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Microdosing/microtracing clinical trials using accelerated mass spectrometry in clinical drug development

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Microtracing/microdosing is an innovative technology that can revolutionize the current paradigm of clinical drug development. Typically, a very small amount of the drug, i.e., 'microdose', which is less than 100 micrograms (or 30 nmoles for proteins), is administered to humans. Since this is much smaller than 1/100 of the pharmacologically active dose, microtracing/microdosing technology can be employed at a very early stage of clinical drug development even when there is limited animal toxicology data. Furthermore, in order to trace minute doses, an accelerator mass spectrometer (AMS) is required and the compound should be labeled, typically with 14C. The microtracing/microdosing study allows clinical drug development scientists for generating the intravenous pharmacokinetics, mass balance, metabolite profiling, and absolute bioavailability data much easier, faster, and at a significantly lower cost. Based on this understanding, this study investigated the current status and employment of AMS-based microtracing/microdosing studies in actual drug development. To achieve this objective, we performed an extensive search of the literature and public information, Delphi focus group interviews, surveys, and personal communications with the key players in the field. The number of the clinical studies that used 14C and AMS dramatically increased from only 3 in 2001-2005 to 59 in 2011-2015. The survey showed that 31.6% of new drug development scientists were planning to perform microtracing/microdosing studies. Furthermore, 73.7% of survey responders replied that they would consider AMS-based microtracing/microdosing studies if there is a well-established service provider. This study confirmed that the frequency of AMS-based microtracing/microdosing studies for drug development has been in a steady increase for the past decade or so. This increase was partly because several issues of AMS application in the previous era, such as dose-linearity, sample pre-processing, and high cost, have been adequately addressed. In conclusion, AMS-based microtracing/microdosing studies have been steadily employed in actual drug development, which is expected to increase further in the future.

Recent Publications

1. Kim YK, Kim A, Park SJ, Lee H. New tablet formulation of tacrolimus with smaller interindividual variability may become a better treatment option than the conventional capsule formulation in organ transplant patients. Drug Design Dev Ther. 2017 (11): 2861-2869
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Biography

Howard Lee is the Founder and Director of the Center for Convergence Approaches in Drug Development (CCADD). Dr. Lee serves as a Professor at the Department of Transdisciplinary Studies, Graduate School of Convergence Science and Technology, Seoul National University. Dr. Lee is also appointed at Seoul National University College of Medicine and Hospital, affiliated with the Department of Clinical Pharmacology and Therapeutics. Dr. Lee previously served as Head of Global Strategy and Planning, Clinical Trials Center, SNUH. As of August 2017, Dr. Lee was appointed Chair of the Graduate Program in Clinical Pharmacology, Seoul National University. Dr. Lee has spearhead the introduction of Accelerator Mass Spectrometry (AMS)-enabled exploratory early clinical drug development studies to the Korean biopharmaceutical R&D sector, which has awarded Dr. Lee 2 government grants.

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