



RESEARCH CONFERENCES

ESF-UB Conference in Biomedicine

Pharmacogenetics and Pharmacogenomics: Practical Applications in Routine Medical Practice

Hotel Eden Roc, Sant Feliu de Guixols (Costa Brava)
• Spain
6-11 June 2010

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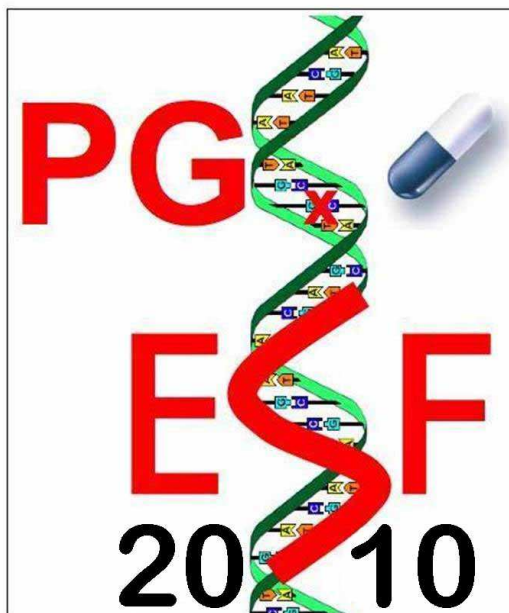
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Highlights & Scientific Report



Conference Highlights

Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)

The third ESF-UB Conference in Biomedicine on Pharmacogenetics and Pharmacogenomics took place in Sant Feliu de Guixols, Spain from June the 6th to June the 10th: it was focused on « *Practical Applications in Routine Medical Practice* ».

Pharmacogenetics started in the fifties and was for a long time restricted in a small research area. In the nineties, the knowledge obtained on drug metabolism (cytochrome P450s) and its pharmacokinetics consequences was progressively integrated into guidances published by European and American drug agencies for drug companies. Pharmacogenetics labels appeared in some drug summarized product characteristics at the beginning of the century, but individual pharmacogenetic testing remained advised or recommended, but seldom compulsory. Few years later, tumoral genetic testing became mandatory before the prescription of several anti tumor drugs.

Due to this rapid evolution of pharmacogenetics in the recent years, from basic science to translational research and to personalised medicine we thought 2 years ago that it would be interesting to summarize which pharmacogenetic information might be useful for patient's therapy and try to make some recommendations on which pharmacogenetic tests should be performed in routine medicine and what could be the advices we might give to physicians for some pharmacogenetic tests.

We planned different sessions on the most important areas of medicine where pharmacogenetics might be presently useful: a whole day was dedicated to oncology covering constitutional as well as tumoral pharmacogenomics. Additional sessions were dedicated to cardiovascular drugs, adverse drug reactions, and organ transplantation. A last session was planned to raise discussions between pharmaceutical companies, drug agencies and reimbursement companies.

Plenary discussion sessions at the end of each day, allowed to summarize the major informations of the day and to define which tests for which drugs should be proposed in routine medical practice and what type of comments should be given for each pharmacogenetic test (Contra indication? Which molecule to choose in the class? What dose to recommend?). We tried to make our best to make the youngest of us to participate to these discussions.

Two night poster sessions were held to be sure to obtain scientific discussion between junior and senior participants. Both sessions had a great success.

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Scientific Report

Executive Summary

(2 pages max)

The third ESF-UB Conference in Biomedicine on Pharmacogenetics and Pharmacogenomics in Sant Feliu de Guixols, Spain was focused on « *Practical Applications in Routine Medical Practice* ».

Our aim was to define among the mass of scientific data obtained during the last sixty years in the field of pharmacogenetics and pharmacogenomics which ones could be useful for patients in routine medical medicine and what could be the informations given to physician for a specific drug and a specific pharmacogenetic test. We focused on several areas such as oncology, adverse drug reactions, cardiovascular drugs and organ transplantation. During specific plenary discussion sessions, several cases were discussed and could lead to practical recommendations such as CYP2D6 for Tamoxifene in post menopausal breast cancer, TPMT for azathioprine in inflammatory bowel disease, VKORC1 and CYP2C9 for individualizing the dose of oral anticoagulants, HLAB*5701 allele for abacavir and flucloxacillin hypersensitivity reactions, CYP3A5 for individualizing the dose of tacrolimus in renal transplantation, K-ras for cetuximab to define responder patients in metastatic colon cancer, EGFR for gefetinib to define responder patients in non small cell lung cancer.

Conclusion of the discussions and practical informations will be published this year (2010) in "Pharmacogenomics".

Scientific Content of the Conference

(1 page min.)

- *Summary of the conference sessions focusing on the scientific highlights*
- *Assessment of the results and their potential impact on future research or applications*

Oncology session: three major interventions should be mentioned:

The first by Miguel A Molina was on EGFR pharmacogenomics in non small cell lung cancer. This team from Barcelona published this year in the New England Journal of medicine the results of a national survey indicating the usefulness of tumoral EGFR pharmacogenomics in order to define tumour, which will respond (activating mutations) to EGFR antagonist (tyrosine kinase inhibitors). The authors also stressed on new techniques available to have the best diagnostic accuracy and to identify as soon as possible mutations such as T790M that will confer resistance to gefetinib or erlotinib. Such results are really at the top of scientific knowledge, an additional paper published in the NEJM 3 weeks after the conference confirming the results from Molina et al.

Hiltrud Brauch made the second major intervention from Stuttgart showing that women with loss of function alleles of CYP2D6 (an enzyme that bioactivates the prodrug Tamoxifene) have a poorer response to Tamoxifene. These results were recently published in the Journal of clinical oncology, JAMA and cancer research in the last years giving an excellent basis for a rationale individualized prescription based on a pharmacogenomics test.

Pierre Laurent-Puig made the third major talk from Paris concerning Tumoral mutation in K-ras, which confer resistance to monoclonal antibodies raised against EGFR in metastatic colon cancer. Following the work of this team, the European agency introduced a pharmacogenetic label for these EGFR antagonists indicating that tumours showing such K-ras mutation should not be treated with this drug.

In the Cardiovascular session, two major drugs received our attention: oral anticoagulants and clopidogrel.

There are now prescribing algorithms to find the best warfarin (oral anticoagulant) dose depending on the individual VKORC1 and CYP2C9 genotypes. The FDA has now proposed these algorithms in warfarin SPC's in April 2010. A large European randomized trial (financed by the seventh European PC) is going to start this year to test the benefit of such a pharmacogenomics prescription for warfarin but also other oral anticoagulants used in Europe (phenprocoumon and acenocoumarol). The leader of the project made this European presentation.

A recent work published in the New England Journal of medicine in 2009 has shown that patients with loss of function alleles of CYP2C19 (an enzyme that bioactivates the prodrug clopidogrel) have a poorer response to clopidogrel after a myocardial infarction. Different groups have meanwhile confirmed this result. One of the members of the initial work made a talk in Sant Feliu and it was concluded that patients after an MI treated by stenting and carrying a CYP2C19 loss of function allele should receive prasugrel (Independent of CYP2C19 activity) instead of clopidogrel.

In the ADR session, the results of recent genome wide association studies, highlighted several HLA alleles, namely HLAB*5701 to predict either abacavir hypersensitivity or Flucloxacillin drug induced liver injury, a recent work published this year in Nature genetics.

Forward Look

(1 page min.)

- Assessment of the results
- Contribution to the future direction of the field – identification of issues in the 5-10 years & timeframe
- Identification of emerging topics

▪ Is there a need for a foresight-type initiative?

The thematic of the future (fourth) pharmacogenetics/pharmacogenomics in 2012 has been discussed during the meeting and summarized during the business session: "Pharmacogenomics of common diseases" and will pay attention to the future results provided by the next generation sequencing as well as the epigenetics data.

Atmosphere and Infrastructure

- The reaction of the participants to the location and the organization, including networking, and any other relevant comments

The atmosphere was excellent; participants had long friendly discussion during the sessions as well as the poster nights. At the beginning of the meeting most of the participants did not know each other's. There was a fairly good exchange between senior and junior participants and many collaborations started during the meeting between different European groups.

The infrastructure is marvellous, the hotel is very pleasant and the working people are very kind with the meeting participants. Food was very fine (Mediterranean cooking) and room OK.



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Date & Author:

June 2010 the 28

Laurent Becquemont Chair of the meeting