Overview and requirements of animal experiments in drug discovery

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Japan is one of the few countries that has the infrastructure to support drug discovery. Drug discovery is an important industry that will support Japan’s future, and is expected to be a driving force for further improving infrastructure and improving medical care. The drug discovery process is based on basic research (2-3 years), non-clinical studies (3-5 years), clinical trials (3-7 years) and applications for new drug approval and approval review (1-2 years). In addition, research on formulation and manufacturing of new drug is needed. Animal studies are often performed in efficacy, safety and pharmacokinetic studies as non-clinical studies. Based on the essential values of efficacy and safety, easy-to-use, security and reliability, and information on use form a pyramid of drug value. Therefore, animal testing in drug discovery requires accuracy, reproducibility, reliability (GLP etc.), and global applicability. There is also a need for speed for market launch as soon as possible and social understanding (legal compliance, animal welfare, etc.). This symposium was designed to share the current status and proposition of efficacy, safety, pharmacokinetic and pharmaceutical research in drug discovery animal research. Animal experiments in drug discovery are very important for creating new drugs, but there were few opportunities for discussion at JALAS annual meeting. In recent years, it has been desired to transmit value in order to improve social understanding of animal experiments. We hope this symposium will be an opportunity.
Current status and issues of animal experiments in pharmacological research

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The overall success rate in drug development is very low, due to the lack of the expected efficacy in clinical trials. In this talk, I will focus on improving the translation from animal to human as well as from human to animal as a challenge to discover effective drug targets in humans. We have previously applied the parameters in clinical trials to pharmacology research, that is, the translation from bedside to benchside has made it possible to align the direction of basic research with that of clinical research. Also, I will talk an example of analysis utilizing the drug discovery support platform, TargetMine (https://targetmine.mizuguchilab.org), which can perform pathway analysis while freely moving between mouse and rat and human molecular data. In recent years, various fields, including drug discovery, medical care, and healthcare have high expectations for the performance and potential of AI. We also develop AI to gather the precise clinical information from clinical sites and use AI based on the vast amount of existing knowledge data that humans cannot process at all. Now, even if a drug target is proposed by AI technology, the certainty of the target must be verified with some animal model. Therefore, development of humanized mice and mice transplanted with human tissues is also an important issue. The time has come when you can approach clinical conditions with complementary use of clinical data and animal experimental data.
While animal experiments are considered to be indispensable in drug discovery research at this time, pharmaceutical companies are responding to the growing demands for animal experimentation ethics in the course of the times. However, the voices against animal testing are not eliminated. Perhaps there is a perception that drug discovery research is a closed professional activity by a researcher or a company, and this may be due to "opacity" and "difficulty". Researches on drug safety assessment play an important role on the process of drug candidates becoming human drugs in drug discovery. Because of its importance, the researches involves many regulations and organizations. There are ethical, economic and social aspects as well as science. There are also various things that are considered to be important, depending on the individual's position. I feel that this is the part that leads to "difficulty". The speaker is not a researcher involved in safety research. I will introduce the current status and issues of safety research from the standpoint of animal management and research support, and also from the perspective of studying animal experiment welfare at the Japan Pharmaceutical Manufacturers Association. We hope that this session will deepen our understanding with those who are not familiar with animal experiments in drug discovery and the general public, and will help the various issues of animal experiments be solved socially.
Based on ICH Harmonised Guideline, a well-structured Common Technical Document (CTD) is prepared and submitted to the respective regulatory authorities for drug applications. The data of pharmacokinetic studies are contained in "2.6 Nonclinical Written and Tabulated Summaries" of Module 2.

The sequence of the Pharmacokinetics Written and Tabulated Summary should be as follows:

2.6.4 Pharmacokinetics Written Summary
2.6.4.1 Brief Summary
2.6.4.2 Methods of Analysis
2.6.4.3 Absorption
2.6.4.4 Distribution
2.6.4.5 Metabolism (interspecies comparison)
2.6.4.6 Excretion
2.6.4.7 Pharmacokinetic Drug Interactions
2.6.4.8 Other Pharmacokinetic Studies
2.6.4.9 Discussion and Conclusions
2.6.5 Pharmacokinetics Tabulated Summary

I would like to talk my views on the current status and issues of animal experiments in pharmacokinetic studies based on recent public information.
Animal Experiments in Pharmaceutical Research and Development

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The mission in pharmaceutical research is to contribute to society by providing easy-to-use and high-quality products. Recently, it has become rather difficult to discover and develop new low-molecular-weight compounds as pharmaceutical drugs. Thus, as noteworthy strategies, new dosage forms using novel formulation technologies with compounds that have been used as pharmaceuticals are invented and developed. The formulation technologies have great potential to maximize the benefit of patients by changing the timing of the absorption and distribution of the compounds. And animal experiments almost always play an important role from the very early stages of pharmaceutical technology research to the late stage for product optimization. However, anatomical and physiological differences between humans and laboratory animals precisely affect the evaluation of pharmaceutical technology. We must understand the anatomical / physiological characteristics / differences for appropriate evaluation. It is also important to devise experimental conditions to compare to human physiological conditions when necessary, aside from 3Rs that must be sufficiently considered.