

Pharmacovigilance Strategy to Maximise Drug Safety



Programme Book

4 March 2011

**Kai Chong Tong, Postgraduate Education Centre
Prince of Wales Hospital, HONG KONG**

Organisers

Centre for Food and Drug Safety

Faculty of Medicine
The Chinese University of Hong Kong

Department of Health

The Government of the Hong Kong SAR

Co-organiser

Medication Safety Committee

Hospital Authority, Hong Kong

Supported by:



Welcome message from the Director of Health

It gives me great pleasure to extend a warm invitation to you to attend the Second Annual Symposium on Pharmacovigilance.

As we all know, pharmacovigilance is the science and activities of collecting, monitoring, researching, assessing and evaluating information from healthcare providers, pharmaceutical industries and patients on the adverse effects of medicines. The purpose of these activities is to enhance the rational use of medicines and pharmaceutical care to patients. As drugs become more potent and sophisticated, pharmacovigilance also plays an increasingly vital role for optimising drug treatment and management of drug side effects. I encourage healthcare professionals to take an active part in pharmacovigilance through the reporting of adverse effects of drugs to the Department of Health. I am confident that this Second Symposium will provide an ideal platform for experts to share new knowledge on pharmacovigilance strategy to maximise drug safety and to enrich all participants with a rewarding experience.

I wish to express my heartiest congratulation to the Organising Committee for coming up with such a comprehensive and coherent programme and I also wish the Symposium every success.

Dr. P.Y. Lam, JP
Director of Health
The Government of the Hong Kong SAR

Welcome message from the President of ISoP

Thank you very much for inviting the International Society of Pharmacovigilance (ISoP) to support the Second Annual Symposium on Pharmacovigilance to be held in the city of Hong Kong on the 4th of March 2011.

At ISoP, our interests have and continue to be the provision of affordable training in pharmacovigilance and the development of tools and strategies to ensure that medicines are safe and that patients and health professionals use these medicines safely and rationally. By encouraging research in pharmacovigilance, promoting regular exchange of information through symposia and workshops and by contributing to education on drug safety, ISoP provides significant scientific and professional leadership to all working in the field of drug safety. The global nature of our membership and our frequent interactions with global normative and technical agencies such as CIOMS and the WHO ensures that ISoP maintains a broad global view of all issues on drug safety with significant inputs from both developed and developing countries. We are therefore pleased about the initiatives in Hong Kong which would go a long way to strengthen patient safety in Hong Kong and across the world, and ISoP is looking forward to collaborating with you and the Department of Health to organize further events in Hong Kong next year.

On behalf of ISoP, it is my greatest pleasure and privilege to congratulate the CUHK and the Department of Health for organising this important meeting and for the impressive list of topics assembled for what would be an immensely beneficial and successful Second Annual Symposium on Pharmacovigilance. I wish you a very successful symposium and the warmest regards from your colleagues in drug safety from across the world.

Dr. Alexander Dodoo
President
International Society of Pharmacovigilance

Welcome message from the President of HKAPI

On behalf of the Hong Kong Association of the Pharmaceutical Industry (HKAPI), I would like to express the warmest congratulations to the Organising Committee and welcome you all to the Second Annual Symposium on Pharmacovigilance, 4 March 2011.

Pharmacovigilance is a vital process for capturing complete safety information about a drug throughout its life cycle. The objective is to reduce the frequency and the severity of adverse effects of drugs, while maintaining or improving their efficacy and effectiveness. This important discipline should improve patient care and safety, which is the ultimate concern of the government, health care service providers, the community, health care professionals and the pharmaceutical industry. Continuing education and training in pharmacovigilance helps promote the culture of safety and safe, effective and quality use of drugs.

This Annual Symposium provides a good opportunity for both health care professionals and pharmaceutical associates to learn about the pharmacovigilance strategy to maximise drug safety. There is also the opportunity to meet the experts and other participants. I sincerely hope you will enjoy this informative programme and you will have a great opportunity to share experiences with friends and colleagues.

Dr. Sian C.S. Ng

President

The Hong Kong Association of the Pharmaceutical Industry

Welcome message from the Chairman of the Organising Committee

On behalf of the Organising Committee, we would like to welcome you to the Second Annual Symposium on Pharmacovigilance in Hong Kong on 4 March 2011. This important meeting on drug safety and pharmacovigilance is organised by the Centre for Food and Drug Safety, Faculty of Medicine, the Chinese University of Hong Kong, the Department of Health and the Medication Safety Committee, Hospital Authority of Hong Kong. The Symposium is supported by the International Society of Pharmacovigilance, Division of Clinical Pharmacology, Department of Medicine and Therapeutics and School of Pharmacy of the Chinese University of Hong Kong and the Hong Kong Association of the Pharmaceutical Industry.

Modern drugs provide significant health benefits in the prevention and treatment of diseases and by improving the quality of life of patients. Drugs that reach the market have favourable benefit-risk profiles, meaning that the benefits (when the drugs are used for the approved indications and dosages in the appropriate patients) outweigh the risks of adverse effects. In general, more information is needed about use in certain subject groups and their effectiveness and safety under real-life conditions, especially when other drugs are used concomitantly and genetic factors are important. In order to maximise benefits and prevent harm to the patients, systems to ensure the safe use of medicines are vital. Pharmacovigilance is defined by the World Health Organization as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem. The ultimate aim is to improve patient care and safety in relation to the use of medicines.

This one-day Symposium focuses on the pharmacovigilance strategy to maximise drug safety. We greatly appreciate the contributions from the renowned speakers, who agree to share their expertise with the participants. The Symposium will also provide the participants with the opportunity to share ideas how we can work together to meet the needs for safe and effective medicines.

We wish to thank all the speakers, chair persons, participants and the supporting organisations for their contributions to the success of this Symposium.

Professor Thomas Y.K. Chan, JP
Chairman, Organising Committee
Director, Centre for Food and Drug Safety, Faculty of Medicine, CUHK

Organisers, Co-organiser and Supporting Organisations

Organisers

Centre for Food and Drug Safety, Faculty of Medicine
The Chinese University of Hong Kong

Department of Health
The Government of the Hong Kong SAR

Co-organiser

Medication Safety Committee
Hospital Authority, Hong Kong

Supporting Organisations

International Society of Pharmacovigilance

Division of Clinical Pharmacology, Department of Medicine and Therapeutics
The Chinese University of Hong Kong

School of Pharmacy
The Chinese University of Hong Kong

The Hong Kong Association of the Pharmaceutical Industry

Organising Committee and Secretariat

Organising Committee

Prof. Thomas Y.K. Chan, JP (Chairman)

Dr. Jones C.M. Chan

Prof. Vincent H.L. Lee

Prof. Brian Tomlinson

Ms. Linda Woo

Dr. Raymond S.M. Wong (Secretary)

Dr. Michael C.H. Chan

Dr. Joseph Lui

Ms. Karen S.Y. Wong

Prof. Hong-Hao Zhou

Secretariat

Ms. Maggie Lee, Centre for Food and Drug Safety, Faculty of Medicine, CUHK

Tel: 2632 3907, Fax: 2646 8756, E-mail: maggielee@cuhk.edu.hk

Website: <http://www.med.cuhk.edu.hk/cfds>

Target Participants

Health care professionals involved in pharmacovigilance, regulatory affairs, public health, risk management, quality assurance, drug safety research and clinical trials, DTC members, DSC members, academics and pharmaceutical associates

Faculty

Prof. Thomas Y.K. Chan

Director, Centre for Food and Drug Safety, Faculty of Medicine, and

Professor, Division of Clinical Pharmacology

Department of Medicine and Therapeutics

The Chinese University of Hong Kong

Dr. Sian C.S. Ng

President

The Hong Kong Association of the Pharmaceutical Industry

Prof. Munir Pirmohamed

NHS Chair of Pharmacogenetics, and

Professor, Department of Molecular and Clinical Pharmacology, and

Deputy Director, MRC Centre for Drug Safety Sciences

The University of Liverpool, UK

Prof. Brian Tomlinson

Professor of Medicine and Therapeutics, and

Head of Division of Clinical Pharmacology

Department of Medicine and Therapeutics

The Chinese University of Hong Kong

Prof. Winai Wananukul

Associate Professor, Division of Clinical Pharmacology and Toxicology

Department of Medicine

Faculty of Medicine

Ramathibodi Hospital

The Mahidol University, Thailand

Prof. Martin C.S. Wong

Associate Professor, School of Public Health and Primary Care

The Chinese University of Hong Kong

Ms. Linda Woo

Chief Pharmacist, Department of Health

The Government of the Hong Kong SAR

Prof. Joyce H.S. You

Associate Professor, School of Pharmacy

The Chinese University of Hong Kong

Prof. Hong-Hao Zhou

Member of the Chinese Academy of Engineering

Chair Professor of Pharmacology and Clinical Pharmacology, and

Dean, Institute of Clinical Pharmacology, and

Director, Pharmacogenetics Research Institute, and

Director, National Training Centre for Clinical Pharmacology

The Central South University, China

Programme

8:30 – 9:00 REGISTRATION

9:00 – 9:05 **Welcome Remarks**

Prof. T.F. Fok, SBS, JP
Dean, Faculty of Medicine
The Chinese University of Hong Kong

9:05 – 9:15 **Opening Address**

Dr. P.Y. Lam, JP
Director of Health
The Government of the Hong Kong SAR

Prof. Thomas Y.K. Chan, JP
Chairman, Organising Committee, and
Director, Centre for Food and Drug Safety, Faculty of Medicine
The Chinese University of Hong Kong

9:15 – 11:00 **Pharmacovigilance to Ensure Drug Safety**

Chair Persons:

Prof. Hong-Hao Zhou
Prof. Brian Tomlinson

9:15 – 10:00 **How We Monitor the Safety of Medicines in the UK**

Prof. Munir Pirmohamed

10:00 – 10:45 **Safety Monitoring of Medicines in Children and Pregnant Women**

Prof. Thomas Y.K. Chan

10:45 – 11:00 **Questions and Answers**

11:00 – 11:15 TEA BREAK

11:15 – 12:45 Pharmacovigilance in Drug Regulation

Chair Persons:

Prof. Munir Pirmohamed

Prof. Vincent H.L. Lee

11:15 – 12:00 Pharmacogenetics and Pharmacogenomics in Clinical Trials

Prof. Hong-Hao Zhou

12:00 – 12:30 Pharmacovigilance in Clinical Trials

Prof. Brian Tomlinson

12:30 – 12:45 Questions and Answers

12:45 – 14:00 LUNCH

14:00 – 15:45 Regulatory Aspects of Pharmacovigilance

Chair Persons:

Prof. Thomas Y.K. Chan

Dr. Heston Kwong

14:00 – 14:30 Overview of Drug Registration in China

Prof. Hong-Hao Zhou

14:30 – 15:00 Regulation of Pharmaceutical Products in Hong Kong

Ms. Linda Woo

15:00 – 15:30 Pharmacovigilance of Vaccines and Snake Antivenoms

Prof. Winai Wananukul

15:30 – 15:45 Questions and Answers

15:45 – 16:00 TEA BREAK

16:00 – 17:55 Building Capacity and Improving Pharmacovigilance Process

Chair Persons:

Prof. Bernard M.Y. Cheung

Dr. Joseph Lui

16:00 – 16:35 Role of Pharmacoepidemiology in Drug Evaluation

Prof. Martin C.S. Wong

16:35 – 17:10 Pharmacovigilance in the Pharmaceutical Industry

Dr. Sian C.S. Ng

17:10 – 17:40 Communicating Drug Safety Information

Prof. Joyce H.S. You

17:40 – 17:55 Questions and Answers

17:55 – 18:00 CLOSING REMARKS

Prof. Brian Tomlinson

Prof. Vincent H.L. Lee

How We Monitor the Safety of Medicines in the UK

Prof. Munir Pirmohamed, The University of Liverpool, UK

Adverse drug reactions are important for the UK— work conducted by us has shown that 6.5% of all admissions to NHS hospitals are due to ADRs, while about 15% of patients develop ADRs while in hospital. Taken together, these result in about 8000 beds in UK hospitals being occupied by patients with ADRs, at a cost of about £1 billion annually. The UK has both active and passive ADR surveillance systems. The yellow card system, which is a spontaneous reporting system, was started in 1964 and currently receives about 20,000 reports per year. Over the last 10 years, the scheme has been extended to other reporter groups including most recently to patients. Like most spontaneous reporting schemes, the main limitations are under-reporting and inability to define the numerator and denominator. The yellow card scheme therefore acts as signal generation pathway, and is particularly important for less common ADRs. In order to validate signals, medicine safety monitoring is supplemented by pharmacoepidemiological approaches including the use of the General Practice Research Database, which is now utilised by regulators, industry and academics and has generated more than 500 publications. More novel approaches are also being evaluated including the use of reporting through electronic prescribing systems and safety registers. The MHRA, the UK regulatory agency, keeps prescribers informed of drug safety issues through its monthly publication Drug Safety Update, while it also has a specific advisory committee on pharmacovigilance. The EU has also introduced new legislation recently which is aimed at strengthening drug safety monitoring in member states, including the UK.

Safety Monitoring of Medicines in Children and Pregnant Women

Prof. Thomas Y.K. Chan, The Chinese University of Hong Kong, Hong Kong

Monitoring the safety of medicines in children and pregnant women is of great importance as only limited information about their efficacy and safety is generated during pre-marketing drug developments. Moreover, conditions for use in clinical trials often differ from those in clinical practice. Post-marketing surveillance is therefore required to ascertain the safety and effectiveness of medicines, especially if population sub-groups, genetic factors, longer term use, drug-drug and drug-disease interactions are involved.

Paediatric pharmacovigilance can be defined as the process of evaluating and improving the safety of medicines used in paediatric patients of all ages. The aims are to detect serious and new adverse drug reactions (ADRs), determine the epidemiology and preventability of ADRs, increase awareness, reduce ADRs, plan risk management strategies and establish the safety of medicines in clinical trials. Several issues about medicines used by children necessitate the need for effective pharmacovigilance. Many medicines used in children are not specifically marked for use in this age group. There may be a lack of appropriate formulations for young children. Diseases and drug toxicity in children are different from those seen in adults. The susceptibility to ADRs may change according to age and stage of development.

It is important to understand the potential effects of taking medicines during pregnancy and the risks involved. The factors to be considered include effects on the pregnancy, effects on labour and delivery and the possible risks on the foetuses (e.g. structural abnormalities and impaired physiological function and alterations to growth). Inevitably, all new drugs have not been studied in women who are, or become, pregnant. It is therefore necessary to collect and analyse drug safety data in pregnancy. Pregnancy registries (or prospective pregnancy follow-up studies) are recommended for medicines that are likely to be used in women of child-bearing potential. Other important sources of drug safety information include cohort studies, databases with linkage to medical records and drug information centres.

Stakeholders in the process of pharmacovigilance include the regulatory authorities, health care professionals, health care systems, the pharmaceutical industry and the patients. Their participation and contribution help ensure safety monitoring of medicines in children and pregnant women is effective and only the safest products are available for use.

Pharmacogenetics and Pharmacogenomics in Clinical Trials

Prof. Hong-Hao Zhou, The Central South University, China

Pharmacogenetics is the study of the role of inheritance in inter-individual variation in drug response. Pharmacogenomics is the use of DNA sequence information to measure and predict the reactions of individuals to drugs. Often, these two terms are used interchangeably. Pharmacogenetics and pharmacogenomics help to select patients who are likely to respond well or safely. The main interest of clinical trial in pharmacogenetics and pharmacogenomics is in identifying patients for whom we can predict drug efficacy and in sparing patients from avoidable adverse effects. To get this information in the case of antihypertensive therapy, we set up a prospective clinical trial with both different dosage of metoprolol based on genotype of CYP2D6 and $\beta 1$ genotyping and a fixed conventional dose in two groups of hypertensive to compare the antihypertensive efficacy of metoprolol. Reductions of blood pressure were differently in these two groups. Major methods of clinical trial to be used in pharmacogenetics and pharmacogenomics are: 1. prospective controlled study in selected genotype of a given gene in normal volunteers. Normally the small number of wild type homozygote or mutation, heterozygote was tested to assess the role of a given gene on PK or PD of a drug. The function of this study is to identify the role of gene variation of a biomarker. 2. Prospective controlled study to compare the selected genotype directed treatment schedule and traditional treatment schedule in large number grouped patients. The function of this study is to find practical treatment schedule that could be guiding clinical practice, i.e. personalized pharmacotherapy. 3. Pharmacogenomics clinical trial also involves in the disease genetics for disease prognostic and diagnosis: rare Mendelian diseases and common complex diseases' susceptibility genes. In drug R&D, current applications of clinical trial in pharmacogenetics and pharmacogenomics are interpretation of clinical trial results, data quality, study design, and biomarkers. In Phase I studies, it could explain outliers or patient-to-patient variability in PK; exclude or include specific patients; normalize genotype frequencies; bridge to other racial populations. In phase II/III studies, it could identify genetically defined groups with more pronounced or rapidly progressing disease; exclude or include at risk individuals; stratify studies based on genotypes; clinical response; risk of adverse drug reactions, develop drugs for specific groups, identify genetic markers associated with clinical outcomes. Currently the clinical trial in pharmacogenetics and pharmacogenomics faced to many challenge issues. The issues raised by Ethics Committees are specify genes, sample ownership, length of storage period, scope of sample use for future research, commercial purpose of samples, limited sample withdrawal period, patient confidentiality and data privacy, investigator role in access/use of samples and data, disclosure of individual results to patients. For the issue of Ethical, Legal and Social Implications, we should answer the questions: who should have access to personal genetic information, and how will it be used, who owns and controls

genetic information, how does personal genetic information affect an individual and society's perceptions of that individual, do healthcare personnel properly counsel parents about the risks and limitations of genetic technology, how is the reliable and useful of fetal genetic testing, how will genetic tests be evaluated and regulated for accuracy, reliability, and utility, should testing be performed when no treatment is available, should parents have the right to have their minor children tested for adult-onset diseases, are genetic tests reliable and interpretable by the medical community, who owns genes and other pieces of DNA. Currently, there is little regulation at the central government level for these issues. Also, there are no agreeable comments in the experts.

Pharmacovigilance in Clinical Trials

Prof. Brian Tomlinson, The Chinese University of Hong Kong, Hong Kong

Clinical trials at all phases of drug development provide the opportunity to identify the relatively common adverse effects of new drugs and to look for signals that adverse effects may be more frequent in particular individuals or populations. Historical examples of drugs that have reached late stages of development, or have been marketed but subsequently withdrawn, demonstrate how the process of drug development can be improved to increase the safety data available in the early stages. For instance, the potential for drugs to cause prolongation of the QT interval has been well recognized in recent years and early phase studies now provide careful monitoring to detect this effect. However, such studies typically exclude subjects with baseline abnormality of the QT interval and if the drug related effect only occurs in susceptible individuals it may be missed. Likewise, in clinical trials those patients taking other medications which might interact with the investigational product are often excluded and the problem of serious adverse drug interactions may not be realised until the drug is used outside of the protected environment of the clinical trial as illustrated by the interaction between cerivastatin and gemfibrozil resulting in rhabdomyolysis. It is therefore essential to perform thorough studies of the clinical pharmacology at an early stage to identify the pathways of drug metabolism and the drug transporters involved in the disposition of the new compound so that important pharmacogenetic effects or potential drug interactions can be predicted and avoided.

Unexpected off target effects can be difficult to identify. The novel cholesteryl ester transfer protein (CETP) inhibitor torcetrapib is an obvious example where the adverse effects of increased levels of aldosterone and increased blood pressure were not fully appreciated until it became obvious in the cardiovascular outcome trial that these were offsetting the potential benefits from the impressive increase in HDL cholesterol. Similarly, such potential adverse effects have been recognised in relation to new treatments for type 2 diabetes and the FDA has initiated new guidelines for evaluating the potential cardiovascular risk that may be associated with these drugs which may be independent of their effects on glycaemic control. Some rare adverse effects, such as liver toxicity, may be difficult to identify until the drug is used in much larger numbers of patients but with increasing understanding of the mechanisms and possible underlying genetic susceptibility to such effects it may become possible to predict these problems at an earlier stage and to make the process of drug development more safe and efficient.

Overview of Drug Registration in China

Prof. Hong-Hao Zhou, The Central South University, China

Many reasons why China needs to globalize the drug research and development. Firstly, China has been having excellent human resources, high-level research/skills, government programs/support. These factors created an attractive drug research and development resources to the possibility of expansion of the regions to global pharmaceuticals. Secondly, China could provide a clinical trial sources for the R&D of drugs that addresses regional illnesses, such as tropical diseases, viral diseases, malignant tumors, etc. Thirdly, the deeds of ideal international companies for incorporation of new compounds and technology to improve the level of drug R&D in China. Chinese government actively encourages MNCs to establish R&D centers in China. It has funded many high-tech parks including Zhongguanchu Science and Technology Park, in Beijing, Zhangjiang High Tech Park in Shanghai, China Medical City in Taizhou, Biolake in Wuhan, Bio and Information Industry Park in Changsha. Accordingly, the globalize pharmaceuticals need to translate the drug R&D from developed areas to China since the market with a huge population, vigorous momentum of economic development, rich resources of clinical cases and potentially huge pharmacy market. In the past decade China has been in the global expansion of international drug company R&D. As early as 2002, Otsuka established clinical R&D center in Beijing. The number of acceptance of clinical research application in China has been increasing in recent years. In 2009, the number of application by foreign enterprise was 517 and the international multi-center application was 205. In 2009, 13 new compounds of chemical drugs (category 1.1) were approved by SFDA. The evaluation of foreign trial data would consider the global trial data, regional trial data and country level trial data and would know that does the drug's safety and efficacy profile provide adequate risk/benefit to the treated patient population. The ethnic pharmacokinetic (PK) data is also important in the evolution of clinical trial data of a new drug application. The challenge of clinical trial in China includes slow regulator process, less experience in conducting CT according to ICH GCP and blood/tissue export permit, etc. China needs to improve their drug R&D regulation and application process.

Regulation of Pharmaceutical Products in Hong Kong

Ms. Linda Woo, Department of Health, The Government of the Hong Kong SAR

Following a series of incidents which caused public concern about the safety of drugs manufactured locally in March 2009, a Review Committee on the Regulation of Pharmaceutical Products in Hong Kong (the Review Committee) was set up by the Government and was tasked to strengthen the regulatory regime of pharmaceutical products. The Review Committee was chaired by the Permanent Secretary for Food and Health (Health) with a broad representation of members from the pharmaceutical sector, the medical profession, academia, patients groups and consumer representatives.

In early January 2010, the Review Committee completed its 9-month study and put forward 75 recommendations which covered improvements in areas from manufacturing to retailing so that a high safety standard could be attained at all levels. The Government and the Legislative Council have accepted all the recommendations. Some recommendations can be implemented with existing resources whereas some will require legislative amendments and/or additional resources. A Steering Committee chaired by the Deputy Director of Health was established in the Department of Health (DH) to steer and monitor the implementation of the recommendations of the Review Committee.

Since the release of the Review Committee report, DH has deployed existing resources and implemented some of the recommendations. In the regulation of drug manufacturers, microbiological monitoring for non-sterile drugs was included during the manufacturing process and the industrial experience of the authorised persons was increased. On the pre-market control of drugs, bioavailability and bioequivalence studies as a registration requirement has been introduced by phases beginning with anti-epileptic drugs and the processing time for clinical trial applications has been shortened. On the regulation of importers/exporters, wholesalers and retailers, a pilot electronic import and export licensing system to track the movement of unregistered pharmaceutical products is being developed and at the same time, Code of Practice for importers/exporters, wholesalers and retailers are being drafted. On post-market control of drugs, a monthly drug bulletin has been published in the website of DH to keep the public and healthcare providers informed of important drug information.

With regards to those recommendations that require legislative amendments, a consultancy has been engaged to conduct a Regulatory Impact Assessment Study to gather views and opinions from the different stakeholders and DH plans to present the relevant instructions to the Legislative Council for discussion within 2011.

Furthermore, with additional resources, the Pharmaceutical Service will be expanded into a dedicated office on drugs to strengthen the regulatory role of the Government in enhancing drug safety. The office will plan and direct the implementation of measures relating to drug safety and it is the long-term commitment of the Government in ensuring drug safety, protecting public health and restoring public confidence in the use of drugs.

It is the believe that the key to the success in raising the standard of the pharmaceutical sector in Hong Kong lies in an effective regulatory regime, the commitment and determination of the professionals to practise to their highest standards and the trade to perform responsibly.

Pharmacovigilance of Vaccines and Snake Antivenoms

Prof. Winai Wananukul, The Mahidol University, Thailand

In general, adverse events (AEs) of any drug vary among the method of studies and populations. Incidences from spontaneous reports are usually lower than intensive monitoring. Population of high concern has higher AEs than those of less concerned population. Adverse events of vaccine in this recent year were overwhelming by Influenza A (H1N1) vaccine. This was because there were many rumors about the vaccine all over the world. From spontaneous report studies of the H1N1 influenza vaccine in general population in various countries, the AEs ranged from 15.2 to 34.0 per 100,000. A study of AEs in health personnel of a university hospital was 515 per 100,000. However, the majority of the AEs were non-serious reaction. Major or life threatening AEs from various studies were low. The common AEs were fatigue, fever, headache, reaction at injection site and myalgia. Many studies suggested that the incidences of Guillain-Barre' syndrome in the population before and after vaccination were not significantly different.

Antivenom is immunoglobulin which is usually pepsin-refined F(ab')₂ fragment of whole IgG from the plasma of a horse, mule or donkey (equine) or sheep (ovine) which has been immunized with the venoms of one or more species of snake. The efficacy and safety of the antivenom depend on the type of these antivenins. The AEs from antivenom administration include early reactions and late reactions. The acute reactions are both true anaphylaxis and anaphylactoid reaction. In most cases, these reactions are not truly "allergy". Complement activation by IgG aggregates is the more likely mechanism for these anaphylactoid reactions. The common AE is urticaria. Incidence of early adverse reactions ranged from 5% to 43%. However, the mortality rate of these reactions was low.

Role of Pharmacoepidemiology in Drug Evaluation

Prof. Martin C.S. Wong, The Chinese University of Hong Kong, Hong Kong

Pharmacoepidemiology is the study of the use of and the effects of drugs in large numbers of people. It applies the methods of epidemiology to the content area of clinical pharmacology, and is an effective tool to capture useful data for clinicians, researchers and policy-makers.

There are many potential contributions of pharmacoepidemiology to the evaluation of drugs. It provides information which supplements data available from premarketing studies, allowing better quantitation of the incidence of known adverse and beneficial effects of medications, and hence safe marketing of pharmaceutical products. It also generates new types of information not available in premarketing studies, like discovery of undetected medication effects, evaluation of drug utilization patterns and their adherence profiles, assessment of effects of drug overdoses, reassurance about drug safety, association between medication use and clinical outcomes, as well as analysis of the cost-effectiveness of different prescription practices.

From the academic point of view, the use of pharmacoepidemiological techniques from large clinical datasets could offer additional support for randomized controlled trials, which might be limited by the relatively small numbers of patients studied, the occasionally strict inclusion and exclusion criteria in subject recruitment, and the short time period designed for patient observation. Some exemplars include the General Practice Research Database (GPRD) in the UK, the United HealthCare Research Databases in the US, and the Italian National Health Service Database in Italy. However, some limitations like the absence of potential confounding variables and indication bias must be adequately addressed and controlled by appropriate statistical techniques before their utilization.

In order to best utilize large datasets in generating findings of significant implications, the accuracy and completeness of information in the datasets are important prerequisites. In this seminar, the various roles of pharmacoepidemiology in drug evaluation will be further elaborated. This is followed by illustration of some international studies using clinical datasets leading to high impact publications, as well as some studies conducted in Hong Kong. The future direction of developing pharmacoepidemiology studies in collaborative research efforts will be highlighted.

Pharmacovigilance in the Pharmaceutical Industry

Dr. Sian C.S. Ng, The Hong Kong Association of the Pharmaceutical Industry, Hong Kong

Pharmacovigilance is the pivotal process for ensuring a pharmaceutical product remains on the market. In today's world, the drug industry faces the challenges of increasingly complex and continuously changing regulations, a higher level of inter-disciplinary expertise is required to ensure effective and safe drugs are put into the market. Moreover, the arena of drug safety continues to be in the media spotlight so it is important that the patient is the primary focus. Multinational pharmaceutical companies are trying the best to make sure pharmacovigilance is handled effectively with the correct tools so as to detect and have quick response to any safety concerns with a product.

Many people believe that pharmaceutical companies are dishonest and only focus on profit making. In fact R&D pharmaceutical companies are putting a lot of efforts on drug safety and pharmacovigilance processes in order to ensure patient health. The aims of pharmacovigilance within the industry are essentially the same as those of regulatory agencies; that is to protect patients from unnecessary harm by identifying previously unrecognised drug hazards, elucidating pre-disposing factors, refuting false safety signals and quantifying risk in relation to benefit.

To ensure a vigorous pharmacovigilance monitoring is taken place, different courses of actions are being conducted during the processes of drug discovery, clinical trials, pre-marketing as well as post marketing phases. In particular, post-authorisation safety studies are carried out specifically to evaluate product safety in different patient groups after the product is launched to a wider population. There are also Pharmacovigilance Spontaneous Reporting and Periodic Safety Update Reports to monitor the aspects of product safety and adverse reactions. Patient is always the primary focus of any pharmaceutical company. In present days, pharmacovigilance is handled comprehensively with the correct tools and pharmacovigilance in the industry will continue to grow and develop as a discipline.

Communicating Drug Safety Information

Prof. Joyce H.S. You, The Chinese University of Hong Kong, Hong Kong

Availability of important drug information, education and effective communication at all stages of drug development and at post-market use are essential for rational drug therapy and patient safety. Prescribers and patients need information about the established benefits and harms of a drug. Drug safety information enables prescribers to avoid using a drug in circumstances of particular risk, to choose preventive strategies, to design appropriate monitoring plan for harm when the risk is defined, and to recognise an adverse reaction when it occurs. Patients also need to know about harms of drug treatment to decide on likely balance of benefit to harm. Empowering the patients with drug safety information during the prescribing process could enhance the patient adherence to drug therapy. Yet what is the best way to communicate drug safety?

The way in which important, emerging drug safety information is communicated to the public and health-care professionals has changed remarkably over the past decade. In an environment of instant and global electronic communication, and in response to the challenge of meeting the public's expectations of transparency and accountability, we need communication tools to incorporate early communications about ongoing safety reviews, and policies that describe what and when to communicate. The present seminar will discuss the different levels at which drug safety information is obtained and communicated, and examine how the content of drug safety information and its significance, and the method of communication at each level can be improved.



Sponsors for the Second Annual Symposium on Pharmacovigilance:



Department of Health
The Government of the Hong Kong SAR



Centre for Food and Drug Safety
Faculty of Medicine, The Chinese University of Hong Kong



Pfizer Corporation



AstraZeneca Hong Kong Limited



Novartis Pharmaceuticals (HK) Ltd.