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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.
Dear Reader,

We would like to welcome you to the January 2017 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.

Each month we draw your attention to a selection of articles 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
LITERATURE

This month's selected articles

Both papers demonstrate that the rate of immunogenicity is very low with tocilizumab, an anti-IL6R very broadly used in the treatment of RA: between 0 and 1.5%. It may explain that this drug is almost as efficient in monotherapy than in association with methotrexate. Interestingly, healthy donors show the same frequency of naive TCZ-specific and infliximab-specific CD4+ T cell precursors. Thus, the low prevalence of ADAs to TCZ might result from interleukin-6 blockade.

Low immunogenicity of tocilizumab in patients with rheumatoid arthritis.

Immunogenicity of tocilizumab in patients with rheumatoid arthritis.
Immunogenicity

Non-neutralizing antibodies against factor VIII and risk of inhibitor development in patients with severe hemophilia A.
Cannavò A, Valsecchi C, Garagiola I, Palla R, Mannucci PM, Rosendaal FR, Peyvandi F.

Immunogenicity of Human Interferon-Beta-Containing Pharmaceuticals.
Nazarov VD, Lapin SV, Mazing AV, Evdoshenko EP, Totolian AA.

A Therapeutic Uricase with Reduced Immunogenicity Risk and Improved Development Properties.

Influence of anti-TNF immunogenicity on safety in rheumatic disease: a narrative review.

Influence of IL6R gene polymorphisms in the effectiveness to treatment with tocilizumab in rheumatoid arthritis.
Maldonado-Montoro M, Cañadas-Garre M, González-Utrilla A, Ángel Calleja-Hernández M.
Pharmacogenomics J. 2016 Dec 13.

Five-year Efficacy and Safety of Tocilizumab Monotherapy in Patients with Rheumatoid Arthritis Who Were Methotrexate- and Biologic-naïve or Free of Methotrexate for 6 Months: the AMBITION Study.
Jones G, Wallace T, McIntosh MJ, Brockwell L, Gómez-Reino JJ, Sebba A.

Methods

Development of Statistical Methods for Analytical Similarity Assessment.
Tsong Y, Dong X, Shen M.
Harmonization of Infliximab and Anti-Infliximab Assays Facilitates the Comparison Between Originators and Biosimilars in Clinical Samples.
Inflamm Bowel Dis. 2016 Apr;22(4):969-75.

Rapid Test for Infliximab Drug Concentration Allows Immediate Dose Adaptation.

Biomarkers

Serum IL-33, a new marker predicting response to rituximab in rheumatoid arthritis.

STAT6 and STAT1 Pathway Activation in Circulating Lymphocytes and Monocytes as Predictor of Treatment Response in Rheumatoid Arthritis.

Biosimilars

Infliximab Biosimilars in the Treatment of Inflammatory Bowel Diseases: A Systematic Review.
Radin M, Sciascia S, Roccatello D, Cuadrado MJ.

The Role of Biosimilars in Inflammatory Bowel Disease.
Paramsothy S, Cleveland NK, Zmeter N, Rubin DT.

FDA’s approach to regulating biosimilars.
Lemery SJ, Ricci MS, Keegan P, McKee AE, Pazdur R.

On Hybrid Parallel-Crossover Designs for Assessing Drug Interchangeability of Biosimilar Products.
Chow SC, Song F, Cui C.

Rheumatoid Arthritis

Biological Agents In Rheumatoid Arthritis: A Cross-Link Between Immune Tolerance And Immune Surveillance.
Talotta R, Atzeni F, Batticciotto A, Benucci M, Bongiovanni S, Sarzi-Puttini P.

Risk of serious adverse effects of biological and targeted drugs in patients with rheumatoid arthritis: a systematic review meta-analysis.

A genetic risk score composed of rheumatoid arthritis risk alleles, HLA-DRB1 haplotypes, and response to TNFi therapy results from a Swedish cohort study.
Jiang X, Askling J, Saevarsdottir S, Padyukov L, Alfredsson L, Viatte S, Frisell T.

Anti-TNF treatment response in rheumatoid arthritis patients with moderate disease activity: a prospective observational multicentre study (MODERATE).

Maintenance of efficacy and safety with subcutaneous golimumab in rheumatoid arthritis patients with low disease activity who previously received TNF inhibitors.
Wakabayashi H, Inada H, Nishioka Y, Hasegawa M, Sudo A, Nishioka K.

IL-1 Inhibition in Systemic Juvenile Idiopathic Arthritis.
Giancane G, Minoia F, Davi S, Bracciolini G, Consolaro A, Ravelli A.
Genetic architecture distinguishes systemic juvenile idiopathic arthritis from other forms of juvenile idiopathic arthritis: clinical and therapeutic implications.

Infection, malignancy, switching, biosimilars, antibody formation, drug survival and withdrawal, and dose reduction: what have we learned over the last year about tumor necrosis factor inhibitors in rheumatoid arthritis?
Ianculescu I, Weisman MH.

Biological agents in polyarticular juvenile idiopathic arthritis: A meta-analysis of randomized withdrawal trials.
Amarilyo G, Tarp S, Foeldvari I, Cohen N, Pope TD, Woo JM, Christensen R, Furst DE.

Efficacy of biologic therapy across individual juvenile idiopathic arthritis subtypes: A systematic review.
Davies R, Gaynor D, Hyrich KL, Pain CE.

Biologic Therapy in Inflammatory and Immunomediated Arthritis: Safety Profile.
Luchetti MM, Balloni A, Gabrielli A.
Inflammatory Bowel Disease

The biologics of ulcerative colitis.
Macaluso FS, Renna S, Orlando A, Cottone M.

Anti-Integrins in Ulcerative Colitis and Crohn’s Disease: What Is Their Place?
Khanna R, Mosli MH, Feagan BG.

Vedolizumab in the treatment of Crohn’s disease.
Tarabar D, Hirsch A, Rubin DT.

Editorial: adalimumab or infliximab as monotherapy, or in combination with an immunomodulator, in the treatment of Crohn’s disease.
Christensen B, Sparrow MP.

Systemic lupus erythematosus

Targeting the interferon pathway with sifalimumab for the treatment of systemic lupus erythematosus.
Greth W, Robbie GJ, Brohawn P, Hultquist M, Yao B.

Multiple Sclerosis

Einarson TR, Bereza BG, Machado M.
Delbue S, Comar M, Ferrante P.
Immunotherapy. 2016 Dec 22.

Depletion of CD52 positive cells inhibits the development of CNS autoimmune disease, but deletes an immune-tolerance promoting CD8 T cell population. Implications for secondary autoimmunity of alemtuzumab in multiple sclerosis.
Immunology. 2016 Dec 7.

Serum Lipid Profile Changes Predict Neurodegeneration in Interferon-B1a Treated Multiple Sclerosis Patients.

Vitamin D supplementation reduces relapse rate in relapsing-remitting multiple sclerosis patients treated with natalizumab.
Laursen JH, Søndergaard HB, Sørensen PS, Sellebjerg F, Oturai AB.

Hemophilia

New findings on inhibitor development: from registries to clinical studies.
Peyvandi F, Ettingshausen CE, Goudemand J, Jiménez-Yuste V, Santagostino E, Makris M.

Clinical evaluation of glycoPEGylated recombinant FVIII: Efficacy and safety in severe haemophilia A.

Opinions/Commentaries/ Across diseases reviews

Antibodies to watch in 2017.
Reichert JM.
MAbs. 2016 Dec 14:0.
Remarkable Pharmacokinetics of Monoclonal Antibodies: A Quest for an Explanation.
Reijers JA, Moerland M, Burggraaf J.
Clin Pharmacokinet. 2016 Dec 20

REGULATION

FDA
Guidance
Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product

EMA
Scientific guidance on post-authorisation efficacy studies - First version, adopted
Draft guideline on the clinical investigation of human normal immunoglobulin for intravenous administration (IVIg), draft: consultation open
Guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches, adopted (updated)

Opinion/decision on a Paediatric investigation plan (PIP): Humira, Adalimumab
Therapeutic area: Dermatology/Immunology-Rheumatology-Transplantation/Ophthalmology/Gastroentology-Hepatology (updated)

Human medicines European public assessment report (EPAR): Simponi, golimumab
Revision: 26, Authorised

Biosimilar medicines (updated)

Clinical pharmacology and pharmacokinetics: questions and answers (updated)

Referral: Article 31 referrals, Factor VIII (updated)

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use guideline Q3C (R5) on impurities: guideline for residual solvents - Step 5, adopted (updated)