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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 Relevance 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 June 2013 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 highlighted the results of the ADACTA study published by The Lancet in May, which for the first time allowed a direct efficacy comparison between two biotherapeutics in rheumatoid arthritis patients.

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

Around thirty per cent of rheumatoid arthritis (RA) patients take biological disease-modifying antirheumatic drugs as monotherapy. In this paper published in The Lancet in May this year, Gabay et al. on behalf of the ADACTA* study investigators, report on a phase IV multi-center, randomized, double-blind, parallel group study designed to permit for the first time a direct efficacy comparison between two biotherapeutics.

Tocilizumab-a humanized IL-6 receptor-inhibiting monoclonal antibody, and adalimumab-a fully human IgG anti-TFNα, had previously shown efficacy and acceptable safety as single-agent therapy in patients, with adalimumab being indeed the most common first-line biological in RA therapy as of today.

The present study is a phase 4 superiority study conducted in 76 centres in 15 countries with 326 patients enrolled.The patients enrolled were aged at least 18 years and has severe RA for 6 months or more and were intolerant to methotrexate or were inappropriate for continued methotrexate treatement. Moreover, none of them had previously received biotherapy for RA.

The reduction in signs and symptoms of RA in adult patients with severely active disease receiving either tocilizumab or adalimumab was evaluated and compared, using the change in disease activity score 28 joints (DAS28) from baseline to week 24 as the primary endpoint (DAS28 score greater than 5.1 indicates severe active disease, less than 3.2, low disease activity, and less than 2.6 is considered remission).Tocilizumab used alone led to a significantly and clinically meaningful greater improvement in DAS28 from baseline to week 24 compared to adalimumab monotherapy. Higher response rates for tocilizumab were also observed for all secondary key endpoints of the study (DAS28 less than 3.2, less than 2.6, ACR 20, 50, 70 responses, EULAR good, good or moderate responses at week 24). Safety was compable among the treatment groups, however more patients in the tociluzumab group than in the adalimumab group had increased LDL-cholesterol, increased alanine aminotransferase concentrations, and reduced platelet and neutrophils counts.

Interestingly, the authors also identified potential baseline predictors of response amongst which e.g. anticyclic citrullinated peptide positivity, geographical regions, sex, age, or C-reactive protein levels. However, none of them predicted efficacy after statistical analysis.

*ADACTA : ADalimumab ACTemrA

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REGULATION

EMA

Human medicines European Public Assessment Report (EPAR): Benlysta, belimumab
Revision: 6, Authorised
May 2013

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