

TABLE OF CONTENTS

INTRODUCTION	2
WELCOME	3
LITERATURE	4
This month's selected article	4
Immunogenicity	5
Methods	5
Biomarkers	5
Systemic Lupus Erythematosus	6
Rheumatoid Arthritis	7
Inflammatory Bowel Disease	7
Multiple Sclerosis	8
Hemophilia	8
Basic immunology	9
Opinions/Commentaries	9
REGULATION	11
EMA	11
OTHER NEWS	12
Announcement	12
Forthcoming conferences	12

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 April 2013 **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 selected a review by Choy et al. published in *Nature Reviews Rheumatology* recapitulating current and future biologic therapies for Rheumatoid Arthritis, highlighting difficulties faced by clinicians when given the opportunity to choose from several effective new options.

In addition, you will find in this issue some regulatory news on biopharmaceuticals and an update on forthcoming conferences of interest.

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

Rheumatoid arthritis (RA) patients failing to respond to conventional DMARD therapy are nowadays offered an alternative treatment by means of biologic therapy. Current approved biotherapeutics for RA treatment include cytokines blockers (anti-TNF α and TNF α receptor, anti-IL-6 and IL-6 receptor, anti-IL-1) and lymphocyte targeting agents (anti-CD20, CTLA4 fusion protein).

The list of putative biotherapeutic agents for RA treatment is rapidly expanding, with other cytokines such as IL-17, IL-23 and signal transduction pathway blockers (e.g. anti-JAK pathway) now reaching the late stages of clinical development. Small-molecule inhibitors of signal transduction pathway and cytokines blockers have indeed been the main focus of new therapies development efforts in the recent years.

However, in absence of reliable biomarkers and clear understanding of the molecular basis of efficacy or lack thereof of each biotherapeutic agent, clinicians are faced with a difficult choice. In this paper, Choy et al. review the modes of action of each of these types of therapy and consider the challenges associated with their use in clinical practice.

[The problem of choice: current biologic agents and future prospects in RA.](#)

Choy EH, Kavanaugh AF, Jones SA.

Nat Rev Rheumatol. 2013 Feb 19

Immunogenicity

[Subcutaneous abatacept for the treatment of rheumatoid arthritis.](#)

Schiff M.

Rheumatology. 2013 Mar 5.

[Late immune tolerance induction in an adult with severe haemophilia A and high-responder inhibitor: 1-year outcome.](#)

Faradji A, Lavigne-Lissalde G, Grunebaum L, Desprez D, Feugeas O, Lapalud P.

Haemophilia. 2012 Sep;18(5):e388-91

[The frequency of anti-infliximab antibodies in patients with rheumatoid arthritis treated in routine care and the associations with adverse drug reactions and treatment failure](#)

Krintel SB, Grunert VP, Hetland ML, Johansen JS, Rothfuss M, Palermo G, Essieux L, Klause U.

Rheumatology. 2013 Mar 4

Methods

[External Quality Assessment of Factor VIII Inhibitor Assays.](#)

Bonar RA, Favaloro EJ, Marsden K.

Semin Thromb Hemost. 2013 Feb 22

[Monitoring of adalimumab and antibodies-to-adalimumab levels in patient serum by the homogeneous mobility shift assay.](#)

Wang SL, Hauenstein S, Ohrmund L, Shringarpure R, Salbato J, Reddy R, McCowen K, Shah S, Lockton S, Chuang E, Singh S.

J Pharm Biomed Anal. 2013 Feb 1;78-79C:39-44.

Biomarkers

[Biomarkers in Multiple Sclerosis: An Up-to-Date Overview.](#)

Katsavos S, Anagnostouli M.

Mult Scler Int. 2013;2013:340508

[The type I IFN signature as a biomarker of preclinical rheumatoid arthritis.](#)

Lübbers J, Brink M, van de Stadt LA, Vosslander S, Wesseling JG, van Schaardenburg D, Rantapää-Dahlqvist S, Verweij CL.

Ann Rheum Dis. 2013 Feb 23.

[Rheumatoid factor does not predict response to TNF antagonists in rheumatoid arthritis: Three centers experience.](#)

Salgado E, Campos J, Moreira-Navarrete V, Mulero J, Navarro F, Pérez-Pampín E, Carmona L, Gómez-Reino J.
Joint Bone Spine. 2013 Feb 28.

[Metabolic profiling predicts response to anti-TNF \$\alpha\$ therapy in patients with rheumatoid arthritis.](#) Kapoor SR, Filer A, Fitzpatrick MA, Fisher BA, Taylor PC, Buckley CD, McInnes IB, Raza K, Young SP.

Arthritis Rheum. 2013 Mar 4.

Systemic Lupus Erythematosus

[Persistent memory B cell down-regulation after 6-year remission induced by rituximab therapy in patients with systemic lupus erythematosus.](#)

Iwata S, Saito K, Tokunaga M, Tanaka Y.
Lupus. 2013 Feb 19.

[Belimumab: targeted therapy for lupus.](#)

Chugh PK, Kalra BS.
Int J Rheum Dis. 2013 Feb;16(1):4-13.

[Down-regulation of interferon signature in systemic lupus erythematosus patients by active immunization with interferon \$\alpha\$ -kinoid.](#)

Lauwerys BR, Hachulla E, Spertini F, Lazaro E, Jorgensen C, Mariette X, Haelterman E, Grouard-Vogel G, Fanget B, Dhellin O, Vandepapelière P, Houssiau FA.
Arthritis Rheum. 2013 Feb;65(2):447-56.

[B-Cell Targeted Therapies in Systemic Lupus Erythematosus : Successes and Challenges.](#)

Harvey PR, Gordon C.
BioDrugs. 2013 Mar 2.

[B-cell-targeted therapies in systemic lupus erythematosus.](#)

Chan VS, Tsang HH, Tam RC, Lu L, Lau CS.
Cell Mol Immunol. 2013 Mar;10(2):133-42.

Rheumatoid Arthritis

[Effects of subcutaneous and intravenous golimumab on inflammatory biomarkers in patients with rheumatoid arthritis: results of a phase 1, randomized, open-label trial.](#)

Doyle MK, Rahman MU, Frederick B, Birbara CA, de Vries D, Toedter G, Wu X, Chen D, Ranganath VK, Westerman ME, Furst DE.

Rheumatology . 2013 Feb 14.

[Exposure-Exposure Relationship of Tocilizumab, an Anti-IL-6 Receptor Monoclonal Antibody, in a Large Population of Patients With Rheumatoid Arthritis.](#)

Levi M, Grange S, Frey N.

J Clin Pharmacol. 2013 Feb;53(2):151-9.

[Harms of TNF inhibitors in rheumatic diseases: a focused review of the literature.](#)

Jain A, Singh JA.

Immunotherapy. 2013 Mar;5(3):265-99

[Longterm Safety and Efficacy of Tocilizumab in Patients with Rheumatoid Arthritis: A Cumulative Analysis of Up to 4.6 Years of Exposure.](#)

Genovese MC, Rubbert-Roth A, Smolen JS, Kremer J, Khraishi M, Gómez-Reino J, Sebba A, Pilson R, Williams S, van Vollenhoven R.

J Rheumatol. 2013 Mar 1

[Targeting Interleukin-6 in Rheumatoid Arthritis](#)

Md Yusof MY, Emery P.

Drugs. 2013 Mar 1.

[Anti-TNF Therapy Reduces Serum Levels of Chemerin in Rheumatoid Arthritis: A New Mechanism by Which Anti-TNF Might Reduce Inflammation.](#)

Herenius MM, Oliveira AS, Wijbrandts CA, Gerlag DM, Tak PP, Lebre MC.

PLoS One. 2013;8(2):e57802

Inflammatory Bowel Disease

[Certolizumab pegol in the treatment of Crohn's disease.](#)

Ferrante M, Vermeire S, Rutgeerts P.

Expert Opin Biol Ther. 2013 Apr;13(4):595-605

[Elective switching from infliximab to adalimumab in stable Crohn's disease.](#)

Hoentjen F, Haarhuis BJ, Drenth JP, de Jong DJ.
Inflamm Bowel Dis. 2013 Mar;19(4):761-6.

[Cost-per-remission analysis of infliximab compared to adalimumab among adults with moderate-to-severe ulcerative colitis.](#)

Lofland JH, Mallow P, Rizzo J.
J Med Econ. 2013 Feb 27.

Multiple Sclerosis

[Immunotherapy of Multiple Sclerosis : The State of the Art.](#)

Karussis D.
BioDrugs. 2013 Feb 20

[Treating multiple sclerosis with monoclonal antibodies: a 2013 update.](#)

Deiß A, Brecht I, Haarmann A, Buttman M.
Expert Rev Neurother. 2013 Mar;13(3):313-35.

[Natalizumab treatment decreases serum IgM and IgG levels in multiple sclerosis patients.](#)

Selter RC, Biberacher V, Grummel V, Buck D, Eienbröcker C, Oertel WH, Berthele A, Tackenberg B, Hemmer B.
Mult Scler. 2013 Feb 25.

[The benefits and risks of alemtuzumab in multiple sclerosis.](#)

Ontaneda D, Cohen JA.
Expert Rev Clin Immunol. 2013 Mar;9(3):189-91

Hemophilia

[Identification and Multidimensional Optimization of an Asymmetric Bispecific IgG Antibody Mimicking the Function of Factor VIII Cofactor Activity.](#)

Sampei Z, Igawa T, Soeda T, Okuyama-Nishida Y, Moriyama C, Wakabayashi T, Tanaka E, Muto A, Kojima T, Kitazawa T, Yoshihashi K, Harada A, Funaki M, Haraya K, Tachibana T, Suzuki S, Esaki K, Nabuchi Y, Hattori K.
PLoS One. 2013;8(2):e57479

[Current status and future prospects for the prophylactic management of hemophilia patients with inhibitor antibodies.](#)

Teitel JM, Sholzberg M.

Blood Rev. 2013 Mar;27(2):103-9.

Basic immunology

[The signal peptide of the tumor-shared antigen Midkine hosts CD4+ T cell epitopes.](#)

Kerzerho J, Schneider A, Favry E, Castelli FA, Maillère B.

J Biol Chem. 2013 Apr 3

Opinions/Commentaries

[To target or not to target APRIL in systemic lupus erythematosus: that is the question!](#)

Morel J, Hahne M.

Arthritis Res Ther. 2013 Feb 25;15(1):107

[First-line therapy in adult Crohn's disease: who should receive anti-TNF agents?](#)

Danese S, Colombel JF, Peyrin-Biroulet L, Rutgeerts P, Reinisch W.

Aliment Pharmacol Ther. 2013 Mar 13

[Canakinumab in pediatric rheumatic diseases](#)

Wulffraat NM, Woo P.

Expert Opin Biol Ther. 2013 Apr;13(4):615-22.

[Letter: are infliximab and adalimumab similar for Crohn's disease in clinical practice?](#)

Tursi A, Elisei W, Picchio M, Penna A.

Aliment Pharmacol Ther. 2013 Apr;37(7):763-4

[Letter: should immunosuppressive therapy be started with adalimumab in Crohn's disease?](#)

Tursi A, Elisei W, Picchio M, Penna A.

Aliment Pharmacol Ther. 2013 Apr;37(7):763-4

[Letter: should immunosuppressive therapy be started with adalimumab in Crohn's disease? Authors' reply.](#)

Reenaers C, Louis E, Belaiche J, Seidel L, Keshav S, Travis S.

Aliment Pharmacol Ther. 2013 Apr;37(7):752-3

[Regulatory T cells: recommendations to simplify the nomenclature.](#)

Abbas AK, Benoist C, Bluestone JA, Campbell DJ, Ghosh S, Hori S, Jiang S, Kuchroo VK, Mathis D, Roncarolo MG, Rudensky A, Sakaguchi S, Shevach EM, Vignali DA, Ziegler SF.

Nat Immunol. 2013 Apr;14(4):307-8.

REGULATION

EMA

[Human medicines European Public Assessment Report \(EPAR\): Orenzia, abatacept](#)

Revision: 13, Authorised

March 2013

[Scientific guideline: Reflection paper on Immune Tolerance Induction in haemophilia A patients with inhibitors, adopted](#)

Adopted

March 2013



Scientific
Guideline.pdf

[Overview of comments received on 'Reflection paper on Immune Tolerance Induction in haemophilia A patients with inhibitors](#)

March 2013



WC500140786
comments.pdf

[Pending EC decision: MabThera, rituximab](#)

Opinion date: 21-Mar-2013

[Guidance for Industry : Enrichment Strategies for Clinical Trials to Support Approval of Human Drugs and Biological Products](#)



Draft guidance
FDA.pdf

OTHER NEWS

Announcement



The IMI-founded  is now open for business ! For more information, please visit : [Nature](#)

Forthcoming conferences

June	EULAR	12-15, Madrid, Spain	http://www.eular.org
	EAACI/WAO	22-26, Milan, Italy	http://www.eaaci-wao2013.com
	FOCIS	27-30, Boston, Massachusetts, USA	http://www.focisnet.org/FOCIS/

July	Tumor Necrosis Factor 2013	7-10, Quebec, Canada	http://www.tnf2013.com/index.html
August	International Congress of Immunology	22-27, Milan, Italy	http://www.ici2013.org/home/
September	World Congress on Inflammation	21-25, Natal, Brazil	http://www.inflammation2013
	World Congress of Neurology	21-26 Vienna, Austria	http://www2.kenes.com