ABIRISK

Making novel drugs safer for patients

A growing number of medicines are based on biological molecules such as proteins and monoclonal antibodies. These novel drugs have resulted in new, more effective treatments for a number of serious conditions. Yet sometimes these medicines trigger a response from the patient's immune system, which can decrease the effectiveness of the drug or cause severe side effects. The aim of the IMI-funded ABIRISK project is to shed new light on the factors behind this immune response. The project, which represents the first concerted effort to solve this problem, will aid in the creation of new, safer biopharmaceuticals and also generate tools to determine how individual patients are likely to respond to them both in clinical trials and after release to the market.

Biopharmaceuticals are drugs that are biological in origin (i.e. are made of proteins or DNA for example) and are manufactured using biotechnology. A number of biopharmaceuticals are already in use and have dramatically improved quality of life for patients with serious, hard to treat conditions such as multiple sclerosis, Crohn's disease, diabetes, rheumatoid arthritis, haemophilia A and some cancers. However, in some patients, biopharmaceuticals can trigger an immune reaction, a phenomenon known as immunogenicity. When this happens, the immune system produces antibodies (ADAs) that neutralise the drug, which can reduce the effectiveness of the biopharmaceutical. In some patients, the immune response causes side effects such as a rash, chest pains, or a fall in blood pressure. In the most severe cases, it can trigger anaphylactic shock and even prove fatal.

Immunogenicity – the known unknowns

Diverse factors appear to be involved in immunogenicity. On the drug side, both the compound and the route and duration of administration seem to play a role, while on the patient side, the type of disease, age, genetic background and interactions with other medicines may be risk factors.

Therefore it is extremely hard to predict which biopharmaceuticals will have immunogenicity problems; although many tests exist, these are not always accurate. Furthermore, knowing which patients are at greatest risk of mounting an immune response to a given biopharmaceutical is extremely difficult.

Reducing the risks

Yet even though immunogenicity continues to pose a problem in the development of new drugs, until now there has been no major effort to solve the problem.

Enter the ABIRISK project, which aims to give biopharmaceuticals a much-needed boost and represents the first concerted effort to tackle the immunogenicity problem by bringing together leading experts from hospitals, academia, industry, and small companies. The project will set up laboratory tests to probe the immunogenicity of several biopharmaceuticals that are already used on patients. The scientists will then match their test findings with the effect the drug actually has on patients. This will help the team to develop tools that are better at predicting immunogenicity during drug development.

Many pharmaceutical companies, academic institutions and patient registries have large amounts of data on biopharmaceuticals and patients' responses to them. In ABIRISK, these diverse databases

ABIRISK at a glance

Full project title: Anti-Biopharmaceutical Immunization: Prediction and Analysis of Clinical Relevance to Minimize the Risk

Start date: 01/03/2012

Duration: 60 months

Total cost: €34.9 million

Project coordinator: GlaxoSmithKline

Managing entity: INSERM

Project external website: www.abirisk.eu (design in progress)

will be assembled into a single immunogenicity databank that will help researchers pinpoint the factors that influence a drug's immunogenicity and patients' risk of it. This will allow the researchers to generate tools that will accurately predict whether a patient will mount an immune response to a biopharmaceutical and how that immune response will affect the efficacy and safety of the drug.

Safer, more effective drugs for patients

Immunogenicity means many patients today are denied the life-changing benefits of biopharmaceuticals. ABIRISK will ultimately result in a new generation of biopharmaceuticals with lower immunogenicity that can be safely and effectively used by more patients. In addition, the project will allow clinicians to determine which patients will respond best to which biopharmaceutical, thereby preventing patients from suffering the side effects of a drug that does not suit them.

For Europe's pharmaceutical industry, better tests will help companies identify the safest, most effective biopharmaceuticals and weed out those that pose a high immunogenicity risk earlier in the drug development process. This will save companies both time and money. Finally, by adding to our knowledge of the mechanisms behind immunogenicity, the project will help to improve regulatory guidelines for the approval of biopharmaceuticals.

Project Partners

EFPIA member companies

- GlaxoSmithKline Research & Development Limited, Brentford, UK
- Bayer Pharma AG, Berlin, Germany
- IPSEN Innovation S.A.S, Paris, France
- Merck KGaA, Darmstadt, Germany
- Novartis Pharma AG, Basel, Switzerland
- Novo Nordisk A/S, Bagsværd, Denmark
- Pfizer Limited, Sandwich, UK
- Sanofi-Aventis Research and Development, Paris, France
- UCB Pharma S.A., Brussels, Belgium

Universities, research organisations, public bodies, non-profit groups

- Institut National de la Santé et de la Recherche Médicale (INSERM), Paris, France
- Academisch Medisch Centrum, Amsterdam, the Netherlands
- Academisch Ziekenhuis Leiden – Leids Universitair Medisch Centrum, Leiden, the Netherlands
- Centre National de la Recherche Scientifique, Paris, France
- Commissariat a L'Energie Atomique et aux Energies Alternatives, Paris, France
- DRK-Blutspendedienst Baden-Württemberg – Hessen gemeinnützige GmbH, Mannheim, Germany
- Fondazione per l'Istituto di Ricerca in Biomedicina, Bellinzona, Switzerland
- Fundació Institut de Recerca de L'hospital Universitari Vall D'hebron, Barcelona, Spain
- Groupe d'Etudes Therapeutiques des Affections Inflammatoires du Tube Digestif, Paris, France
- Istituto Giannina Gaslini, Genova, Italy
- Johann Wolfgang Goethe Universität, Klinikum und Fachbereich Medizin, Frankfurt, Germany
- Karolinska Institutet, Stockholm, Sweden
- Klinikum rechts der Isar der Technischen Universitaet Muenchen, Munich; Germany
- Medizinische Universität Innsbruck, Innsbruck, Austria
- Paul-Ehrlich-Institut, Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel, Langen, Germany
- Queen Mary and Westfield, University of London, London, UK
- Rambam Medical Center, Haifa, Israel
- Region Hovedstaden, Hillerød, Denmark
- Università di Firenze, Firenze, Italy
- Universitaetsklinikum Bonn, Bonn, Germany
- Universitätsklinikum Düsseldorf, Düsseldorf, Germany
- University College London, London, UK
- University Hospital Basel, Basel, Switzerland
- Univerzita Karlova v Praze, Prague , Czech Republic;

Small and medium-sized enterprises (SMEs)

- ALTA Ricerca e Sviluppo in Biotecnologie S.r.l.u, Siena, Italy
- Biomonitor A/S, Copenhagen, Denmark

Financing

IMI funding	€18.2 million
EFPIA in kind contribution	€9.6 million
Other contributions	€7.1 million
Total project cost	**€34.9 million**

Contacts

Project Coordinator

Daniel Sikkema, GlaxoSmithKline
Tel.: +1 610 270 6054
E-mail: dan.x.sikkema@gsk.com

Managing Entity for EU funds

Marc Pallardy, INSERM UMR 996
Tel.: +33 1 46 83 54 92
E-mail: marc.pallardy@u-psud.fr

This project is funded by the Innovative Medicines Initiative (IMI), a public-private partnership between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA), under Grant Agreement n. 115303

Last updated: March 2012