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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 rheumatism (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 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 draw attention to the results of a phase 2b clinical trial published by The Lancet, which evaluated the efficacy and safety of a new version of daclizumab (high yield produced) in multiple sclerosis.

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

LITERATURE

This month's selected article

Interleukin-2 receptor alpha (IL-2R alpha) has lately emerged as a new target for Multiple Sclerosis (MS). Former clinical studies had demonstrated the efficacy of intravenous and subcutaneous daclizumab (a monoclonal antibody directed to CD25/IL-2 R alpha chain) when used in combination with IFN β in relapsing-remitting multiple sclerosis (RRMS).

In this publication in *The Lancet* this summer, Gold et al. on behalf of the SELECT study investigators reported on a Phase 2b study designed to determine the efficacy and safety of daclizumab alone in RRMS patients. A new form of daclizumab -high-yield process or daclizumab HYP, which only differs from previous versions of daclizumab in its glycosylation pattern, resulting in decreased antibody-dependent cellular cytotoxicity activity was investigated.

The study was conducted on 621 eligible RRMS patients between February 2008 and May 2010 in 76 clinical centres throughout Europe and India, randomly assigned to receive daclizumab HYP 150 mg, daclizumab HYP 300 mg, or placebo.

The primary end point was the annualised relapse rate at week 52. Secondary endpoints included cumulative number of new gadolinium-enhancing lesions on brain MRI; newly enlarging T2 hyperintense lesions at week 52; proportion of relapsing patients at week 52 and change in MSIS-29 physical impact score. Confirmed disability progression as measured by change in EDSS score between baseline and week 52 was amongst the chosen tertiary endpoints.

At 52 weeks, Daclizumab HYP treatment resulted in a 54% reduction in annualised relapse rate compared to placebo for the 150 mg arm and 50% reduction for the 300 mg arm. The proportion of relapsing patients was also significantly lower in treated (150 mg, 19%; 300 mg, 20%) than placebo groups (36%). As well, compared with placebo, the risk of 3-month sustained disability progression at week 52 was reduced by 57% and 43% in the daclizumab HYP 150 mg and daclizumab HYP 300 mg groups respectively.

Expansion of CD56^{bright} NK cells in peripheral blood has been consistently observed in peripheral blood of daclizumab-treated MS patients. Increased in CD56^{bright} NK cells counts in treated versus placebo groups were observed in the current study too, accompanied with a 7-10% decrease in CD4⁺ and CD8⁺ T cells.

Interestingly, **immunogenicity** of daclizumab HYP was assessed with an enzyme-linked immunosorbent assay with acid dissociation to identify antidrug antibodies. Positive samples were subsequently tested for

neutralising antibodies in a cell-based assay. At week 24, neutralising antibodies to daclizumab HYP were detected in 2% of patients in the daclizumab groups (five patients in the 150 mg group and one in the 300 mg

dose group). In some patients, these antibodies were transient, and at week 52 only 1 patient in each daclizumab group had neutralising antibodies.

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Revision: 25, Authorised
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Therapeutic area: Haematology-Hemostaseology (updated)

August 2013

[Human medicines European public assessment report \(EPAR\): Benlysta, belimumab](#)

Revision: 7, Authorised

August 2013

[Human medicines European public assessment report \(EPAR\): Simponi, golimumab](#)

Revision: 14, Authorised

August 2013

OTHER NEWS

Announcement

[Drug Channels: Meet the Top Ten Drugs of 2018](#)