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INTRODUCTION

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-founded ABIRISK project **"Anti-Biopharmaceutical Immunization: Prediction and Analysis of Clinical Re to Minimize the Risk",** is to shed new light on the factors behind this immune response. The project, which represents the first concerted effort to solve this problem, officially kicked off March 1st, 2012. ABIRISK project will aid in the creation of new, safer **biopharmaceuticals (BPs)** 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.

The ABIRISK consortium (presently made up of thirty-five partners, twenty-four of which are academic institutions, nine are EFPIA member companies and two are small and medium enterprises, with thirteen countries represented), has been designed to meet all of these requirements in order to target three types of disorders: **Hemophilia A, Multiple sclerosis and Inflammatory diseases: inflammatory rheumatisms (including rheumatoid arthritis) and inflammatory bowel diseases.**

ABIRISK Project will collect data both retrospectively from patients suffering from various types of diseases and treated with various BPs at European centers with a high level of experience in clinical research and will prospectively recruit additional patients in dedicated studies during the 5 years of this program. Guidelines and Standard Operating Protocols for the study of anti-drug immunization will be established and used to standardize the collection of prospective data from these patients.

ABIRISK Project thus represents a unique opportunity to create an interdisciplinary task force of clinical centers especially designed to study immune responses against biopharmaceuticals.

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WELCOME

Dear Reader,

We would like to welcome you to the April 2015 the **ABIRISK Scientific Newsletter**. The Scientific Newsletter gives you a monthly update on the most relevant literature related to ABIRISK topics published around the globe, both inside and outside ABIRISK consortium.

This month, we chose to draw attention Deehan *et al.* on the management of unwanted immunogenicity of therapeutic proteins, mainly reporting on discussions that took place at the European Immunogenicity Platform annual symposium in February 2014.

In addition, you will find in this issue some regulatory news on biopharmaceuticals

We look forward to your visit on **ABIRISK** website for more information and updates on the program.

Enjoy reading !

Best wishes

The ABIRISK management team

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LITERATURE

This month's selected article

The introduction of biopharmaceuticals products (BPs) has been a critical step forward in the treatment of many severe diseases. A major limitation to the use of BPs remains the development of anti-drug antibodies (ADA) in a subset of patients. ADA may decrease the efficacy of BPs by neutralizing them or modifying their clearance, and they may be associated with BP-specific hypersensitivity reactions. The prediction, prevention and cure of anti-drug immunogenicity are thus major goals in biopharmaceutical drug development and patient safety.

In this paper, Deehan et al. review the critical topics discussed at the February 2014 European Immunogenicity Platform Symposium around unwanted BPs immunogenicity.

Namely, they report that a better understanding of BPs immunogenicity and a potential reduction of its clinical consequences may rely upon : 1) the use of innovative *in silico*, *in vitro* and *in vivo* immunogenicity prediction tools; 2) further improvement of ADA assays performance, in particular with respect to sensitivity and drug tolerance thresholds; 3) refined analysis of the clinical relevance of ADA in treated patients.

Such multidisciplinary and integrated approach is the one chosen by the ABIRISK consortium to analyze the mechanisms and consequences of immunization against biopharmaceutical products in Hemophilia A, Multiple sclerosis and in Inflammatory diseases: inflammatory rheumatisms -including adult and juvenile rheumatoid arthritis- and inflammatory bowel diseases.

Managing unwanted immunogenicity of biologicals.
Deehan M, Garcês S, Kramer D, Baker MP, Rat D, Roettger Y, Kromminga A.
Autoimmun Rev. 2015 Mar 2.

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Immunogenicity

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Structure-based development and optimization of therapy antibody drugs against TNFα.
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Animal models

Animal models of rheumatoid arthritis: How informative are they?
McNamee K, Williams R, Seed M.
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Mouse Models of Multiple Sclerosis: Lost in translation?
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Cathepsin S inhibition suppresses systemic lupus erythematosus and lupus nephritis because cathepsin S is essential for MHC class II-mediated CD4 T cell and B cell priming.
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Update on the Autoimmune Pathology of Multiple Sclerosis: B-Cells as Disease-Drivers and Therapeutic Targets.
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REGULATION

EMA

Scientific guideline: Final guideline on adjustment for baseline covariates in clinical trials
Adopted
March 2015

Scientific guideline: Guideline on clinical investigation of medicinal products for the treatment of systemic lupus erythematosus and lupus nephritis.
Adopted
March 2015

Overview of external comments received on the 'Guideline on clinical investigation of medicinal products for the treatment of systemic lupus erythematosus, and lupus nephritis'
March 2015

Human medicines European public assessment report (EPAR): MabThera, rituximab
Revision: 35, Authorised
March 2015

Orphan designation: Vatreptacog alfa (activated)
Updated
March 2015

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