

## TABLE OF CONTENTS

INTRODUCTION	2
WELCOME	3
LITERATURE	4
This month's selected articles	4
Immunogenicity	5
Methods	6
Animal models	6
Biomarkers	6
Systemic Lupus Erythematosus	7
Rheumatoid Arthritis	8
Inflammatory Bowel Diseases	8
Multiple Sclerosis	9
Haemophilia	10
Basic immunology	10
Opinions/Commentaries/Across diseases reviews	10
REGULATION	11
EMA	11

## 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 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 December 2015 **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*



## LITERATURE

### This month's selected articles

1. A comprehensive review of the immunopathological mechanisms underlying Multiple Sclerosis :

[Immunopathology of multiple sclerosis.](#)

Dendrou CA, Fugger L, Friese MA.

Nat Rev Immunol. 2015 Sep 15;15(9):545-58.

2. Juvenile idiopathic arthritis differs from adult rheumatoid arthritis by the symptoms. It is interesting to see that the two disease also differ by their HLA-DRB association :

[HLA-DRB1\\*11 and variants of the MHC class II locus are strong risk factors for systemic juvenile idiopathic arthritis.](#)

Ombrello MJ et al. ; International Childhood Arthritis Genetics (INCHARGE) Consortium; British Society of Pediatric and Adolescent Rheumatology BSPAR Study Group.

Proc Natl Acad Sci U S A. 2015 Nov 23

## Immunogenicity

[The Association between Clinical Response to Ustekinumab and Immunogenicity to Ustekinumab and Prior Adalimumab.](#)

Chiu HY, Chu TW, Cheng YP, Tsai TF.  
PLoS One. 2015 Nov 13;10(11):e0142930.

[From the Bench to Clinical Practice: Understanding the Challenges and Uncertainties in Immunogenicity Testing for Biopharmaceuticals.](#)

Gunn GR, Sealey DC, Jamali F, Meibohm B, Ghosh S, Shankar G.  
Clin Exp Immunol. 2015 Nov 24

[A Randomized, Phase I Pharmacokinetic Study Comparing SB2 and Infliximab Reference Product \(Remicade®\) in Healthy Subjects.](#)

Shin D, Kim Y, Kim YS, Körnicke T, Fuhr R.  
BioDrugs. 2015 Nov 17.

[Engineering less immunogenic and antigenic FVIII proteins.](#)

Pratt KP.  
Cell Immunol. 2015 Nov 2.

[Immunogenicity evaluation strategy for a second-generation therapeutic, PEG-IFN- \$\beta\$ -1a.](#)

White JT, Crossman M, Richter K, Berman M, Goyal J, Subramanyam M.  
Bioanalysis. 2015 Nov;7(21):2801-11.

[Immunogenicity of infliximab and adalimumab: what is its role in hypersensitivity and modulation of therapeutic efficacy and safety?](#)

Murdaca G, Spanò F, Contatore M, Guastalla A, Penza E, Magnani O, Puppo F.  
Expert Opin Drug Saf. 2015 Nov 11:1-10.

[Immunogenicity of anti-TNF biologic agents in the treatment of rheumatoid arthritis.](#)

Mok CC, Tsai WC, Chen Y, Wei JC.  
Expert Opin Biol Ther. 2015 Nov 11

[To clear or to fear: An innate perspective on factor VIII immunity.](#)

Lai JD, Georgescu MT, Hough C, Lillicrap D.  
Cell Immunol. 2015 Oct 28

## Methods

[Serum trough infliximab levels: A comparison of three different immunoassays for the monitoring of CT-P13 \(infliximab\) treatment in patients with inflammatory bowel disease.](#)

Malíčková K, Ďuricová D, Bortlík M, Hind'oš M, Machková N, Hrubá V, Lukáš M, Zima T, Lukáš M.  
Biologicals. 2015 Oct 23. pii: S1045-1056(15)00110-4.

[Therapeutic drug monitoring of infliximab: performance evaluation of three commercial ELISA kits.](#)

Schmitz EM, van de Kerkhof D, Hamann D, van Dongen JL, Kuijper PH, Brunsveld L, Scharnhorst V, Broeren MA.  
Clin Chem Lab Med . 2015 Nov 20

## Animal models

[Clinical efficacy of a new CD28-targeting antagonist of T cell co-stimulation in a non-human primate model of collagen-induced arthritis.](#)

Vierboom MP, Breedveld E, Kap YS, Mary C, Poirier N, Hart BA, Vanhove B.  
Clin Exp Immunol. 2015 Nov 5.

[Companion animals: Translational scientist's new best friends.](#)

Kol A, Arzi B, Athanasiou KA, Farmer DL, Nolta JA, Rebhun RB, Chen X, Griffiths LG, Verstraete FJ, Murphy CJ, Borjesson DL.  
Sci Transl Med. 2015 Oct 7;7(308):308ps21.

[Characterization of a genetically engineered mouse model of hemophilia A with complete deletion of the F8 gene.](#)

Chao BN, Baldwin WH, Healey JF, Parker ET, Shafer-Weaver K, Cox C, Jiang P, Kanellopoulou C, Lollar P, Meeks SL, Lenardo MJ.  
J Thromb Haemost. 2015 Nov 20

## Biomarkers

[Cultured blood T-cell responses predict anti-TNF therapy response in patients with ulcerative colitis.](#)

Magnusson MK, Strid H, Isaksson S, Bajor A, Lasson A, Ung KA, Öhman L.  
Aliment Pharmacol Ther. 2015 Jun;41(11):1149-61.



[Immunologic and MRI markers of the therapeutic effect of IFN- \$\beta\$ -1a in relapsing-remitting MS.](#)

Tao Y, Zhang X, Zivadinov R, Dwyer MG, Kennedy C, Bergsland N, Ramasamy D, Durfee J, Hojnacki D, Hayward B, Dangond F, Weinstock-Guttman B, Markovic-Plese S.

Neurol Neuroimmunol Neuroinflamm. 2015 Nov 12;2(6):e176

[Increased pretreatment serum IFN- \$\beta\$ / \$\alpha\$  ratio predicts non-response to tumour necrosis factor  \$\alpha\$  inhibition in rheumatoid arthritis.](#)

Wampler Muskardin T, Vashisht P, Dorschner JM, Jensen MA, Chrobot BS, Kern M, Curtis JR, Danila MI, Cofield SS, Shadick N, Nigrovic PA, St Clair EW, Bingham CO 3rd, Furie R, Robinson W, Genovese M, Striebich CC, O'Dell JR, Thiele GM, Moreland LW, Levesque M, Bridges SL Jr, Gregersen PK, Niewold TB.

Ann Rheum Dis. 2015 Nov 6

[Association Between Response to Etrolizumab and Expression of Integrin alpha E and Granzyme A in Colon Biopsies of Patients with Ulcerative Colitis.](#)

Tew GW, Hackney JA, Gibbons D, Lamb CA, Luca D, Egen JG, Diehl L, Anderson JE, Vermeire S, Mansfield JC, Feagan BG, Panes J, Baumgart DC, Schreiber S, Dotan I, Sandborn WJ, Kirby JA, Irving PM, De Hertogh G, Van Assche GA, Rutgeerts P, O'Byrne S, Hayday A, Keir ME.

Gastroenterology. 2015 Oct 29.

## Systemic Lupus Erythematosus

[Further thoughts about the Illuminate studies of tabalumab in SLE.](#)

Isenberg D.

Ann Rheum Dis. 2015 Nov 3.

[Safety and Efficacy of Belimumab to Treat Systemic Lupus Erythematosus in Academic Clinical Practices.](#)

Hui-Yuen JS, Reddy A, Taylor J, Li X, Eichenfield AH, Bermudez LM, Starr AJ, Imundo LF, Buyon J, Furie RA, Kamen DL, Manzi S, Petri M, Ramsey-Goldman R, van Vollenhoven RF, Wallace DJ, Askanase A.

J Rheumatol. 2015 Nov 1.

## Rheumatoid Arthritis

### [Tailored first-line biologic therapy in patients with rheumatoid arthritis, spondyloarthritis, and psoriatic arthritis.](#)

Cantini F, Niccoli L, Nannini C, Cassarà E, Kaloudi O, Giulio Favalli E, Becciolini A, Biggioggero M, Benucci M, Li Gobbi F, Grossi V, Infantino M, Meacci F, Manfredi M, Guiducci S, Bellando-Randone S, Matucci-Cerinic M, Foti R, Di Gangi M, Mosca M, Tani C, Palmieri F, Goletti D; Italian board for the Tailored Biologic therapy (ITABIO). Semin Arthritis Rheum. 2015 Oct 22

### [A safety evaluation of canakinumab for the treatment of systemic onset juvenile idiopathic arthritis.](#)

Wulfraat NM.  
Expert Opin Drug Saf. 2015 Nov 14:1-7.

### [Twenty-eight-week results from the REALISTIC phase IIIb randomized trial: efficacy, safety and predictability of response to certolizumab pegol in a diverse rheumatoid arthritis population.](#)

Weinblatt ME, Fleischmann R, van Vollenhoven RF, Emery P, Huizinga TW, Cutolo M, van der Heijde D, Duncan B, Davies O, Luijckens K, Dougados M.  
Arthritis Res Ther. 2015 Nov 15;17(1):325.

### [Efficacy and safety of tabalumab, an anti-BAFF monoclonal antibody, in patients with moderate-to-severe rheumatoid arthritis and inadequate response to TNF inhibitors: results of a randomised, double-blind, placebo-controlled, phase 3 study.](#)

Schiff M, Combe B, Dörner T, Kremer JM, Huizinga TW, Veenhuizen M, Gill A, Komocsar W, Berclaz PY, Ortmann R, Lee C.  
RMD Open. 2015 Aug 12;1(1):e000037.

## Inflammatory Bowel Diseases

### [Review article: the potential mechanisms of action of rifaximin in the management of inflammatory bowel diseases.](#)

Sartor RB.  
Aliment Pharmacol Ther. 2016 Jan;43 Suppl 1:27-36.

### [Anti-TNF- \$\alpha\$ therapies for the treatment of Crohn's disease: the past, present and future.](#)

Berns M, Hommes DW.  
Expert Opin Investig Drugs. 2015 Nov 28



[Clinical relevance and inter-test reliability of anti-infliximab antibodies and infliximab trough levels in patients with inflammatory bowel disease.](#)

Guiotto C, Daperno M, Frigerio F, Vizzini M, Cerruti R, Ercole E, Cosimato M, Lavagna A, Germano L, Migliardi M, Rocca R.  
Dig Liver Dis. 2015 Oct 31.

[Long-term assessment of clinical response to adalimumab therapy in refractory ulcerative colitis.](#)

Hussey M, Mc Garrigle R, Kennedy U, Holleran G, Kevans D, Ryan B, Breslin N, Mahmud N, McNamara D.  
Eur J Gastroenterol Hepatol. 2015 Nov 19

[Vedolizumab for the treatment of ulcerative colitis.](#)

Neal S, Brian B, Remo P.  
Expert Opin Biol Ther. 2015 Nov 15.

[Optimizing anti-TNF \$\alpha\$  therapy: Serum Levels of Infliximab and Adalimumab Associate With Mucosal Healing in Patients with Inflammatory Bowel Diseases.](#)

Ungar B, Levy I, Yavne Y, Yavzori M, Picard O, Fudim E, Loebstein R, Chowers Y, Eliakim R, Kopylov U, Ben-Horin S.  
Clin Gastroenterol Hepatol. 2015 Oct 29

[Letter: stool adalimumab detection in ulcerative colitis and Crohn's disease--authors' reply.](#)

Rosen MJ, Minar P, Vinks AA.  
Aliment Pharmacol Ther. 2015 Jul;42(2):241.

[Letter: stool adalimumab detection in ulcerative colitis and Crohn's disease.](#)

Roblin X, Paul S.  
Aliment Pharmacol Ther. 2015 Jul;42(2):240.

## Multiple Sclerosis

[Monoclonal antibody therapies for the treatment of relapsing-remitting multiple sclerosis: differentiating mechanisms and clinical outcomes.](#)

Lycke J.  
Ther Adv Neurol Disord. 2015 Nov;8(6):274-293.

[Transcriptional response to interferon beta-1a treatment in patients with secondary progressive multiple sclerosis.](#)

Gurevich M, Miron G, Falb RZ, Magalashvili D, Dolev M, Stern Y, Achiron A.  
BMC Neurol. 2015 Nov 21;15(1):240.

## Haemophilia

### [Hunting down factor VIII in the immunopeptidome.](#)

Hartholt RB, Peyron I, Voorberg J.  
Cell Immunol. 2015 Nov 5.

### [Structure of the Human Factor VIII C2 Domain in Complex with the 3E6 Inhibitory Antibody.](#)

Wuerth ME, Cragerud RK, Clint Spiegel P.  
Sci Rep. 2015 Nov 24;5:17216.

## Basic immunology

### [Stable inhibitory activity of regulatory T cells requires the transcription factor Helios.](#)

Kim HJ, Barnitz RA, Kreslavsky T, Brown FD, Moffett H, Lemieux ME, Kaygusuz Y, Meissner T, Holderried TA, Chan S, Kastner P, Haining WN, Cantor H.  
Science. 2015 Oct 16;350(6258):334-9.

### [A mechanism for expansion of regulatory T-cell repertoire and its role in self-tolerance.](#)

Feng Y, van der Veeke J, Shugay M, Putintseva EV, Osmanbeyoglu HU, Dikiy S, Hoyos BE, Moltedo B, Hemmers S, Treuting P, Leslie CS, Chudakov DM, Rudensky AY.  
Nature. 2015 Nov 25.

## Opinions/Commentaries/Across diseases reviews

### [Revisiting the Mechanisms of CNS Immune Privilege.](#)

Louveau A, Harris TH, Kipnis J.  
Trends Immunol. 2015 Oct;36(10):569-77.

### [IMMUNOLOGY. From transient infection to chronic disease.](#)

Nathan C.  
Science. 2015 Oct 9;350(6257):161.

## REGULATION

### EMA

[Overview of comments received on the 'Guideline on clinical investigation of medicinal products for the treatment of juvenile idiopathic arthritis'](#)

November 2015

[Human medicines European public assessment report \(EPAR\): Extavia, interferon beta-1b,](#)

Revision: 18, Authorised

November 2015

[Human medicines European public assessment report \(EPAR\): Betaferon, interferon beta-1b](#)

Revision: 26, Authorised

November 2015

[Human medicines European public assessment report \(EPAR\): Remicade, infliximab](#)

Revision: 45, Authorised

November 2015

[Orphan designation: recombinant porcine factor VIII \(B-domain-depleted\) for the treatment of haemophilia A](#)

Updated

November 2015

[Pending EC decision: Benepali, etanercept](#)

Opinion date : 19 Nov 2015

[Pending EC decision: Cimzia, certolizumab pegol](#)

Opinion date : 19 Nov 2015

[Scientific guideline: Guideline on clinical investigation of medicinal products for the treatment of juvenile idiopathic arthritis](#)

**Adopted**

November 2015



WC500196719.pdf



[Work plan for the CVMP Immunologicals Working Party 2016](#)

November 2015

[Human medicine European public assessment report \(EPAR\): Humira, adalimumab](#)

Revision: 42, Authorised

November 2015

[Human medicines European public assessment report \(EPAR\): Enbrel, etanercept](#)

Revision :46, authorised

November 2015