ABIRISK

EXTERNAL NEWSLETTER

ISSUE 5 - MARCH 2014

WWW.ABIRISK.EU

Dear colleagues, dear friends and supporters of ABIRISK,

we are pleased to present you the fifth 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)

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PROJECT NEWS

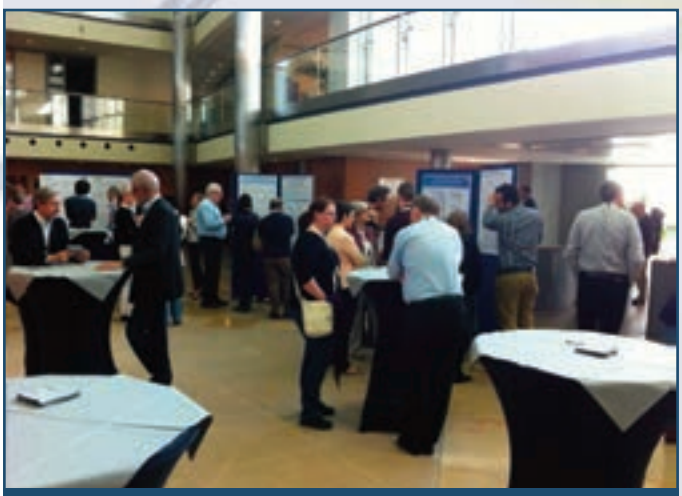
ABIRISK GENERAL ASSEMBLY
March 12th and 13th 2014
UCB PHARMA - ALLÉE DE LA RECHERCHE 60, 1070 ANDERLECHT - BRUSSELS, BELGIUM

The Oral Presentation Session

On the 11th, 12th and 13th of March 2014, the **Third Annual Meeting of ABIRISK Project** was held in Brussels (Belgium) at UCB Pharma Headquarter.

ABIRISK Third Annual Meeting was organized only for the partners of the project and more than 100 participants attended ABIRISK General Assembly in Brussels.

The meeting started with the ABIRISK Executive Project Management Team and Steering Committee meetings, followed by the General Assembly. The first day of the ABIRISK General Assembly agenda included the update on main project successes, issues and challenges for the second year of the project, an overview on ABIRISK project management and dissemination activities, some presentations from Work Packages (WPs) Leaders on WPs update and deliverables, and WPs' sub-meetings.



The Poster Session

WPs' sub-meetings were followed by the presentation of **Bonita Rup** (ABIRISK Partner 29 Pfizer Limited) on the **"Terms and Definitions for Describing and Interpreting Unwanted Immunogenicity against Biopharmaceuticals"** document recently finalized by **ABIRISK Consortium members** and currently submitted for publication. As anticipated in the **previous issue of the ABIRISK External Newsletter,** a prerequisite to understanding the impact of immunogenicity is to provide clear definitions around terms and concepts related to immunogenicity, its prediction, and associated clinical events. Agreement on terms and definitions to describe and implement these new and emerging aspects of immunogenicity science will be also an outcome of the **ABIRISK goals.** Bonita's presentation aimed to overview the current status of terms and definitions document with recommended communication strategy.

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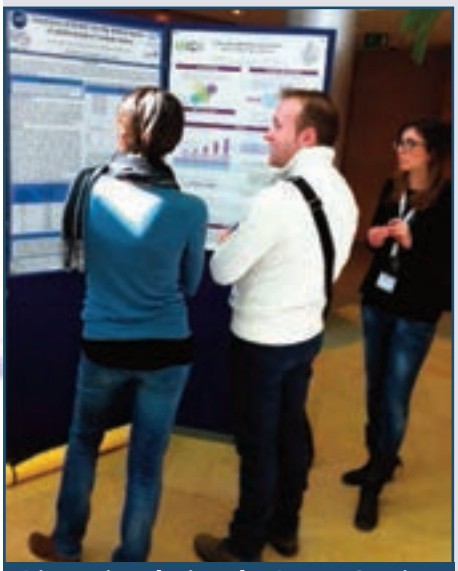
Discussion during the Poster Session

The second day of the ABIRISK General Assembly was completely dedicated to science and it 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 by the ABIRISK Consortium members. 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 as well as with ABIRISK Scientific Advisory Board members have taken place during all scientific sessions.

Scientific sessions were followed by the presentation of **Maria Teresa De Magistris** (Innovative Medicine Initiative - IMI; ABIRISK Scientific Officer) titled **"The Innovative Medicines Initiative: overview and achievements".**

The presentation of **Maria Teresa De Magistris** was focused on IMI projects organization, aims and major achievements obtained so far and on some information related to the future calls belonging to IMI 2 Work Programme.


Comments from the ABIRISK Scientific Advisory Board

The Third ABIRISK Annual Meeting was closed by the **ABIRISK Scientific Advisory Board** report focused on main strengths and weaknesses of the project and giving crucial suggestions to ABIRISK Consortium members on how optimize resources and efforts during the third year of the project.

The ABIRISK Project Consortium during Third Annual Meeting of ABIRISK Project in Brussels - March 2014

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ABIRISK PRESENTED AT KEY IMMUNOGENICITY MEETINGS

At the **6th Open Scientific European Immunogenicity Platform (EIP) Symposium on Immunogenicity of Biopharmaceuticals** (Lisbon, Portugal, 24-26 February 2014) an entire section **(Section 7)** on day 3 has been dedicated to A**BIRISK Project**. **Section 7 of the Symposium** was chaired by **Daniel Kramer** (ABIRISK Partner 14 Merck KGaA) and opened by **Marc Pallardy** (INSERM, ABIRISK Managing Entity) presentation focused on the achievements obtained by ABIRISK during the second year of the project and planning of 2014 activities. Marc's talk was followed by **Liz Jury** (ABIRISK Partner 8 University College London - UCL) **"Cellular characterization and mechanisms of the AD immune response"** and **Bernard Maillère** (ABIRISK Partner 5 Commissariat a L'Energie Atomique et aux Energies Alternatives - CEA) **"Evaluation and development of technologies for predicting immunogenicity"** presentations. Session 7 was closed by **Christian Ross Pedersen** (EIP Chairman and ABIRISK Partner 35 Novo Nordisk A/S) talk **"Closing remarks and outlook".**

Anna Fogdell-Hahn (ABIRISK Partner 17 Karolinska Institutet – KI) was invited to present ABIRISK Project at the **Pfizer Immunogenicity Meeting** (Oslo, Norway, 12 February 2014). Meeting presentations gave to the audience an overview on clinical immunogenicity data from the perspective of different European countries with particular emphasis on biopharmaceuticals immunogenicity risks.

UPCOMING EVENTS

APRIL

CORAL GABLES SYMPOSIUM "UNDERSTANDING IMMUNOGENICITY: THE FUTURE FORETOLD"
Coral Gables Symposia provide a unique forum for thought leaders to address the principal concerns regarding the immunogenicity of biopharmaceuticals; in their development, regulation, and clinical use. Coral Gables Symposia provides delegates with a convivial environment designed to foster the exchange of ideas. Coral Gables symposium 2014 aims to establish improved approaches to the major challenges confronting those active in the field.

The 2014 Coral Gables Symposium will focus on an understanding of the mechanisms that can lead to an immune response against biopharmaceutical products and the consequences of such immunogenicity on clinical outcome and patient safety.
6th-8th April - Miami, U.S.A

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MAY

THE AMERICAN ASSOCIATION OF IMMUNOLOGISTS (AAI) ANNUAL MEETING

Join us in Pittsburgh for the world's leading annual all-immunology event worldwide and:
- Find the latest developments in your field
- Hear lectures by the world's most prominent immunologists and poster presentations by scientists at e every career stage
- Network with colleagues from more than 40 countries, and
- See the newest tools and techniques to benefit your research!

2nd-6th, May - Pittsburgh, U.S.A.

PROTEIN AND ANTIBODY ENGINEERING SUMMIT (PEGS) TENTH ANNUAL MEETING

Over 1,600 participants will gather in Boston's vibrant seaport district for open forum discussions and collaboration at CHI's flagship biologics event "PEGS the essential protein engineering summit".
The continued success of PEGS is driven by the growth in biologics worldwide, the quality of scientific programming presented and valuable networking opportunities.
5th-9th May - Boston, USA

2014 AMERICAN ASSOCIATION OF PHARMACEUTICAL SCIENTISTS (AAPS) – NATIONAL BIOTECHNOLOGY CONFERENCE

One Conference—Four Program Themes: Biomanufacturing; Biomarker and PK/PD; Research and Discovery; Immunogenicity and Administration Routes
An integrated program will examine both theory and application from multiple perspectives including discovery, development, engineering, and regulatory aspects.
19th-21rd May - San Diergo, USA

NEW PUBLICATIONS PRODUCED BY ABIRISK PROJECT

Human leukocyte antigen and interferon beta preparation influence risk of developing neutralizing anti-drug antibodies in multiple sclerosis.
Link J, Ryner ML, Fink K, Hermanrud C, Lime I, Brynedal B, Kockum I, Hillert J, Fogdell-Hahn A
PLoS One. 2014 Mar 7;9(3):e90479.

A significant proportion of patients with multiple sclerosis who receive interferon beta (IFNβ) therapy develop neutralizing antibodies (NAbs) that reduce drug efficacy.

The main objective of the present study performed by **ABIRISK Partner Karolinska Institutet** was to investigate if HLA class I and II alleles are associated with development of NAbs against IFNβ. To this aim, the authors analyzed whether NAb status and development of NAb titers high enough to be biologically relevant (>150 tenfold reduction units/ml) correlated with the HLA allele group carriage in a cohort of 903 Swedish patients with multiple sclerosis treated with either intramuscular IFNβ-1a, subcutaneous IFNβ-1a or subcutaneous IFNβ-1b.

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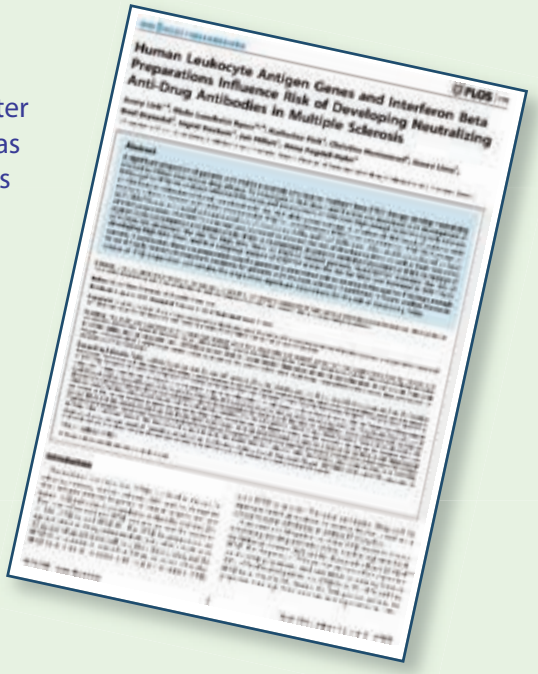
Results reported in this study indicated that carriage of HLA-DRB1*15 was associated with increased risk of developing NAbs and high NAb titers. After stratification based on type of IFNβ preparation, HLA-DRB1*15 carriage was observed to increase the risk of developing NAbs as well as high NAb titers against both subcutaneous and intramuscular IFNβ-1a. Furthermore, in patients receiving subcutaneous IFNβ-1a carriage of HLA-DQA1*05 decreased the risk for high NAb titers. In IFNβ-1b treated patients, HLA-DRB1*04increased the risk of developing high NAb titers, and in a subgroup analysis of DRB1*04 alleles the risk for NAbs was increased in DRB1*04:01 carriers.

In conclusion, this study reported that there is a preparation-specific genetically determined risk to develop NAbs against IFNβ high enough to be clinically relevant in treatment decisions for patients with multiple sclerosis if confirmed in future studies. However, choice of IFNβ preparation still remains the single most significant determinant for the risk of developing NAbs.


Human Leukocyte Antigen Genes and Interferon Beta Preparations Influence Risk of Developing Neutralizing Anti-Drug Antibodies in Multiple Sclerosis

RECENT PUBLICATIONS GENERATED BY ABIRISK PARTICIPANTS OUTSIDE THE PROJECT

Predictive immunogenicity of Refacto.
Delignat S, Repessé Y, Gilardin L, Dimitrov JD, Lone YC, Kaveri SV, Lacroix-Desmazes S.
Haemophilia. 2013 Dec 30.

Body fluid biomarkers in multiple sclerosis.
Comabella M, Montalban X.
Lancet Neurol. 2014 Jan;13(1):113-26.

Relationship between inflammation and infliximab pharmacokinetics in rheumatoid arthritis.
Ternant D, Ducourau E, Perdriger A, Corondan A, Le Goff B, Devauchelle-Pensec V, Solau-Gervais E, Watier H, Goupille P, Paintaud G, Mulleman D.
Br J Clin Pharmacol. 2013 Dec 19

Sarilumab, a fully human monoclonal antibody against IL-6Rα in patients with rheumatoid arthritis and an inadequate response to methotrexate: efficacy and safety results from the randomised SARIL-RA-MOBILITY Part A trial.
Huizinga TW, Fleischmann RM, Jasson M, Radin AR, van Adelsberg J, Fiore S, Huang X, Yancopoulos GD, Stahl N, Genovese MC.
Ann Rheum Dis. 2013 Dec 2.

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Risk acceptance in multiple sclerosis patients on natalizumab treatment.
Tur C, Tintoré M, Vidal-Jordana A, Bichuetti D, Nieto González P, Arévalo MJ, Arrambide G, Anglada E, Galán I, Castilló J, Nos C, Río J, Martín MI, Comabella M, Sastre-Garriga J, Montalban X.
PLoS One. 2013 Dec 10;8(12):e82796.

Spanish consensus on the use of natalizumab (Tysabri®)-2013.
Fernández O, García-Merino JA, Arroyo R, Alvarez-Cermeño JC, Izquierdo G, Saiz A, Olascoaga J, Rodríguez-Antigüedad A, Prieto JM, Oreja-Guevara C, Hernández MA, Moral E, Meca J, Montalbán X.
Neurologia. 2013 Dec 18. pii: S0213-4853(13)00243-0.

Smokers run increased risk of developing anti-natalizumab antibodies.
Hedström A, Alfredsson L, Lundkvist Ryner M, Fogdell-Hahn A, Hillert J, Olsson T.
Mult Scler. 2013 Dec 5.

Aggregation of human recombinant monoclonal antibodies influences the capacity of dendritic cells to stimulate adaptive T-cell responses in vitro.
Rombach-Riegraf V, Karle AC, Wolf B, Sordé L, Koepke S, Gottlieb S, Krieg J, Djidja MC, Baban A, Spindeldreher S, Koulov AV, Kiessling A.
PLoS One. 2014 Jan 21;9(1):e86322

Anti-Interferon Beta Antibody Titers Strongly Correlate Between Two Bioassays and In Vivo Biomarker Expression, and Indicates That a Titer of 150 TRU/mL Is a Biologically Functional Cut-Point.
Hermanrud C, Ryner ML, Engdahl E, Fogdell-Hahn A.
J Interferon Cytokine Res. 2014 Jan 20.

Biomarkers of treatment response in multiple sclerosis.
Buck D, Hemmer B.
Expert Rev Neurother. 2014 Feb;14(2):165-72.

Safety and effectiveness of adalimumab in patients with rheumatoid arthritis over 5 years of therapy in a phase 3b and subsequent postmarketing observational study.
Burmester GR, Matucci-Cerinic M, Mariette X, Navarro-Blasco F, Kary S, Unnebrink K, Kupper H.
Arthritis Res Ther. 2014 Jan 27;16(1):R24.

Clinical, radiographic and immunogenic effects after 1 year of tocilizumab-based treatment strategies in rheumatoid arthritis: the ACT-RAY study.
Dougados M, Kissel K, Conaghan PG, Mola EM, Schett G, Gerli R, Hansen MS, Amital H, Xavier RM, Troum O, Bernasconi C, Huizinga TW.
Ann Rheum Dis. 2014 Jan 28.

Review article: anti-adhesion therapies for inflammatory bowel disease.
Lobatón T, Vermeire S, Van Assche G, Rutgeerts P.
Aliment Pharmacol Ther. 2014 Jan 30.

Multiple sclerosis in 2013: Novel triggers, treatment targets and brain atrophy measures.
Montalban X, Tintoré M.
Nat Rev Neurol. 2014 Feb;10(2):72-3.a

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The challenges of measuring disability accumulation in relapsing-remitting multiple sclerosis: evidence from interferon beta treatments.
Kieseier BC.
Expert Rev Neurother. 2014 Jan;14(1):105-20.

Do immunoglobulin levels and CD4 cell count interact during Rituximab treatment?
Mulleman D.
Arthritis Rheumatol. 2014 Jan 27. doi: 10.1002/art.38361.

Direct and indirect rituximab-induced T-cell depletion.
Thibault G, Mulleman D.
Arthritis Rheum. 2014 Jan 8.

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 has been visited by a monthly average of over 7 hundred people worldwide in the last 12 months!

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