Workshop

Biomarkers and Companion Diagnostics

24 September 2009

Malmö University Hospital
Malmö, Sweden

TRAVEL
From Kastrup airport
12 min by train to Malmö South (Svågertorp) + a short taxi drive
or
30 km by car directly from Kastrup to Malmö University Hospital
[There is a fee for the passing the Öresund bridge by car]

TAXI SKÅNE +46 (0)46 330 330

Workshop
Biomarkers and Companion Diagnostics

24 September 2009

Venue: Malmö University Hospital, CRC-building, Entrance 72,
Locality: Seminar room 60-12-015, 12th floor (2:ond from street level)

Overview Programme

09.30 - 10.00	**Registration with coffee/tea**
10.00 - 10.20	**Welcome - Intention with this meeting** (Gunnar Hörnsten, CEFFORT AB)
Plenary program:	
10.20 - 10.50	**Biomarkers in development of drugs for respiratory diseases** (Magnus Korsgren, AstraZeneca)
10.55 - 11.25	**Genetic markers predicting dyslipdemia, cardiovascular disease and type 2 diabetes** (Marju Orho-Melander, Lund University)
11.30 - 11.45	Short break
11.50 - 12.20	**Identifying indications and patients where a new drug is efficient** (Jesper Dahlgaard, Medical Prognosis Institute)
12.25 - 12.55	**Therapeutic drug monitoring and clinical pharmacogenetics at Karolinska today** (Erik Eliasson, Karolinska Institutet)
13.00 - 14.00	Lunch and networking
14.00 - 14.30	**Health economics of biomarkers and companion diagnostics** (Christian Asseburg, The Swedish Institute for Health economics)
14.35 - 15.05	**Science base for competitive development of high value companion diagnostics** (Henrik Winther, DAKO A/S)
15.10-15.30	Coffee
15.35 - 16.20	**Discussions:** • Towards a mutually beneficial integrated approach in support of treatment decisions • Creation of incremental values across the value chain: drug development, diagnostics and clinical/laboratory chemistry/pharmacology (Chaired by Jan-Gunnar Gustafsson, Bio Evaluation AB)
16.30 - 16.40	**Suggestion to a CEFFORT®: New cost effective tools for improved treatment out-comes** (Gunnar Hörnsten, CEFFORT AB)
16.40 - 17.00	**Discussion and Closing remarks**
17.00	**Drinks**

The intention with this meeting
(Gunnar Hörnsten, CEO, CEFFORT AB)

Abstract: Following on the traditions of NbiNet and DiagISN, this meeting contributes to information exchange and development of business and R&D in the Nordic region.

A key ambition is to support our members in the strengthening of their international competitiveness. This is done e.g. through improved communication on areas where industry can make a difference in developing new products that simultaneously improves Health care economy, the efficacy and quality of treatments including patient care.

Person: Gunnar Hörnsten has more than 25 years of experience within Biotechnology. He has established and coordinated/managed Networks and larger R&D programmes involving many participants (total exceeding 150) on the Nordic market since 1994. With a PhD from Linköping Institute of Technology he has worked cross-diciplinary within Life Sciences. His speciality area involves analytics within Microbiology and Biotechnology. Founder of Hörnstens Analytica in 1992. Founder and CEO of CEFFORT AB in 2009.

Biomarkers in development of drugs for respiratory diseases (Magnus Korsgren, AstraZeneca)

Abstract: Drug development is a costly and time consuming exercise. When a molecule is identified as a potential drug candidate 7-10 years of development remains to make it a marketed drug and 4 of 5 drug candidates will fail for one reason or another during this time. To be able to accurately predict long term positive effects or side effects from relatively short clinical trials is thus of paramount importance to the pharmaceutical industry.

Personalized health care (right drug to right patient) will be increasingly important in order to identify patients most likely to get optimal benefit of a certain treatment. The use of different biomarkers to achieve these goals will be discussed.

Person: Associate Professor Magnus Korsgren is Disease Area Medical Leader, Respiratory and Inflammation Therapeutic Area, AstraZeneca R&D. In his role, he is involved in a range of drug development activities spanning from target selection to phase II clinical trials. Magnus Korsgren obtained his medical degree and completed higher specialist medical training in Clinical Pharmacology in Lund, Sweden. He has 15 years experience in the respiratory research field and has a special interest in phase I and II clinical testing of new therapies for asthma and COPD.

Genetic markers predicting dyslipidemia, cardiovascular disease and type 2 diabetes
(Marju Orho-Melander, Lund University)

Abstract: Using genome-wide association-studies (GWAS) and large replication efforts we have mapped 30 loci (17

novel) that contribute to variation in lipoprotein concentrations and created a genetic risk score to predict cardiovascular disease (CVD). GWAS studies have identified > 20 genetic loci for T2D and >15 that contribute to genetic predisposition to obesity. Aiming to better biological understanding and genetic risk assessment, life style recommendations, prevention and treatment possibilities of dyslipidemia, obesity and CVD, our studies now focus on: 1) Gene-diet interactions between the identified lipid- and obesity genes and dietary factors; 2) Improving the genetic risk score to predict CVD by adding information on all validated gene variants and testing if such score adds significant clinical information regarding individual risk assessment beyond classical risk factors; 3) Characterization of intermediate phenotypes associating with genetic markers associating with lipids/lipoproteins/obesity by relating them to levels of classical CVD risk factors, lipid subfractions, fatty liver and other insulin resistance and inflammation markers.

Person: Marju Orho-Melander is associate professor of experimental endocrinology and senior lecturer in medical research (multifactorial human genetics) at the Lund University, Department of Clinical Sciences. She defended her thesis on human glycogen synthase genes in 1999 and has since then been devoted her research on genetic causes of type 2 diabetes, metabolic syndrome, cardiovascular disease and dyslipidemia. During the last years her group has focused on identification of genes regulating lipid levels from genome wide association studies and successfully utilized this information to predict cardiovascular disease in population. Dr Orho-Melander has published 65 papers in international scientific journals.

Identifying indications and patients where a new drug is efficient (Jesper Dahlgaard, Medical Prognosis Institute)

Abstract: Being able to select the patient sub population where a novel drug is efficient is the new paradigm for both the drug development industry and the treating clinician.

Biomarkers that can be used to select the responding patients for particular drugs are crucial in this process. Here we present a DNA chip based universal Drug Response Predictor (DRP) based on gene expression. The presented DRP is based on in vitro data from a large number of cell lines treated with the drug leading to both high accuracy and efficiency in response prediction. As can be seen from the presented data on e.g. Belinostat and others, the DRP is unrivalled in its ability to select a cancer type that will respond to a drug. In conclusion new methods like the presented DRP can save costs for clinical trials as well as reduce wasted patent time and the cost/benefit ratio of this application is very low.

Person: Jesper Dahlgaard is Head of Clinical Trials & Development at Medical Prognosis Institute (MPI), Denmark. JD worked from 2001 to 2008 as associate professor and senior scientist at Odense University Hospital (OUH) and at Aarhus University Hospital (AUH) with research on global gene expression in cancer and stem cells. Before he came to MPI he was principal investigator in a national and international collaborative project on prediction of chemo sensitivity in Multiple Myeloma.

Therapeutic drug monitoring and clinical pharmacogenetics at Karolinska today (Erik Eliasson, Karolinska Institutet)

Abstract: The Clinical Pharmacology section of the Karolinska University Laboratory analyse more than 60.000 patient plasma samples per year. The routine analytical spectrum covers more than 100 clinically used drugs and the methodology is mainly based on LC-MS. All analyses are assessed and commented by doctors that consider the plasma concentration in light of individual clinical data on lab requests. The clinical indications for therapeutic drug monitoring (TDM) vary widely; for some drugs being recommended in the drug label with a direct impact on dosage, but in other cases restricted to individual pharmacotherapeutic problems as a missing piece of information or a way to handle variability in pharmacokinetics for instance in the intensive care unit. The same is true for pharmacogenetic analysis where it is possible to distinguish between analyses that should be run prospectively for most patients, or be limited to retrospective investigations of individual problem-cases. Today, genotyping is offered on a routine basis for different CYP-genes, TPMT and HLA-B*5701. An increased use of both TDM and patient genotyping will be discussed; in post-marketing studies on poorly characterised subpopulations of patients, i.e. those at risk of markedly different drug exposure, therapeutic failure or rare, adverse drug reactions.

Person: Erik Eliasson is associate professor in clinical pharmacology at Karolinska Institutet and has the medical responsibility for Therapeutic Drug Monitoring (TDM) and Clinical Pharmacogenetics at Karolinska University Hospital, Stockholm. After a PhD on cytochrome P450 regulation in the laboratory of Magnus Ingelman-Sundberg, Karolinska Institutet, and additional research on drug-induced liver injury as a post-doc at Imperial College School of Medicine, London, Eliasson has had a clinical position at Karolinska Huddinge in combination with research focusing on pharmacogenetics, drug disposition and drug-drug interactions. Last year, he was working at AstraZeneca R&D Södertälje as research physician in early clinical studies on neuroscience drug candidates.

Health economics of biomarkers and companion diagnostics (Christian Asseburg, The Swedish Institute for Health economics)

Abstract: With limited health-care budgets and increasing health-care costs, health economics has become an important tool to help decision-makers optimise spending on health. In many countries, demonstration of treatment value are required when applying for a reimbursement price for a novel drug or treatment. To allow comparisons of treatment value across different diseases, the quality-adjusted life-year (QALY) has become a standard in health-technology assessment (HTA), but disease-specific outcomes may be used in some studies. The result of health-economic evaluation is a "price tag" of a novel treatment in terms of incremental costs per incremental benefits, for example cost per QALY gained.

Whereas HTA methods have established their place in pharmacoeconomics, they are not commonly used in the pricing of diagnostics. However, in terms of treatment outcome, there is a clear benefit of selecting those patients for treatment who are most likely to benefit, according to prior diagnostics or biomarkers. These benefits must be seen in relation to the cost of testing and cost of treatment. A gen-

Workshop organiser

CELS Network www.ceffort.org

Gunnar Hörnsten, CEO
CEFFORT AB

eral introduction to the process of health-technology assessment is presented and illustrated with an example from Sweden. An outline how the current process can be adapted to the co-development of tests and treatments is presented, highlighting the value of testing and implications for the pricing of novel pharmacological agents and the pricing of diagnostic tests. Health-economic modelling may be useful in this setting to determine cost thresholds below which the payer may consider a novel treatment cost-effective.

Person: Dr. Christian Asseburg has applied Bayesian statistical modelling to health economics, first at the Centre of Health Economics at the University of York, England, and currently at the Swedish Institute for Health Economics (IHE) in Lund. His interests include meta-analyses to combine evidence on treatment effectiveness from multiple trials within a disease area. Where data on different relevant quantities are available (for example, number of patients responding to a treatment as well as other measures of patient improvement), hierarchical approaches may be used to reduce decision uncertainty. Christian has worked on several cost-effectiveness models that have been used by decision-makers (e.g. a review of treatments for psoriatic arthritis, for the UK health-technology assessment agency NICE; and a review of treatments for depression for the Swedish TLV).

Science base for competitive development of high value companion diagnostics (Henrik Winther, Director Immuno-Histology, DAKO A/S)

Abstract: Genetic variations, protein expressions variations and activated pathway variations – together described as molecular profiling variations – are key elements when differentiating/sub-classifying cancer patients. These molecular variations are the main drivers in the development of companion diagnostics (pharmDx's) used to enrol cancer patients into more personalized (as opposed to the "one-fits-all" model) drug regimen. Development of a pharmDx requires a close collaboration between the pharmaceutical- and diagnostic company – Dako is a leader within the field of cancer companion diagnostics.

Person: Dr. Henrik Winther has almost 9 years of experience within development of cancer diagnostic antibodies used as confirmatory single reagents or in companion diagnostic assays. He is presently director of Immunohistology and Companion Diagnostics (pharmDx) at Dako. He was educated as a veterinarian and holds a PhD within the topic of "angiogenesis".

Discussions: Chaired by: Jan-Gunnar Gustafsson, Bio Evaluation AB

Person: Jan-Gunnar Gustafsson has 30 years in biotechnology including diagnostics and biopharmaceutical industry. He has broad experience of assay development, manufacturing and process development of biopharmaceuticals, including technology transfer to large-scale production plants. He has also been responsible for marketing, selling, proposals and negotiations 'Fee For Service', including setting up of the strategy for the business. Has performed Due Diligence and set up the legal and business deal. He has an Executive MBA from The Stockholm School of Economics and was member of the board for CBioSep, the Swedish Centre for Bio Separation in Lund, Senior Vice President, Process Development and Manufacturing, Resistentia Pharmaceuticals AB, CEO for Entreprenör-Center Development AB, Uppsala and Klostervine AB.

Suggestion to a CEFFORT®: New cost effective tools for improved treatment out-comes
(Gunnar Hörnsten, CEFFORT AB)

Binding Registration
Biomarkers and Companion Diagnostics

Discount price for members of *CEFFORTs in Life Sciences

early registration (before 090904)	600 SEK/person
final registration deadline 090917	950 SEK/person

Non-members of *CEFFORTs in Life Sciences

early registration (before 090904)	1 950 SEK per person
final registration deadline 090917	2 450 SEK per person

See www.ceffort.org for information on membership

*VAT (25 %) will be added for Swedish participants and participants without international VAT registration number.

Send an email with the information below to:

registration@ceffort.org

Needed information:
- Company/University/Organisation
- Name, email, telephone and address of Participant
- International VAT reg. number (non-swedish participant)

Please: specify which meeting that you register to!

Confirmation of Meeting and Registration (Disclaimer)
A formal confirmation of the meeting will be sent via email to the participants on the day after the final registration date. The organisers takes no responsibility for travel or other costs in the case an unconfirmed meeting is moved to a different venue, cancelled or postponed.

Questions on registration: Call +46 (0)46 286 3351

CEFFORT AB,
Ideon Science Park,
SE-223 70 LUND, Sweden
www.ceffort.biz