ABIRISK

EXTERNAL NEWSLETTER

ISSUE 13 - MARCH 2016

WWW.ABIRISK.EU

Dear colleagues, dear friends and supporters of ABIRISK,

we are pleased to present you the thirteenth 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 GlaxoSmithKline (Dr. Daniel Sikkema, 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)

efpia

imi
Innovative Medicines Initiative

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.'

www.imi.europa.eu

ABIRISK
EXTERNAL NEWSLETTER
ISSUE 13 - MARCH 2016
WWW.ABIRISK.EU

PROJECT NEWS

ABIRISK 2016 GENERAL ASSEMBLY AND FIRST DRUG IMMUNOGENICITY CONFERENCE

On the 29-30 March 2016, the **Fifth General Assembly of ABIRISK Project** was held in Innsbruck (Austria) at the Innsbruck Medical University.

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

The ABIRISK General Assembly

The meeting started with the Work Packages' sub-meetings followed by the ABIRISK Executive Project Management Team 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 fourth 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.

The General Assembly also included the **keynote lecture "European biobanking efforts - The Biobanking and Biomolecular Resources Research Infrastructure (BBMRI-ERIC)"** with the presentations of **Jan-Eric Liton** and **Michaela Mayrhofer (Biobanking and Biomolecular Resources Research Infrastructure-Austria)** titled **"European biobanking efforts" and "ELSI: Ethical, legal and social issues",** respectively.

In order to increase awareness and improve the visibility to the international scientific community on **ABIRISK project** aims, objectives and expectations, this year the **General Assembly scientific day** consisted of a scientific meeting **open also to non-ABIRISK members:**

The First Drug Immunogenicity Conference was held on **1 April 2016** - all day.

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.'
www.imi.europa.eu

ABIRISK
EXTERNAL NEWSLETTER
ISSUE 13 - MARCH 2016
WWW.ABIRISK.EU

The First Immunogenicity Conference included two sessions of oral presentations as well as of poster sessions. All scientific sessions were focused on the most important scientific achievements obtained so far on biopharmaceuticals immunogenicity.

The First Immunogenicity Conference also included the presentations of **Amy Rosenberg (United States Food and Drug Administration - ABIRISK Scientific Advisory Board member)** titled **"Self" and "Foreign" are relative terms from an immunologic perspective: immunogenicity pitfalls in development of therapeutic biologic products"** and **Tim Hickling (ABIRISK Partner 29 Pfizer Limited)** titled **"Applying mathematical modelling to the prediction of therapeutic drug immunogenicity".**

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

The poster session

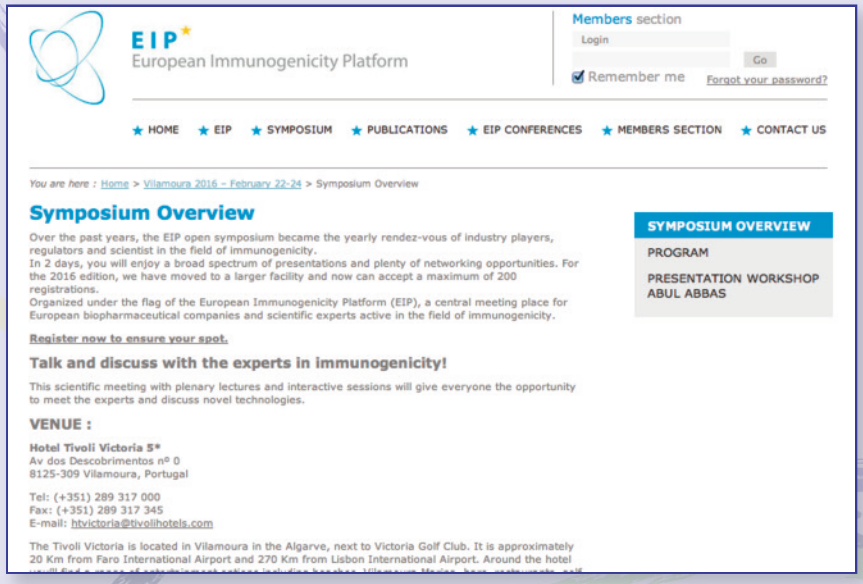
The ABIRISK Consortium in Innsbruck

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.'
www.imi.europa.eu

ABIRISK
EXTERNAL NEWSLETTER
ISSUE 13 - MARCH 2016
WWW.ABIRISK.EU

ABIRISK presented at key immunogenicity meetings

At the **2016 European Immunogenicity Platform (EIP) 8th Annual Symposium**, held in Vilamoura, Portugal, on 22-24 February 2016, **a session was dedicated to the ABIRISK Project. Anna Fogdell-Hahn (ABIRISK Partner 17 Karolinska Institutet), Tim Hickling (ABIRISK Partner 29 Pfizer Limited)** and **Bernard Maillère (ABIRISK Partner 5 Commissariat à L'Energie Atomique et aux Energies Alternatives-CEA)** were invited to give a talk on the scientific update of ABIRISK Work Packages 1-3.



The EIP Annual Symposium acts as a central meeting place for European biopharmaceutical companies and scientific experts active in the field of immunogenicity.

Its scope is: 1) Interaction with authorities regarding immunogenicity guidelines; 2) Formulate active recommendations regarding immunogenicity; 3) Stimulate research addressing the clinical and non-clinical effects of unwanted immunogenicity; and 4) Collaboration between academia and pharmaceutical companies.

The EIP aims to build a broad knowledge-base related to immunogenicity, and to stimulate interactions and developments in the broad field of immunogenicity.
Through its working-group structure, the EIP can react in a focused way on regulatory and scientific evolutions in the immunogenicity-field.

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.'
www.imi.europa.eu

ABIRISK
EXTERNAL NEWSLETTER
ISSUE 13 - MARCH 2016
WWW.ABIRISK.EU

UPCOMING EVENTS

AAPS NATIONAL BIOTECH MEETING

Boston, USA - 16-18 May 2016

The sessions will be focused on four themes examine science from multiple perspectives:

- **Biomarkers**
- **Formulation and Manufacturing**
- **Drug Delivery**
- **Immunogenicity**

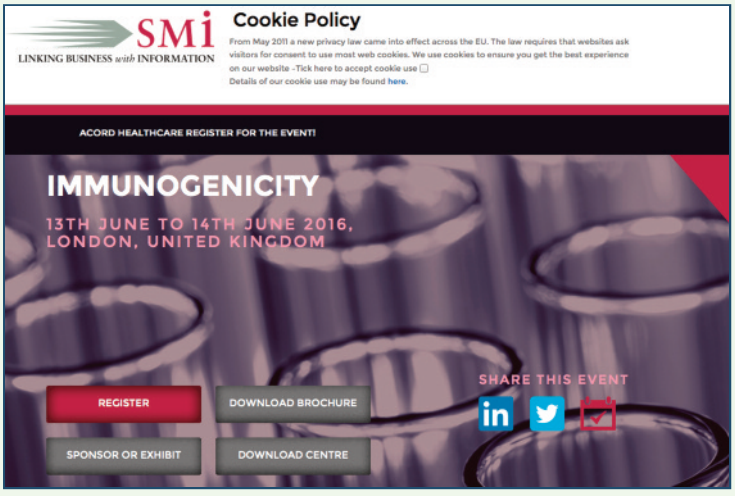
A great opportunity to learn and network with top biotechnology, and bring new ideas back to lab and office.

An integrated program will examine both theory and application from multiple perspectives including discovery, development, engineering, and regulatory aspects. It will be possible to choose the presentation depth preferred: short sunrise sessions, focused day-long short courses, dialogue and debate discussions, and symposia. There will be top speakers from industry, FDA, and academia and over 250 poster presentations featuring the latest scientific developments.

3rd Annual Conference on Immunogenicity

London, UK - 13-14, June 2016

SMi is proud to announce the return of their 3rd annual Immunogenicity event to London in 2016! The challenges for the biopharmaceutical market are different to those from traditional chemical entities. Immunogenicity continues to be a major concern for the field of science, due to its impact on safety and efficacy. The challenging task of immunogenicity assessment of a biopharmaceutical drug's immunogenic potential remains at the forefront of challenges.



Immunogenicity of an antigen is frequently encountered in the context of vaccine development, an area of intense interest currently due to the emergence or re-emergence of infectious pathogens with the potential for worldwide spread. With the global vaccine market expected to reach $84.44 billion by 2022, now is the time engage with industry experts to addresses the real challenges with immunogenicity including assay assessment, the role of aggregation, the introduction of nanobodies and many more!

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.'
www.imi.europa.eu

ABIRISK
EXTERNAL NEWSLETTER
ISSUE 13 - MARCH 2016
WWW.ABIRISK.EU

NEW PUBLICATIONS PRODUCED BY ABIRISK PROJECT

Development and validation of cell-based luciferase reporter gene assays for measuring neutralizing antibodies to interferon beta

Hermanrud Christina, Ryner Malin, Luft Thomas, Jensen Poul Erik, Ingenhoven Kathleen, Rat Dorothea, Deisenhammer Florian, Soelberg Sørensen Per, Bertotti Elisa, Kramer Daniel, Creeke Paul, Fogdell-Hahn Anna, on behalf of the ABIRISK consortium.

J Immunol Methods. 2016 Mar; 430:1-9. doi: 10.1016/j.jim.2016.01.004. Epub 2016 Jan11.

Neutralizing anti-drug antibodies (NAbs) against therapeutic interferon beta (IFNβ) in people with multiple sclerosis (MS) are measured with cell-based bioassays.


Journal of Immunological Methods

Research paper

Development and validation of cell-based luciferase reporter gene assays for measuring neutralizing anti-drug antibodies against interferon beta

The aim of this study was to redevelop and validate two luciferase reporter-gene bioassays, LUC and iLite, using a cut-point approach to identify NAb positive samples. Such an approach is favored by the pharmaceutical industry and governmental regulatory agencies as it has a clear statistical basis and overcomes the limitations of the current assays based on the Kawade principle. The work was conducted following the latest assay guidelines. The assays were re-developed and validated as part of the "Anti-Biopharmaceutical Immunization: Prediction and analysis of clinical relevance to minimize the risk" (ABIRISK) consortium and involved a joint collaboration between four academic laboratories and two pharmaceutical companies.

The LUC assay was validated at Innsbruck Medical University (LUCIMU) and at Rigshospitalet (LUCRH) Copenhagen, and the iLite assay at Karolinska Institutet, Stockholm. For both assays, the optimal serum sample concentration in relation to sensitivity and recovery was 2.5% (v/v) in assay media. A Shapiro-Wilk test indicated a normal distribution for the majority of runs, allowing a parametric approach for cut-point calculation to be used, where NAb positive samples could be identified with 95% confidence. An analysis of means and variances indicated that a floating cut-point should be used for all assays. The assays demonstrated acceptable sensitivity for being cell-based assays, with a confirmed limit of detection in neat serum of 1519ng/mL for LUCIMU, 814ng/mL for LUCRH, and 320ng/mL for iLite. Use of the validated cut-point assay, in comparison with the previously used Kawade method, identified 14% more NAb positive samples.

In conclusion, implementation of the cut-point design resulted in increased sensitivity to detect NAbs. However, the clinical significance of these low positive titers needs to be further evaluated.

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.'
www.imi.europa.eu

ABIRISK
EXTERNAL NEWSLETTER
ISSUE 13 - MARCH 2016
WWW.ABIRISK.EU

RECENT PUBLICATIONS GENERATED BY ABIRISK PARTICIPANTS OUTSIDE THE PROJECT

IgG1 Allotypes Influence the Pharmacokinetics of Therapeutic Monoclonal Antibodies through FcRn Binding
Ternant D, Arnoult C, Pugnière M, Dhommée C, Drocourt D, Perouzel E, Passot C, Baroukh N, Mulleman D, Tiraby G, Watier H, Paintaud G, Gouilleux-Gruart V.
J Immunol. 2015 Dec 18.

The Role of Aggregates of Therapeutic Protein Products in Immunogenicity: An Evaluation by Mathematical Modeling
Yin L, Chen X, Tiwari A, Vicini P, Hickling TP.
J Immunol Res. 2015;2015:401956.

Advances in and Algorithms for the Treatment of Relapsing-Remitting Multiple Sclerosis
Ingwersen J, Aktas O, Hartung HP.
Neurotherapeutics. 2015 Dec 23.

Secukinumab, a novel anti-IL-17A antibody, shows low immunogenicity potential in human in vitro assays comparable to other marketed biotherapeutics with low clinical immunogenicity
Karle A, Spindeldreher S, Kolbinger F.
MAbs. 2016 Jan 28

Effectiveness and safety of abatacept in elderly patients with rheumatoid arthritis enrolled in the French Society of Rheumatology's ORA registry
Lahaye C, Soubrier M, Mulliez A, Bardin T, Cantagrel A, Combe B, Dougados M, Flipo RM, Le Loët X, Shaeverbeke T, Ravaud P, Mariette X, Gottenberg JE; French Society of Rheumatology.
Rheumatology (Oxford). 2016 Jan 27.

Rheumatoid factor and anti-citrullinated protein antibody positivity are associated with a better effectiveness of abatacept: Results from the Pan-European registry analysis
Gottenberg JE, Courvoisier DS, Hernandez MV, Iannone F, Lie E, Canhão H, Pavelka K, Hetland ML, Turesson C, Mariette X, Finckh A.
Arthritis Rheumatol. 2016 Jan 27.

Daclizumab high-yield process reduced the evolution of new gadolinium-enhancing lesions to T1 black holes in patients with relapsing-remitting multiple sclerosis
Radue EW, Sprenger T, Vollmer T, Giovannoni G, Gold R, Havrdova E, Selmaj K, Stefoski D, You X, Elkins J.
Eur J Neurol. 2016 Feb;23(2):412-5.

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.'
www.imi.europa.eu

ABIRISK
EXTERNAL NEWSLETTER
ISSUE 13 - MARCH 2016
WWW.ABIRISK.EU

RECENT PUBLICATIONS GENERATED BY ABIRISK PARTICIPANTS OUTSIDE THE PROJECT

B cell-directed therapies in multiple sclerosis
Gasperi C, Stüve O, Hemmer B.
Neurodegener Dis Manag. 2016 Feb;6(1):37-47.

Achievements, challenges and unmet needs for haemophilia patients with inhibitors: Report from a symposium in Paris, France on 20 November 2014
Dargaud Y, Pavlova A, Lacroix-Desmazes S, Fischer K, Soucie M, Claeyssens S, Scott DW, d'Oiron R, Lavigne-Lissalde G, Kenet G, Escuriola Ettingshausen C, Borel-Derlon A, Lambert T, Pasta G, Négrier C.
Haemophilia. 2016 Jan;22 Suppl 1:1-24.

Tocilizumab and multiple sclerosis: a causal relationship? Clinical Commentary on the case report entitled - MS arising during Tocilizumab therapy for rheumatoid arthritis
Comabella M.
Mult Scler. 2016 Jan 7.

Cytokine profiles show heterogeneity of interferon-β response in multiple sclerosis patients
Hegen H, Adrianto I, Lessard CJ, Millonig A, Bertolotto A, Comabella M, Giovannoni G, Guger M, Hoelzl M, Khalil M, Fazekas F, Killestein J, Lindberg RL, Malucchi S, Mehling M, Montalban X, Rudzki D, Schautzer F, Sellebjerg F, Sorensen PS, Deisenhammer F, Steinman L, Axtell RC.
Neurol Neuroimmunol Neuroinflamm. 2016 Jan 27;3(2):e202.

Effectiveness and Safety of Vedolizumab Induction Therapy for Patients with Inflammatory Bowel Disease
Amiot A, Grimaud JC, Peyrin-Biroulet L, Filippi J, Pariente B, Roblin X, Buisson A, Stefanescu C, Trang-Poisson C, Altwegg R, Marteau P, Vaysse T, Bourrier A, Nancey S, Laharie D, Allez M, Savoye G, Moreau J, Gagniere C, Vuitton L, Viennot S, Aubourg A, Pelletier AL, Bouguen G, Abitbol V, Bouhnik Y; OBSERV-IBD study group and the GETAID.
Clin Gastroenterol Hepatol. 2016 Feb 22.

Design of clinical trials for new products in hemophilia: communication from the SSC of the ISTH
Dimichele DM, Lacroix-Desmazes S, Peyvandi F, Srivastava A, Rosendaal FR; Subcommittee on Factor VIII, Factor IX and Rare Coagulation Disorders.
J Thromb Haemost. 2015 May;13(5):876-9.

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.'
www.imi.europa.eu

ABIRISK
EXTERNAL NEWSLETTER
ISSUE 13 - MARCH 2016
WWW.ABIRISK.EU

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!

Innovative Medicines Initiative

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.'
www.imi.europa.eu