ABIRISK

EXTERNAL NEWSLETTER

ISSUE 17 - APRIL 2017

WWW.ABIRISK.EU

Dear colleagues, dear friends and supporters of ABIRISK,

we are pleased to present you the seventeenth issue of the external newsletter of ***Anti-Biopharmaceutical Immunization: prediction and analysis of clinical relevance to minimize the risk -ABIRISK- Project.***

ABIRISK External Newsletter will be filled with interesting information mainly for all groups external to the ABIRISK consortium that may have an interest in our research and progress.

Please don't hesitate to forward this mail to anyone who could also be interested in reading it. If they want to receive their own newsletter in the future they can write at newsletter@abirisk.eu. If you're not interested in receiving our newsletter anymore, you can unsubscribe via mail.

In order to contribute to the contents of the newsletter, please send news, photos and other material related to ABIRISK areas of research at newsletter@abirisk.eu

We hope you will enjoy reading our latest news.

Best regards,
The ABIRISK management team

THE ABIRISK PROJECT

ABIRISK is an Innovative Medicine Initiative 3rd Call project on Anti-Biopharmaceutical Immunization. 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** 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.

ABIRISK Project aims to provide an integrated approach to **anti-drug immunization**, bringing together, in an extensive and coordinated manner, a large network of clinicians from various specialties with broad experience in the care of patients treated with various type of **biopharmaceutical products** developing **anti-drug antibodies**, biologists familiar with the immune monitoring of patients, scientists specialized in the mechanisms of immunogenicity, methodologists and biostatisticians. In addition the collaboration with a large network of private pharmaceutical industries under the European Federation of Pharmaceutical Industries and Associations (EFPIA), will ensure direct transfer of the experimental findings into **biopharmaceutical product** development and patient management. Collectively, this group will critically evaluate the immunogenicity of existing **biopharmaceutical products** for **Hemophilia A, Multiple Sclerosis,** and **Inflammatory Diseases.** The **ABIRISK consortium**, constituting unique task forces for each of these complementary contributions, should improve our ability to predict immunogenicity and to minimize the risk of immunization against **biopharmaceutical products**.

The **ABIRISK project** consortium is presently made up of **thirty-eight partners, twenty-six** of which are **academic institutions, nine are EFPIA member companies** and **three** are small and medium enterprises **(SMEs).** Thirteen countries are represented: The United Kingdom, France, Italy, Germany, Switzerland, Denmark, Belgium, the Netherlands, Spain, Sweden, Austria, Israel and Czech Republic.

The consortium is co-ordinated by **Novartis Pharma AG (Dr. Sebastian Spindeldreher, Project Coordinator)** and **Institut National de la Santé et de la Recherche Médicale (INSERM; Prof. Marc Pallardy, Managing Entity)**, and will receive over €30 milion funding over 5 years from 1st March 2012.

The list of ABIRISK partners and more information on the project can be found on the website (www.abirisk.eu)

The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n° [115303], resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in kind contribution.'

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PROJECT NEWS

ABIRISK GENERAL ASSEMBLY
6th ANNUAL MEETING
April 26th-28th, 2017
HOTEL BOSCOLO ASTORIA FIRENZE - Via del Giglio, 9 - Firenze - Italy

On the **26-28 April 2017**, the **Sixth General Assembly of the ABIRISK Project** was held in **Florence (Italy)** hosted by ABIRISK Partner 3 Università di Firenze-UNIFI.

ABIRISK Sixth General Assembly was organized only for the partners of the project and more than 70 participants attended ABIRISK General Assembly in Florence.

The Sixth General Assembly in Florence

The meeting started with the ABIRISK Executive Project Management Team meeting followed by the Work Packages and Steering Committee meetings. The second day of the meeting was fully dedicated to the ABIRISK General Assembly. The ABIRISK General Assembly agenda included the update on main project successes, issues and challenges for the last year of the project, an overview on ABIRISK project management activities and ABIRISK sustainability, some presentations from Work Packages leaders on WPs' update and deliverables achieved since the previous General Assembly.

Niek de Vries and Marc Pallardy during the presentation

The General Assembly also included the presentation of **Niek de Vries** (ABIRISK Partner 10 Academisch Medisch Centrum bij de Universiteit van Amsterdam-AMC entitled **"Fingerprinting B and T cell clones to unravel adaptive immune responses in disease".**

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Starting from the previous experience occurred during the previous General Assembly in Innsbruck, the last day of the General Assembly was entirely dedicated to:

THE SECOND ABIRISK DRUG IMMUNOGENICITY CONFERENCE

The Second ABIRISK Drug Immunogenicity Conference included five sessions of oral presentations as well as of poster sessions. All scientific sessions were focused on the most important scientific achievements obtained so far within the ABIRISK Project on biopharmaceuticals immunogenicity.

The Second ABIRISK Drug Immunogenicity Conference was opened by the presentation of **Marc Pallardy** (ABIRISK Partner 2 Institut National de la Santé et de la Recherche Médicale – INSERM; ABIRISK Managing Entity) entitled **"Immunotoxicity of Biopharmaceuticals".**

Amongst speakers, several young scientists have had the opportunity to present recent data generated by their belonging groups in the area of the ABIRISK Project interests. More important, lots of discussions amongst ABIRISK partners and ABIRISK Scientific Advisory Board members have taken place during all scientific sessions.

The poster session during the Second ABIRISK Drug Immunogenicity Conference

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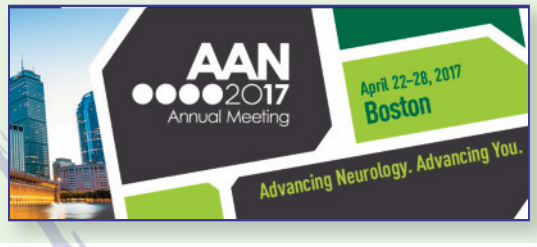
ABIRISK PRESENTED AT KEY IMMUNOGENICITY MEETINGS

At the **Annual Meeting of the American Academy of Neurology**, held in Boston, MA, on 22-28 April 2017, data generated by the ABIRISK project were presented by **Florian Deisenhammer** (ABIRISK Partner 18 Medizinische Universität Innsbruck - IMU; ABIRISK Work Package 1 co-leader) through the talk **"Prediction of long-term persistency of Natalizumab anti-drug antibodies".** The AAN Annual Meeting is the world's largest gathering of neurologists, bringing together more than 10,000 neurology professionals across the globe to network, discuss cutting-edge research, and take part in top-rated education programming across a wide variety of topics.



At the **3rd European Workshop on Protein Aggregation and Immunogenicity**, held in Innsbruck, Austria, on 30-31 January 2017, **Catherine Prades** (ABIRISK Partner 33 Sanofi-Aventis) had been invited to give a talk entitled **"*In-silico* prediction of aggregation and immunogenicity of Biologics".** The Workshop was focused on issues in aggregation and its impact on the immunogenicity of therapeutic proteins. Gathering opinion leaders from academia, industry and regulatory authorities, the conference wi covered a broad range of topics from what causes aggregation of therapeutic proteins in formulation and processing, analytical methods of detecting aggregates, the utility of in vitro and animal models in assessing immunogenicity, to the clinical aspects of therapeutic protein immunogenicity. Options to control aggregates and particles in therapeutic protein formulation and processing were also discussed from a hands-on experience.

At the **61st Annual Meeting of the Society of Thrombosis and Hemostasis Research**, held in Basel, Switzerland, on 15-18 February 2017, **Lilija Miller** (ABIRISK Partner 15 Paul-Ehrlich-Institut, Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel - PEI) was invited to give the talk **"Danger signal-dependent activation of human immune cells by factor VIII products".** The educational and scientific program of the Meeting provided state-of-the-art sessions and plenary lectures given by experts as well as a platform for the presentation of original research in the field of thrombosis and hemostasis. In addition, participants had the possibility to attend satellite symposia organized by pharmaceutical companies and to visit their booths.

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NEW PUBLICATIONS PRODUCED BY ABIRISK PROJECT

Clinical practice of analysis of anti-drug antibodies against interferon beta and natalizumab in multiple sclerosis patients in Europe: a descriptive study of test results

Jenny Link, Ryan Ramanujam, Michael Auer, Malin Ryner, Signe Hässler, Delphine Bachelet, Cyprien Mbogning, Clemens Warnke, Dorothea Buck, Poul Erik Hyldgaard Jensen, Claudia Sievers, Kathleen Ingenhoven, Nicolas Fissolo, Raija Lindberg, Verena Grummel, Naoimh Donnellan, Véronique Berthou, Manuel Comabella, Xavier Montalban, Bernd Kieseier, Per Soelberg Sorensen, Hans-Peter Hartung, Tobias Derfuss, Andy Lawton, Dan Sikkema, Marc Pallardy, Bernhard Hemmer, Florian Deisenhammer, Philippe Broët, Pierre Dönnes, Julie Davidson, Anna Fogdell-Hahn, on b half of the ABIRISK Consortium

PLoS One. 2017 Feb 7;12(2):e0170395.

Antibodies against biopharmaceuticals (anti-drug antibodies, ADA) have been a well-integrated part of the clinical care of multiple sclerosis (MS) in several European countries. ADA data generated in Europe during the more than 10 years of ADA monitoring in MS patients treated with interferon beta (IFNβ) and natalizumab have been pooled and characterizedthrough collaboration within a European consortium.

The aim of this study was to report on the clinical practice of ADA testing in Europe, considering the number of ADA tests performed and type of ADA assays used, and to determine the frequency of ADA testing against the different drug preparations in different countries. A common database platform (tranSMART) for querying, analyzing and storing retrospective data of MS cohorts was set up to harmonize the data and compare results of ADA tests between different countries. Retrospective data from six countries (Sweden, Austria, Spain, Switzerland, Germany and Denmark) on 20,695 patients and on 42,555 samples were loaded into tranSMART including data points of age, gender, treatment, samples, and ADA results.


PLOS ONE

RESEARCH ARTICLE

Clinical practice of analysis of anti-drug antibodies against interferon beta and natalizumab in multiple sclerosis patients in Europe: A descriptive study of test results

Abstract

The previously observed immunogenic difference among the four IFNβ preparations was confirmed in this large dataset. Decreased usage of the more immunogenic preparations IFNβ-1a subcutaneous (s.c.) and IFNβ-1b s.c. in favor of the least immunogenic preparation IFNβ-1a intramuscular (i.m.) was observed. The median time from treatment start to first ADA test correlated with time to first positive test. Shorter times were observed for IFNβ-1b-Extavia s.c. (0.99 and 0.94 years) and natalizumab (0.25 and 0.23 years), which were introduced on the market when ADA testing was already available, as compared to IFNβ-1a i.m. (1.41 and 2.27 years), IFNβ-1b-Betaferon s.c. (2.51 and 1.96 years) and IFNβ-1a s.c. (2.11 and 2.09 years) which were available years before routine testing began. A higher rate of anti-IFNβ ADA was observed in test samples taken from older patients.

Testing for ADA varies between different European countries and is highly dependent on the policy within each country. For drugs where routine monitoring of ADA is not in place, there is a risk that some patients remain on treatment for several years despite ADA positivity. For drugs where a strategy of ADA testing is introduced with the release of the drug, there is a reduced risk of having ADA positive patients and thus of less efficient treatment.

This indicates that potential savings in health cost might be achieved by routine analysis of ADA.

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RECENT PUBLICATIONS GENERATED BY ABIRISK PARTICIPANTS OUTSIDE THE PROJECT

Immunogenicity of tocilizumab in patients with rheumatoid arthritis
Sigaux J, Hamze M, Daien C, Morel J, Krzysiek R, Pallardy M, Maillere B, Mariette X, Miceli-Richard C.
Joint Bone Spine. 2017 Jan;84(1):39-45

Influence of anti-TNF immunogenicity on safety in rheumatic disease: a narrative review
Matucci A, Cammelli D, Cantini F, Goletti D, Marino V, Milano GM, Scarpa R, Tocci G, Maggi E, Vultaggio A.
Expert Opin Drug Saf. 2016 Dec;15(sup1):3-10.

Serum IL-33, a new marker predicting response to rituximab in rheumatoid arthritis
Sellam J, Rivière E, Courties A, Rouzaire PO, Tolusso B, Vital EM, Emery P, Ferraciolli G, Soubrier M, Ly B, Hendel
Chavez H, Taoufik Y, Dougados M, Mariette X.
Arthritis Res Ther. 2016 Dec 13;18(1):294.

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
von Kutzleben S, Pryce G, Giovannoni G, Baker D.
Immunology. 2016 Dec 7

Serum Lipid Profile Changes Predict Neurodegeneration in Interferon-B1a Treated Multiple Sclerosis Patients
Uher T, Fellows K, Horakova D, Zivadinov R, Vaneckova M, Sobisek L, Tyblova M, Seidl Z, Krasensky J, Bergsland N, Weinstock-Guttman B, Havrdova E, Ramanathan M.
J Lipid Res. 2016 Dec 6.

Clinical evaluation of glycoPEGylated recombinant FVIII: Efficacy and safety in severe haemophilia A
Giangrande P, Andreeva T, Chowdary P, Ehrenforth S, Hanabusa H, Leebeek FW, Lentz SR, Nemes L, Poulsen LH, Santagostino E, You CW, Clausen WH, Jönsson PG, Oldenburg J; Pathfinder™2 Investigators.
Thromb Haemost. 2016 Dec 1.

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ABIRISK COMMUNICATION TOOLS

PRESS RELEASE

Updating the original version generated by IMI Communication Office, **ABIRISK kick-off meeting fact sheet** has been created to promote ABIRISK project to broad audience mainly through institutional websites of ABIRISK partners, highlighting that the project has been started.

PROJECT BROCHURE

Official **ABIRISK Brochure** has been created and distributed to ABIRISK partners to disseminate information about the project in any suitable occasion (meetings, congresses, workshops, exhibition, shows or open forum, etc.) to broad audiences.

SCIENTIFIC NEWSLETTER

The **ABIRISK Scientific Newsletter**, an update on ABIRISK topics-related literature and international regulation, is sent to all consortium members and key opinion leaders in the different ABIRISK fields each month, posted on ABIRISK website and advertised on LinkedIn in several Immunogenicity-focused groups.

PROJECT WEBSITE

The main source for information on the project is ABIRISK website (**www.abirisk.eu**) where you will find the list of ABIRISK partners and their contact, more detailed information on the project, recent news on the project, all ABIRISK publications and press release, and the ABIRISK Scientific Newsletter.

ABIRISK WEBSITE IS VISITED EVERY MONTHS BY OVER 1300 PEOPLE WORLDWIDE!

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