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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.
Dear Reader,

We would like to welcome you to the June 2016 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.

From now on, we will draw your attention to a selection of articles each month that we think make a difference in their respective fields.

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
This month's selected article

This month, a large consensus elected this article, which stands as a milestone paper that will change the treatment of haemophilia in the next years dramatically from every second day i.v. protein substitution to weekly to monthly s.c. injection of a FVIII mimetic antibody:

**Factor VIII-Mimetic Function of Humanized Bispecific Antibody in Hemophilia A.**

**Commentary:**
Bispecific antibody mimicking factor VIII.
Nogami K.
Thromb Res. 2016 May;141 Suppl 2:S34-5.
Immunogenicity

Posttranslational Modifications and the Immunogenicity of Biotherapeutics.
Jefferis R.

Adalimumab trough serum levels and anti-adalimunab antibodies in the long-term clinical outcome of patients with Crohn's disease.
Bodini G, Giannini EG, Savarino V, Del Nero L, Pellegatta G, De Maria C, Baldissarro I, Savarino E.

Response to: 'Comparing the immunogenicity of the etanercept biosimilar SB4 with the innovator etanercept: another consideration' by Marshall et al.
Ann Rheum Dis. 2016 May 4

Optimizing Treatment with TNF Inhibitors in Inflammatory Bowel Disease by Monitoring Drug Levels and Antidrug Antibodies.
Steenholdt C, Bendtzen K, Brynskov J, Ainsworth MA.
Inflamm Bowel Dis. 2016 Apr 29.

Methods

An Immunoinhibition Approach to Overcome the Impact of Pre-existing Antibodies on Cut Point Establishment for Immunogenicity Assessment of Moxetumomab Pasudotox.
Schneider AK, Vainshtein I, Roskos LK, Chavez C, Sun B, Liang M.

Quantifying Trace Amounts of Aggregates in Biopharmaceuticals Using Analytical Ultracentrifugation Sedimentation Velocity; Bayesian Analyses and F Statistics.
Wafer L, Kloczewiak M, Luo Y.
AAPS J. 2016 May 16.

Generation of a Highly Specific Monoclonal Anti-Infliximab Antibody for Harmonization of TNF-Coated Infliximab Assays.
Van Stappen T, Brouwers E, Tops S, Geukens N, Vermeire S, Declerck PJ, Gils A.
Animal models

**Animal Models of Rheumatoid Arthritis (I): Pristane-Induced Arthritis in the Rat.**

**Animal models of inflammatory bowel disease: how useful are they really?**
Kolios G.
Curr Opin Gastroenterol. 2016 May 19.

Biomarkers

**Rheumatoid factor, not antibodies against citrullinated proteins, is associated with baseline disease activity in rheumatoid arthritis clinical trials.**
Aletaha D, Alasti F, Smolen JS.

**Stimulating disease activity using multi-biomarker disease activity scores in patients with rheumatoid arthritis treated with abatacept or adalimumab.**
Fleischmann R, Connolly SE, Maldonado MA, Schiff M.

**Dynamic tracking of functional gene modules in treated juvenile idiopathic arthritis.**

Biosimilars

**Biosimilars in rheumatology: understanding the rigor of their development.**
Goel N, Chance K.

**European Experience of Infliximab Biosimilars for the Treatment of Inflammatory Bowel Disease.**
Lakatos P.
Włodarczyk M, Fichna J, Sobolewska-Włodarczyk A.
Pharmacol Rep. 2016 Apr 26

Clinical experience with infliximab biosimilar Remsima (CT-P13) in inflammatory bowel disease patients.
Jahnsen J.

A randomized, controlled trial of efficacy and safety of Anbainuo, a bio-similar etanercept, for moderate to severe rheumatoid arthritis inadequately responding to methotrexate.
Chen XX, Li ZG, Wu HX, Zhao DB, Li XF, Xu JH, Tao Y, Yang NP, Hu SX, Huang AB, Jiang LD, Wang GC, Zhang X, Bao CD.
Clin Rheumatol. 2016 May 16.

Biosimilars in Inflammatory Bowel Disease: Facts and Fears of Extrapolation.
Ben-Horin S, Casteele NV, Schreiber S, Lakatos P.

Systemic Lupus Erythematosus

IL-10-producing forkhead box protein 3-negative regulatory T cells inhibit B-cell responses and are involved in systemic lupus erythematosus.

Arthritis

Circulating CD4+ T-cell number decreases in rheumatoid patients with clinical response to rituximab.
Piantoni S, Scarsi M, Tincani A, Airò P.
Rheumatol Int. 2015 Sep;35(9):1571-3
Complete clinical remission with tocilizumab in two infants with systemic juvenile idiopathic arthritis: a case series.
Maritsi DN, Onoufriou M, Vartzelis G, Eleftheriou D.

Monitoring serum etanercept levels in juvenile idiopathic arthritis: a pilot study.
Alcobendas R, Rodríguez-Vidal A, Pascual-Salcedo D, Murias S, Remesal A, Diego C, Merino R.

**Inflammatory Bowel Diseases**

Biologic therapies in ulcerative colitis: primi inter pares?
Curr Drug Targets. 2016 May 27.

The impact of updated NICE guidelines on biologic treatment of ulcerative colitis: reflections on past practices, the changing present and implications for the future.
Samaan MA, Irving PM.

Cost-effectiveness of adalimumab, infliximab or vedolizumab as first-line biological therapy in moderate-to-severe ulcerative colitis.
Yokomizo L, Limketkai B, Park KT.

Safety of vedolizumab in the treatment of Crohn's disease and ulcerative colitis.
Hagan M, Cross RK.

IBD: Tracking TNF and anti-TNF agents in inflamed gut tissue.
Ray K.

Interleukin-27 as a Novel Therapy for Inflammatory Bowel Disease: A Critical Review of the Literature.
Andrews C, McLean MH, Durum SK.
Inflamm Bowel Dis. 2016 May 26

The role of vedolizumab in patients with moderate-to-severe Crohn's disease and ulcerative colitis.
Shahidi N, Bressler B, Panaccione R.
Multiple Sclerosis

**Activity of secukinumab, an anti-IL-17A antibody, on brain lesions in RRMS: results from a randomized, proof-of-concept study.**

**Immunologic profiles of multiple sclerosis treatments reveal shared early B cell alterations.**

Hemophilia

**A Randomized Trial of Factor VIII and Neutralizing Antibodies in Hemophilia A.**

**Innovative Pharmacological Therapies for the Hemophilias Not Based on Deficient Factor Replacement.**

Basic Immunology

**Antigen processing * Special section: New concepts in antibody therapeutics**
Current Opinion in Immunology
Volume 40, Pages 1-130, June 2016
**Development and maintenance of intestinal regulatory T cells.**
Tanoue T, Atarashi K, Honda K.

**AIRE expands: new roles in immune tolerance and beyond.**
Anderson MS, Su MA.

**REGULATION**

**EMA**

**Human medicines European public assessment report (EPAR): Cimzia, certolizumab pegol**
Revision: 16, Authorised

Pending EC decision: Humira, adalimumab
Opinion date: 26-May-2016

Pending EC decision: Tysabri, natalizumab
Opinion date: 26-May-2016

Pending EC decision: Simponi, golimumab
Opinion date: 26-May-2016

**Human medicines European public assessment report (EPAR): Humira, adalimumab**
Revision: 45, Authorised

Referral: Article 20 procedures, Tysabri, natalizumab (updated)

**Human medicines European public assessment report (EPAR): Tysabri, natalizumab**
Revision: 22, Authorised
Agenda

Programme - Targeted consultation on development of new medicinal products for the treatment of rheumatoid arthritis

Human medicines European public assessment report (EPAR): Enbrel, etanercept
Revision: 48, Authorised

Scientific guideline:
Concept paper on the revision of the 'Guideline on the environmental risk assessment of medicinal products for human use', draft: consultation open