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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.

WELCOME

Dear Reader,

We would like to welcome you to the May 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

LITERATURE

This month's selected articles

1. This work explores methods that are now used in routine labs more frequently. An innovative approach using a “hybrid” method of immunocapture and LCMS for characterisation of ADA. This demonstrates clearly that this hybrid LCMS approach is increasingly becoming an option in the **bioanalytical toolbox for ADA assessment :**

[Development of Immunocapture-LC/MS Assay for Simultaneous ADA Isotyping and Semiquantitation.](#)

Chen LZ, Roos D, Philip E.

J Immunol Res. 2016;2016:7682472.

2. It is not very common to see papers comparing different commercial assays. The results are showing that all three commercially available assays appear suitable for therapeutic drug monitoring of anti-TNF α drugs, allowing sensitive and comparable detection of infliximab, adalimumab and etanercept concentrations. However, differences in specificity, recovery and cross-reactivity are noted :

[A comparison of three assays to quantify infliximab, adalimumab and etanercept serum concentrations.](#)

van Bezooijen JS, Koch BC, Doorn MV, Prens EP, Gelder TV, Schreurs MW.

Ther Drug Monit. 2016 Apr 26.

Immunogenicity

[A Cohesive and Integrated Platform for Immunogenicity Prediction.](#)

Dimitrov I, Atanasova M, Patronov A, Flower DR, Doytchinova I.
Methods Mol Biol. 2016;1404:761-70.

[Correlations between immunogenicity, drug levels, and disease activity in an Italian cohort of rheumatoid arthritis patients treated with tocilizumab.](#)

Benucci M, Meacci F, Grossi V, Infantino M, Manfredi M, Bellio E, Bellio V, Li Gobbi F, Bazzichi L, Moscato P, Caputo D, Saviola G, Talotta R, Sarzi-Puttini P, Atzeni F.
Biologics. 2016 Mar 11;10:53-8.

[Anti-infliximab Antibodies with Neutralizing Capacity in Patients with Inflammatory Bowel Disease: Distinct Clinical Implications Revealed by a Novel Assay.](#)

Weisshof R, Ungar B, Blatt A, Dahan A, Pressman S, Waterman M, Kopylov U, Ben-Horin S, Chowers Y.
Inflamm Bowel Dis. 2016 Apr 26.

[Serum Infliximab, Antidrug Antibodies, and Tumor Necrosis Factor Predict Sustained Response in Pediatric Crohn's Disease.](#)

Stein R, Lee D, Leonard MB, Thayu M, Denson LA, Chuang E, Herskovitz R, Kerbowski T, Baldassano RN.
Inflamm Bowel Dis. 2016 Apr 6.

[Cost-effectiveness of routine measuring of serum drug concentrations and anti-drug antibodies in treatment of rheumatoid arthritis patients with TNF- \$\alpha\$ blockers.](#)

Laine J, Jokiranta TS, Eklund KK, Väkeväinen M, Puolakka K.
Biologics. 2016 Apr 1;10:67-73

Methods

[Nanobodies as therapeutics: big opportunities for small antibodies.](#)

Steeland S, Vandenbroucke RE, Libert C.
Drug Discov Today. 2016 Apr 11.

[Application of a Plug-and-Play Immunogenicity Assay in Cynomolgus Monkey Serum for ADCs at Early Stages of Drug Development.](#)

Carrasco-Triguero M, Davis H, Zhu Y, Coleman D, Nazzal D, Vu P, Kaur S.
J Immunol Res. 2016;2016:2618575.

[A Highly Sensitive and Drug-Tolerant Anti-Drug Antibody Screening Assay for Ixekizumab using Affinity Capture Elution.](#)

Muram TM, Sloan JH, Chain JS, Komocsar WJ, Meiklejohn BI, Blauvelt A, Papp K, Heffernan MP, Qian YW, Konrad RJ.

J Invest Dermatol. 2016 Mar 30.

Animal models

[Mouse Models for Assessing Protein Immunogenicity: Lessons and Challenges.](#)

Jiskoot W, Kijanka G, Randolph TW, Carpenter JF, Koulov AV, Mahler HC, Joubert MK, Jawa V, Narhi LO.
J Pharm Sci. 2016 May;105(5):1567-75.

[Fate of Multimeric Oligomers, Submicron, and Micron Size Aggregates of Monoclonal Antibodies Upon Subcutaneous Injection in Mice.](#)

Kijanka G, Bee JS, Bishop SM, Que I, Löwik C, Jiskoot W.
J Pharm Sci. 2016 May;105(5):1693-704.

Biomarkers

[Precision medicine in multiple sclerosis: biomarkers for diagnosis, prognosis, and treatment response.](#)

Comabella M, Sastre-Garriga J, Montalban X.
Curr Opin Neurol. 2016 Jun;29(3):254-62.

[Estimating 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.
Arthritis Rheumatol. 2016 Apr 25.

[Independent Candidate Serum Protein Biomarkers of Response to Adalimumab and to Infliximab in Rheumatoid Arthritis: An Exploratory Study.](#)

Ortea I, Roschitzki B, López-Rodríguez R, Tomero EG, Ovalles JG, López-Longo J, de la Torre I, González-Alvaro I, Gómez-Reino JJ, González A.
PLoS One. 2016 Apr 6;11(4):e0153140.

Biosimilars

[Clinical outcomes following a switch from Remicade® to the biosimilar CT-P13 in inflammatory bowel disease patients: a prospective observational cohort study.](#)

Smits LJ, Derikx LA, de Jong DJ, Boshuizen RS, van Esch AA, Drenth JP, Hoentjen F.
J Crohns Colitis. 2016 Apr 19.

Systemic Lupus Erythematosus

[Use of rituximab in systemic lupus erythematosus: a single center experience over 14 years.](#)

Aguiar R, Araújo C, Martins-Coelho G, Isenberg D.
Arthritis Care Res (Hoboken). 2016 Apr 25

Arthritis

[Pharmacokinetics and Pharmacodynamics of Canakinumab in Patients With Systemic Juvenile Idiopathic Arthritis.](#)

Sun H, Van LM, Floch D, Jiang X, Klein UR, Abrams K, Sunkara G.
J Clin Pharmacol. 2016 Apr 27.

[Efficacy and safety of CT-P13 \(biosimilar infliximab\) in patients with rheumatoid arthritis: comparison between switching from reference infliximab to CT-P13 and continuing CT-P13 in the PLANETRA extension study.](#)

Yoo DH, Prodanovic N, Jaworski J, Miranda P, Ramiterre E, Lanzon A, Baranauskaite A, Wiland P, Abud-Mendoza C, Oparanov B, Smiyan S, Kim H, Lee SJ, Kim S, Park W.
Ann Rheum Dis. 2016 Apr 29

[Methotrexate monotherapy and methotrexate combination therapy with traditional and biologic disease modifying antirheumatic drugs for rheumatoid arthritis: abridged Cochrane systematic review and network meta-analysis.](#)

Hazlewood GS, Barnabe C, Tomlinson G, Marshall D, Devoe D, Bombardier C.
BMJ. 2016 Apr 21;353:i1777.

[Prediction of remission and low disease activity in disease-modifying anti-rheumatic drug-refractory patients with rheumatoid arthritis treated with golimumab.](#)

Vastesaegeer N, Kutzbach AG, Amital H, Pavelka K, Lazaro MA, Moots RJ, Wollenhaupt J, Zerbini CA, Louw I, Combe B, Beaulieu A, Schulze-Koops H, Dasgupta B, Fu B, Huyck S, Weng HH, Govoni M, Durez P.
Rheumatology (Oxford). 2016 Apr 25.

[Anti-IL-17 therapy in treatment of rheumatoid arthritis: a systematic literature review and meta-analysis of randomized controlled trials.](#)

Kunwar S, Dahal K, Sharma S.
Rheumatol Int. 2016 Apr 22

Inflammatory Bowel Diseases

[Substitution with Alternative Anti-TNF \$\alpha\$ Therapy \(SAVANT\)-Outcomes of a Crohn's Disease Cohort Undergoing Substitution Therapy with Certolizumab.](#)

Boktor M, Motlis A, Aravantagi A, Sheth A, Jordan P, Morris J, Manas K, Hussain N, Cvek U, Trutschl M, Becker F, Alexander JS.
Inflamm Bowel Dis. 2016 Apr 21.

[Comparative Effectiveness and Safety of Anti-Tumor Necrosis Factor Agents in Biologic-Naïve Patients with Crohn's Disease.](#)

Singh S, Heien HC, Sangaralingham LR, Schilz SR, Kappelman MD, Shah ND, Loftus EV Jr.
Clin Gastroenterol Hepatol. 2016 Apr 4. pii: S1542-3565(16)30013-1.

[Maintenance of Efficacy and Continuing Safety of Golimumab for Active Ulcerative Colitis: PURSUIT-SC Maintenance Study Extension Through 1 Year.](#)

Gibson PR, Feagan BG, Sandborn WJ, Marano C, Strauss R, Johanns J, Padgett L, Collins J, Tarabar D, Hebzda Z, Rutgeerts P, Reinisch W.
Clin Transl Gastroenterol. 2016 Apr 28;7:e168.

[Vedolizumab and Infliximab Combination Therapy in the Treatment of Crohn's Disease.](#)

Hirten R, Longman RS, Bosworth BP, Steinlauf A, Scherl E.
Am J Gastroenterol. 2015 Dec;110(12):1737-8.

[Pharmacodynamic assessment of vedolizumab for the treatment of ulcerative colitis.](#)

McLean LP, Cross RK.
Expert Opin Drug Metab Toxicol. 2016 Apr 20.

Multiple Sclerosis

[Parenteral Treatment of Multiple Sclerosis: The Advent of Monoclonal Antibodies.](#)

Singer BA.

Semin Neurol. 2016 Apr;36(2):140-7.

[Alemtuzumab for multiple sclerosis.](#)

Riera R, Porfírio GJ, Torloni MR.

Cochrane Database Syst Rev. 2016 Apr 15;4:CD011203.

[Alemtuzumab and Multiple Sclerosis: Another Note of Caution.](#)

Hohlfeld R, Kumpf T.

JAMA Neurol. 2016 Apr 4

[Interferon-Beta Therapy of Multiple Sclerosis Patients Improves the Responsiveness of T Cells for Immune Suppression by Regulatory T Cells.](#)

Trinschek B, Luessi F, Gross CC, Wiendl H, Jonuleit H.

Int J Mol Sci. 2015 Jul 17;16(7):16330-46.

Hemophilia

[Factor VIII products in haemophilia A: one size fits all?](#)

Mannucci PM, Garagiola I.

Thromb Haemost. 2015 May;113(5):911-4

REGULATION

EMA

Human medicines European public assessment report (EPAR): [Humira](#), adalimumab
Revision: 44, Authorised

Opinion/decision on a Paediatric investigation plan (PIP): MabThera, [Rituximab](#)
Therapeutic area: Immunology-Rheumatology-Transplantation/Oncology (updated)

Human medicines European public assessment report (EPAR): [Inflectra](#), infliximab
Revision: 10, Authorised

Regulatory and procedural guideline:
[Reflection paper on extrapolation of efficacy and safety in paediatric medicine development](#), draft

Pending EC decision: [Humira](#), adalimumab
Opinion date: 01-Apr-2016

[PROTECT: key results and recommendations](#)