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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.
Dear Reader,

We would like to welcome you to the third 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 highlight a review by Wiendl and Gross in Nature Reviews Neurology on the unexpected mechanisms of action of daclizumab in Multiple Sclerosis patients.

In addition, you will find our usual update on regulation within the Immunogenicity field.

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*
IL-2/IL-2 receptor (IL-2R) interactions are central to T cell differentiation, activation and expansion. Two functional forms of IL-2 receptor exist, one of which being the high affinity receptor, a trimer composed of the IL-2Rβ, IL-2Rγc and IL-2Rα (also known as CD25) chains, and primarily expressed by activated T cells. As antigen-specific activated T cells are known to play a major role in the immunopathogenesis of multiple sclerosis disease (MS), disrupting the IL-2/IL-2Rα pathway has been proposed as a new therapeutic approach in MS.

Daclizumab, a humanized IgG1 monoclonal antibody directed against IL-2Rα originally developed and commercialized for prevention of renal allograft rejection, is currently under clinical investigation in MS patients. To date, several clinical trials, including recent randomized double blind comparator studies have established that daclizumab strongly inhibited disease activity and slowed disease progression in patients with MS, with a fairly good tolerability and safety profile.

Interestingly in the present paper, Wiendl and Gross not only review the efficacy and safety data collected through the different clinical studies, but also discuss novel putative mechanisms of action of daclizumab associated with its observed efficacy. When contemplating the use of daclizumab for MS treatment, it was initially postulated that disrupting the IL-2/IL-2R pathway on activated T cells would suppress IL-2-mediated expansion of autoreactive T cell populations, thus resulting in disease amelioration. In fact, a growing body of evidence now supports the hypothesis of the immune balance being ameliorated or restored through enhancement of endogenous mechanisms of immune tolerance, rather than through neutralization of the expansion of deleterious activated T cells.

These so far identified mechanisms involve expansion and stimulation of immune regulatory CD56bright natural killer cells - the most prominent NK cell population in the cerebrospinal fluid, reduction of early T-cell activation through inhibition of IL-2-mediated cross presentation by dendritic cells, and reduction of the of proinflammatory LTi cells.

Modulation of IL-2Rα with daclizumab for treatment of multiple sclerosis.
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Immunogenicity

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Adair P, Su Y, Scott DW.

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Anti-TNF treatments in rheumatoid arthritis: economic impact of dosage modification.
Mixed Treatment Comparison of Efficacy and Tolerability of Biologic Agents in Patients with Rheumatoid Arthritis.
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Monotherapy with tocilizumab or TNF-alpha inhibitors in patients with rheumatoid arthritis: efficacy, treatment satisfaction, and persistence in routine clinical practice
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EMA

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July 2013
Draft- Consultation open
Deadline 15th January 2014

EMA IBS guideline.pdf

Orphan designation: Octocog alfa (liposomal) for the treatment of Haemophilia A
Updated
July 2013

Human medicines European public assessment report (EPAR): NovoSeven, eptacog alfa (activated)
Revision: 27, Authorised
July 2013

Human medicines European public assessment report (EPAR): RoActemra, tocilizumab
Revision: 11, Authorised
July 2013

Human medicines European public assessment report (EPAR): Orencia, abatacept
Revision: 15, Authorised
July 2013

FDA

Biological License Application Approvals: Rixubis, Coagulation Factor IX (Recombinant)
For treatment of Haemophilia B
June 2013
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FDA Guidance for Industry
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FDA Monitoring guideline.pdf

OTHER NEWS

Announcement

Teva and Lonza Announce Mutual Decision to Discontinue Biologics Joint Venture
July 2013