excluding the elderly from candidacy as clinical trial subjects simply due to the old age or shorter life expectancy is not fair.

Therefore, clinical research professionals believe setting a required participation ratio of the elderly in clinical trials when recruiting subjects will be effective in encouraging the participation of the elderly or expanding the support for clinical trials that the elderly is involved in.

In addition, in the case of new drugs that are frequently used by the elderly, making a policy that requires results of elderly clinical trials in order to receive a new drug approval or allowing a special patent extension or insurance benefits should be considered to motivate investigators or pharmaceutical firms.

"In case of old people, the overall metabolic processes such as drug absorption, distribution, and excretion are different from young adults. Also, the elderly usually take a larger number of drugs due to multiple health conditions they have, exposing themselves to a higher risk of having adverse events," said Professor Jae-Yong Chung from the Department of Pharmacology at SNUBH Clinical Trials Center. "Therefore, the elderly should be involved in the process of proving the efficacy and safety of a new drug or treatment," he continued.

"The participation of the elderly is often limited in order to make the result more substantial, but plenty of experience in clinical trials of the elderly will help reduce health care spending in the long run. Therefore, policies that prevent excluding the elderly from clinical trials are needed along with adequate support and incentives that encourage the policy," added Professor Jong-seok Lee, the director of SNUBH Clinical Trials Center.

The result of the study was published in the Korean Geriatric Society Journal of September.

CUH Global Center of Excellence in Early Clinical Trials

Chonbuk National University Hospital Clinical Trials Center (CNUH CTC) has been operating with the goal of securing a world-class performance in early clinical competence in the field of natural medicine, which is emerging as a new pipeline of drug development. In order to achieve its goal, the CNUH CTC provided medical consulting related to the global phase 1 clinical trial of YPL-001 developed by Yungjin Pharm as a treatment for respiratory diseases in the early 2014.

Additionally, the CNUH CTC performed pharmacokinetic linearity evaluation on clinical trials for DW1029M, developed by Dong Wha Pharm, which is a natural medicine for treating diabetic kidney. Moreover, the Center had experience in using the cocktail approach, a technique to evaluate a variety of drug interactions, that was achieved through dosing indicating drugs of metabolizing enzymes and transporting protein at the same time. As a result, the CNUH CTC now possesses the latest technology used to evaluate drug interaction while developing natural medicines.

Currently, the Center is conducting a clinical trial that evaluates the pharmacokinetic interaction of DW1029M, a natural medicine, containing metformin, linagliptin, and rosaflo.

Over the last year, the CNUH CTC has become a Contract Research Organization that offers a variety of services related to phase I clinical trials including consulting of new drug development, performing analysis of pharmacokinetics, providing statistical data, modeling, and the simulation and management of clinical data. Also, it has conducted over 20 pharmacology studies such as evaluating pharmacokinetic properties of healthy volunteers, drug interactions with other drugs and food, and antimicrobial activities. As an institution that has completed WHO prequalification program, the CNUH CTC has especially performed a bioequivalence testing of terizidone capsules that was developed by Dong-A Pharm in order to export to WHO for the first time in Korea. Through this experience, CNUH CTC was able to demonstrate that it holds the global level of clinical performance.