[16:30 – 17:10]

Pharmacogenomics in Clinical Trials

Dr. Setsuo Hasegawa (Sekino Clinical Pharmacology Clinic)

In the advent of post genome era, clinical studies associated with drug development are likely to be changed drastically. Especially, in phase-I studies where healthy adults are voluntarily enrolled for a trial subject, noticeable improvement will be expected. Clinical trials are intended to be implemented in nature to make assessments on both safety and drug efficacy in trial subjects through scientific analysis based on the view point from pharmacokinetics and pharmacodynamics. With introduction of pharmacogenomics, evidence-based medications rested on genome information would become available in addition to improve the safe for subjects and shorten the term of clinical studies more than ever before.

In Japan, clinical investigations on single nucleotide polymorphism (SNP) of drug metabolism have already been set out to conduct clinical trials in classified subject group of extensive metabolizers or poor metabolizers. Especially, the frequency of CYP2C19 poor metabolizers is relatively high (approximately 20%) in Japanese population, and the genetic variations result in differences of their kinetics and pharmacological actions, e.g. clinical responses to proton pump inhibitors which are mainly metabolized by 2C19 in the liver.

We developed a novel automatic SNPs-typing system and applied it for the genotyping CYP2C19. The developed system is based on analysis of a melting curve of probe DNA bound to the target SNP site using a fluorescence quenching probe. The system enables automated and multiplex SNP genotyping from sample preparation. The results of SNP typing are consistent with the results obtained by allele specific primer PCR method. This full automation analyzing system can be translated to the clinical trials, e.g. classification by the genetic variations of metabolizing enzymes or transporters.

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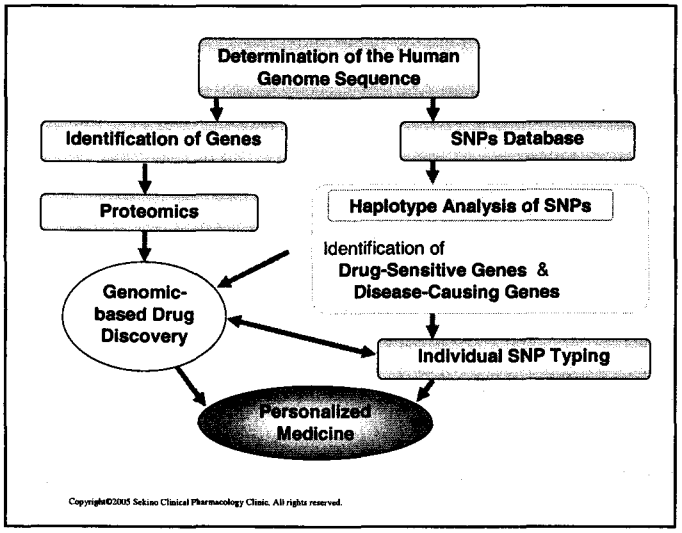

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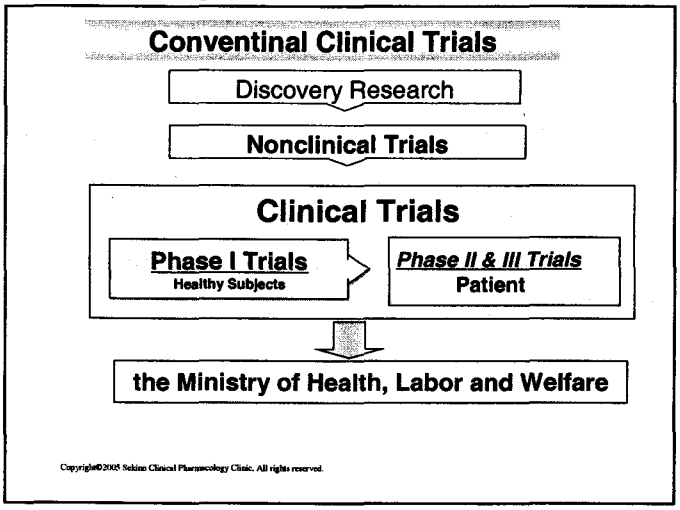

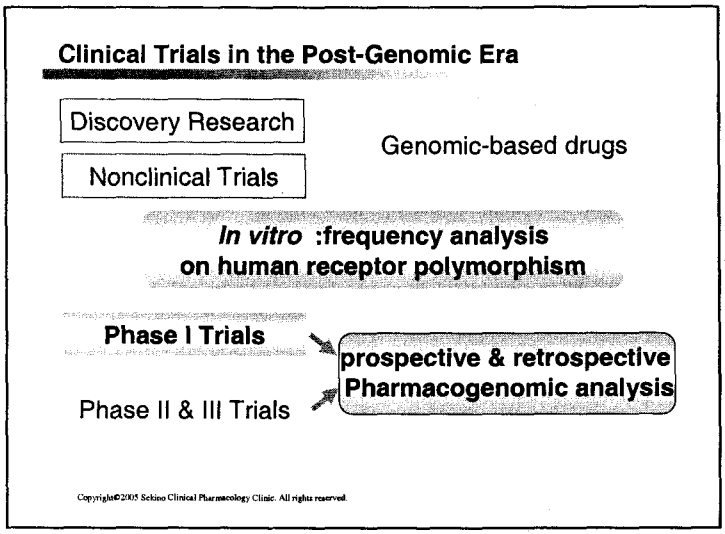

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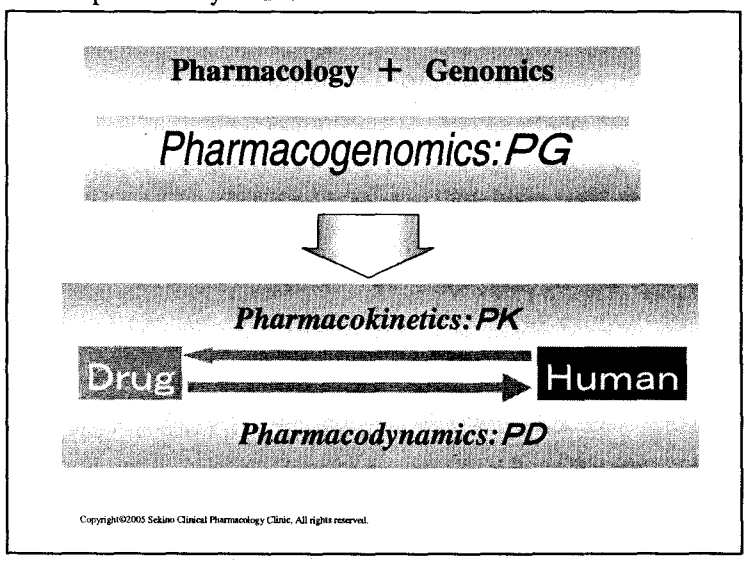


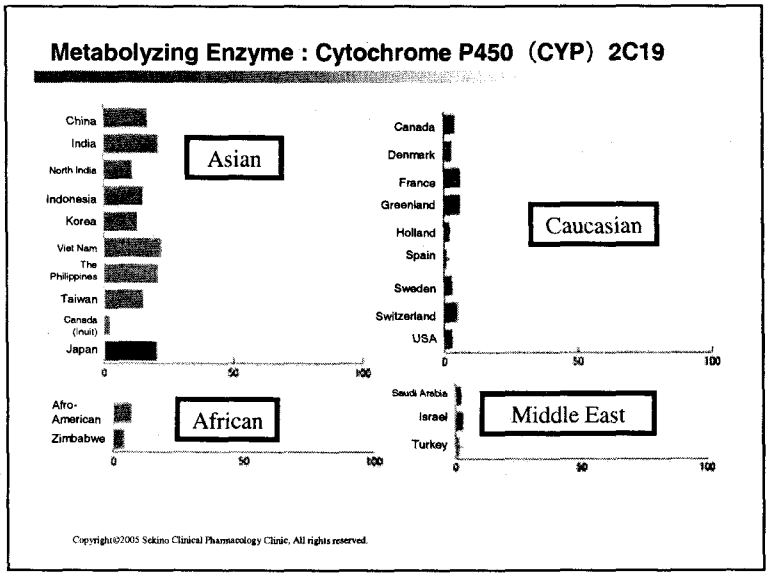
With introduction of pharmacogenomics, evidence-based medications rested on genome information would become available in addition to improve the safe for subjects and shorten the term of clinical trials more than ever before.

In Japan, clinical investigations on single nucleotide polymorphism (SNP) of drug metabolism have already been set out to conduct clinical trials in classified subject group of extensive metabolizers or poor metabolizers.

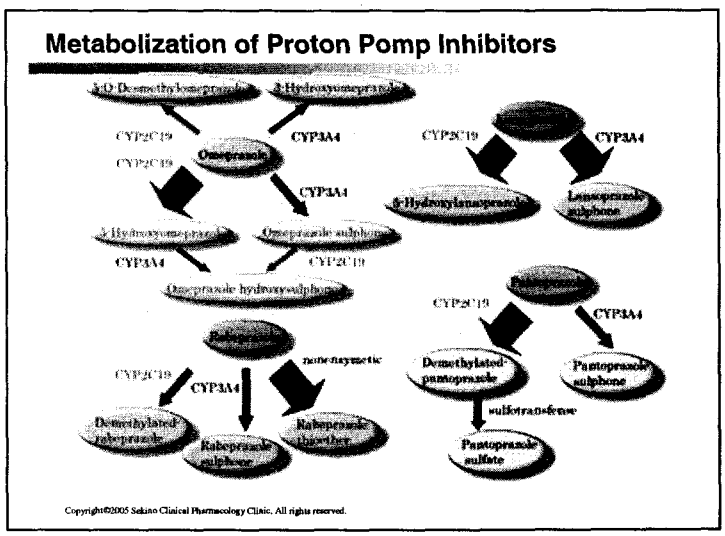
PGt / PGx Studies in Sekino Clinical Pharmacology Clinic

	Biomarkers	Classification		
1: n=72	CYP2C19	EM: 72	PM : exclude	
2: n=72	CYP2C19	EM: 72	PM : exclude	
3: n=32	CYP2C19	EM: 12	IM: 12	PM: 8
4: n=90	CYP2C19	EM: 30	IM: 30	PM: 30
5: n=36	CYP2C19	EM: 18	PM: 18	
	CYP2D6	PM : exclude		
6: n=16	CYP2D6	EM: 10	IM: 6	
7: n=24	CYP2C19	EM: 12	IM: 12	
8: n=18	HLA	HLA-DRB345 · DPB1		
9: n=30	CYP2C9 CYP2C19 CYP3A5 MDR1	Retrospective (banking)		
10: n=20	CYP3A5 MDR1 Receptor X Interleukin Y	Retrospective (banking)		
11: n=31	HLA	HLA-DPB1		
12: n=24	CYP2C19	EM: 12	PM: 12	
13: n=12	CYP2C19	EM: 12		
14: n=16	CYP2C19	EM: 8	PM: 8	
15: n=40	CYP2C9 CYP2C19 CYP3A5 MDR1	Retrospective (banking)		

Especially, the frequency of CYP2C19 poor metabolizers is relatively high (approximately 20%) in Japanese population,

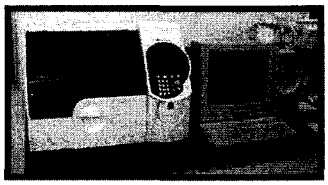


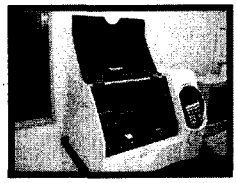
and the genetic variations result in differences of their kinetics and pharmacological actions, e.g. clinical responses to proton pump inhibitors which are mainly metabolized by 2C19 in the liver.



We developed a novel automatic SNP-typing system and applied it for the genotyping CYP2C19.

SNP-typing System ; Research & Development Phase

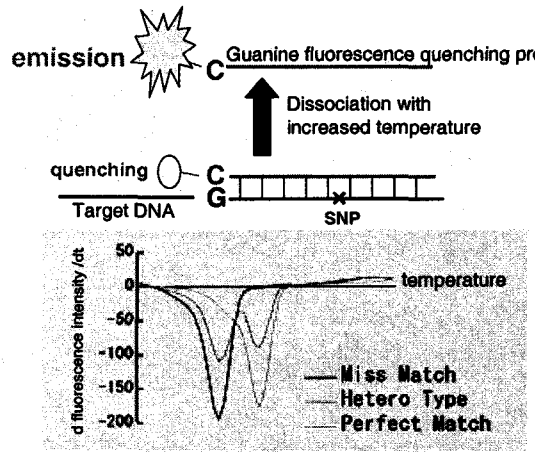




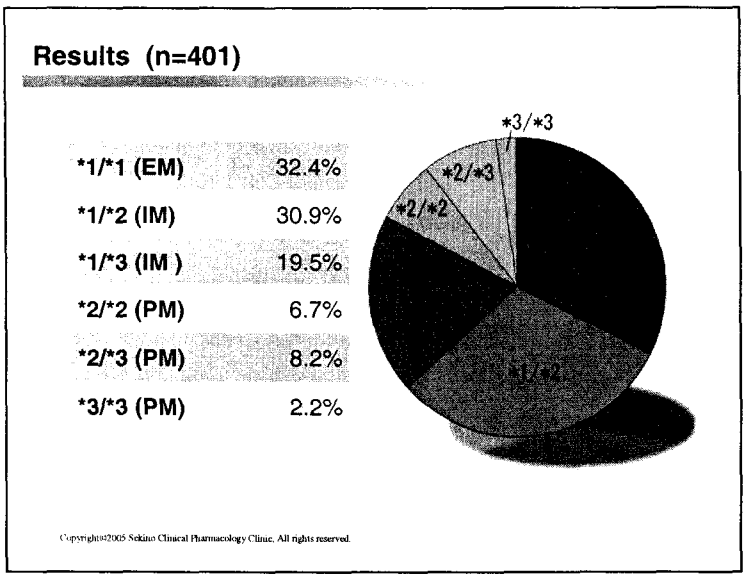
Collaboration with ARKRAY, Inc.
(http://www.arkray.co.jp/english)

ARKRAY handles a wide range of analysis equipment for use in environments as diverse as major hospitals, diagnostic centers and point of care testing. ARKRAY provides the latest equipment for major hospitals and diagnostic centers, easy-to-use, compact testing systems for clinics, and testing equipment for convenient measurement at home or elsewhere for home care.

The developed system is based on analysis of a melting curve of probe DNA bound to the target SNP site using guanine fluorescence quenching probe.



The system enables automated and multiplex SNP genotyping from sample preparation. The results of SNP typing are consistent with the results obtained by allele specific primer PCR method.



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