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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.

WELCOME

Dear Reader,

We would like to welcome you to the November 2014 issue of 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 to the work conducted by van Schouwenburg *et al.* on the functional characterisation of anti-adalimumab antibodies in Rheumatoid arthritis patients.

In addition, you will find in this issue some news on biopharmaceuticals from the regulatory agencies.

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

LITERATURE

This month's selected article

Adalimumab – a therapeutic monoclonal antibody directed against TNFα – elicits strong anti-drug antibody (ADA) responses in Rheumatoid Arthritis (RA) patients albeit being a fully human recombinant protein. Adalimumab ADA have been found to be anti-idiotypic, i.e. directed to the TNFα binding site of the drug. Hence, most adalimumab ADA are neutralizing antibodies (NAbs).

In this paper, van Schouwenburg and colleagues sought to investigate whether the anti-idiotypic ADA response to adalimumab is confined to various epitopes or a single dominant one within the adalimumab complementary determining region (CDR), and explore the diversity of the anti-adalimumab B cell repertoire.

To this aim, antigen-specific memory B cells were isolated and cloned from the peripheral blood of 2 adalimumab ADA positive RA patients. A total of 16 clones were obtained, 8 of IgG1, 7 of IgG4 and 1 of undetermined subclass. All clones exhibited different V(D)J recombination and the CDR1 and CDR2 regions showed a Replacement/Suppression mutation ratio characteristic of antigen-driven maturation. Eleven out of the sixteen clones were expressed as recombinant IgG1 monoclonal antibodies to explore binding affinity to adalimumab and neutralizing capacity. Ten out of eleven clones exhibited high affinity, all proved neutralizing and more interestingly, all could compete with each other for binding to adalimumab, thus confirming that they recognize overlapping regions of adalimumab TNFα binding site. Single amino acid mutations experiments revealed that several B cell epitopes within this region were recognized by the clones. Moreover, differences in propensy to form dimeric and multimeric immune complexes with adalimumab were also observed.

Based on this findings, the authors suggest that adalimumab immunogenicity might be reduced through the introduction of point mutations within the CDRs regions but further studies will be needed to estimate the risk of impairing TNFα specificity and/or generating new immunogenic amino acid sequences.

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REGULATION

EMA

Scientific guideline: Guideline on similar biological medicinal products
Adopted
October 2014

EMA Guideline on similar biological medic

Human medicines European public assessment report (EPAR): Humira, adalimumab
Revision: 36, Authorised
October 2014

Human medicines European public assessment report (EPAR): Extavia, interferon beta-1b
Revision: 14, Authorised
October 2014

Human medicines European public assessment report (EPAR): Kogenate Bayer, octocog alfa
Revision: 26, Authorised
October 2014

Scientific guideline: Draft concept paper on the revision of the guideline on the development of new medicinal products for the treatment of ulcerative colitis, draft: consultation open
Consultation start date 01/10/2014
Consultation end date 31/12/2014

EMA Draft concept paper on the revision