Volumetric absorptive microsampling in pharmacokinetic studies

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Biography: Hua Li is currently a Bioanalytical Research Scientist in the NBE Pharmacokinetics Group in the Biotherapeutics Discovery Department at Boehringer Ingelheim (CT, USA). She earned her MA in molecular, cellular and developmental biology from the University of Kansas (KS, USA). While pursuing her master's degree, she worked as a research assistant on *Caenorhabditis elegans* genetics. After graduation, she started my career as a research associate and laboratory manager at the Stem Cell Center of Yale University (CT, USA). Her main roles included investigating the essential proteins that play a critical role in the division and differentiation of mouse testes stem cells, as well as administrative responsibilities for a laboratory of around 12 people including graduate students, post-docs and laboratory technician. Since 2008, her career has been focusing on the quantitation of pharmacokinetics and pharmacodynamics study of protein therapeutics. Over the past 12 years, she has witnessed a tremendous expansion of new technologies, devices and theories in the pharmacokinetics/pharmacodynamics field, all of which have helped us better serve the patient community all over the world. Hua Li speaks to the *International Journal of Pharmacokinetics* about the use of volumetric absorptive microsampling in pharmacokinetic studies and their methodology on the application of Mitra[®] microsampling for pharmacokinetic bioanalysis of monoclonal antibodies in rats.

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Please introduce yourself & your experience working on pharmacokinetic studies

I joined Boehringer Ingelheim Pharmaceuticals in 2008 when my manager was establishing a new NBE Pharmacokinetics (PK) Group for preclinical research projects. Over the past 12 years, our group has expanded substantially in both size and functions. We are supporting multiple therapeutic indications including cardiovascular, immunology and immuno-oncology with preclinical species PK/pharmacodynamics (PD) bioanalysis and human PK dose prediction and modeling. My work mainly focuses on protein therapeutics PK/PD/anti-drug antibody (ADA) assay development, sample bioanalysis, PK analysis as well as preparing data summary packages for the candidates that successfully pass into development.

Can you briefly summarize the methodology you published in bioanalysis on the ‘application of Mitra[®] microsampling for pharmacokinetic bioanalysis of monoclonal antibodies in rats’?

First, we developed an ELISA to quantitate the two marketed protein therapeutics of interest. Then we developed an incubation condition to retrieve the spiked protein therapeutics from Mitra[®] microsamplers after drying. After confirming satisfactory drug recovery, we then conducted a rat PK study to compare Mitra[®] data with that of serum and liquid whole blood control groups. The three groups of data resulted in good agreement, so we found Mitra[®] microsamplers to be potentially powerful tool for blood sampling during preclinical antibody PK studies. Since only very small volume of blood is needed for accurate quantitation, the Mitra[®] device enables better

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characterization of the pharmacokinetic profile, while substantially reducing the number of animals required for preclinical PK studies [1].

Why has volumetric absorptive microsampling become a technique increasingly used in nonclinical pharmacokinetic studies?

To characterize monoclonal antibody PK/PD accurately, we desire a suitable time course for animal blood sampling. Due to the small body size of rodent animals, the volume and frequency of blood sampling are regulated strictly by Institutional Animal Care and Use Committee. To comply with the regulations, we often have to compromise our sampling schedules by other methods like staggering sampling, which may compromise our data quality. When we apply volumetric absorptive microsampling (VAM) technology such as Mitra[®] microsamplers, blood sampling volume required for bioanalysis is much less than serum or plasma sampling method. Therefore, VAM technology may allow us to increase the quantity and quality of our data while adhering to Institutional Animal Care and Use Committee sampling.

What are the key differences in using VAM for small-molecule pharmacokinetic studies as opposed to larger protein therapeutics?

One obvious difference we noticed during our evaluations is that the recovery process for large-protein therapeutics is easier than that for small molecules. For example, we just needed to soak the dried Mitra[®] microsamplers in PBS with moderate shaking for 1 h at room temperature vs several steps involving several solvents needed for small-molecule recovery.

What are the key considerations for anyone working on preclinical pharmacokinetic studies?

When we work on preclinical pharmacokinetic studies, it is very important to keep in mind of the three Rs: replacement, reduction, and refinement of animal usage. We should make all efforts to deliver high-quality data without unnecessary use of animals. Regarding the application of Mitra[®] microsamplers, since the pharmaceutical industry is developing such a wide variety of therapeutics, each scientist would need to optimize the conditions to retrieve their drugs of interest.

What are the most common challenges of pharmacokinetic studies in modern-day laboratories & what solutions do you use to address these?

Working in a pharmacokinetic laboratory, I often face the challenges of assay development. Because of the new drug concepts and modalities, it is not always easy to develop an appropriate assay to address the goals of each specific project. Not only are we in need of particular reagent pairs for our quantitation target of interest, but also better assay sensitivity and throughput. The challenges motivate us to keep finding ways to increase our knowledge and capabilities. Another challenge of preclinical PK/PD study lies in the number of data sets we desire from every sample of a study. The pharmaceutical industry is evolving so quickly and we are gaining new biological information to apply to our PK/PD characterizations. Therefore, we would like to investigate more aspects of each sample (e.g., more biomarkers). Those needs push us to look for more and better VAM tools so we could obtain more data without increasing blood sample volume.

What emerging technologies are you particularly excited about that are likely to change the future of pharmacokinetic studies?

In the current fast pace of the pharmaceutical industry, every scientist is multi-tasking and responsible for several projects at the same time. I am often running between different assays for different drugs. I would be very excited about assay kits and automation systems that could obtain multiple sets of data from the same set of samples, which would reduce my manual bench work and enable the development of additional new drugs and technologies.

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Reference

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