1st INTERNATIONAL MEETING
FOCUS ON
UPPER & LOWER
AIRWAYS DISEASES
Highlights

Genoa (Italy), February 16-18, 2017

Highlights

Introduction

Prof. Canonica, chairman of the symposium, opened the congress, by highlighting the high scientific level of this meeting focusing on upper and lower airways diseases with the intention to identify these two entities as a continuum and not as two different and quite unrelated diseases. Many top researchers in airway disease field, coming from all the world attended this symposium together with young physicians, pneumologists and allergologists. This congress represented a very unique occasion for a full update on Asthma, COPD and Allergic diseases linked to the Precision Medicine.

To follow the presentations of this congress, click on the link below:
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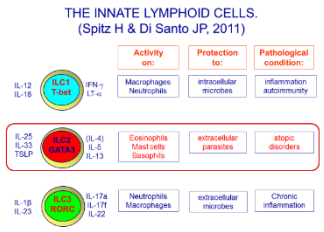
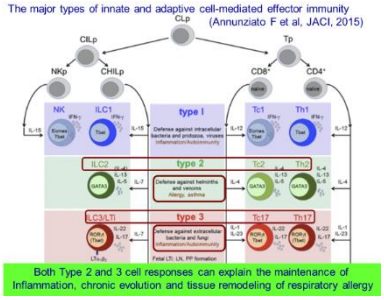
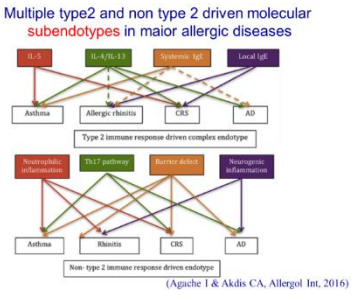
RHINITIS: Pathophysiology aspect



The pathophysiological aspect of Rhinitis was the topic discussed by Prof. Maggi in his lecture. The speaker, coming from Florence (IT), went deeper in his talk by presenting very interesting data starting from the history of the Rhinitis pathophysiology. Going deeper in his presentation, Prof. Maggi, highlighted the role played by the Th2 cells as the main regulator of the immune response, responsible for the onset of the allergic reaction. In the main part of his talk, the speaker presented also very interesting data on the function of the Th17 cells as a new player in the pathophysiology of Rhinitis, able to activate the neutrophil reaction through an alternative pathway, not modulated by the usual mechanisms of control. Prof. Maggi spoke also about the innate lymphoid cells, a novel family of haematopoietic effectors with many effects on eosinophils, mast cells and basophils and responsible for atopic disorders in many pathological conditions. In the last part of his presentation, the speaker presented new data on the plasticity of the so-called effector cells. In conclusion Prof. Maggi pointed out that these pathogenetic mechanisms allow to identify some endotypes of respiratory allergic disorders for their selective treatment with the new biological agents.





- Does the flexibility of Th cells explain the different endotypes of allergic respiratory diseases?
- What are the main mechanisms leading to the Flexibility of differentiated effectors cells?
- What are the main characteristics of the Th17 cells as new players in Asthma pathogenesis?
- What are the main allergic mechanisms associated with the stimulation of the innate immunity?
- What are the main functions of the Th cells already defined?

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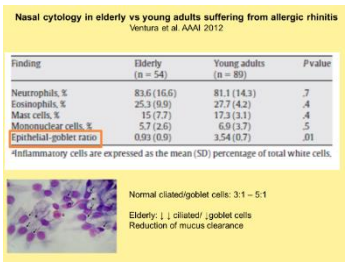
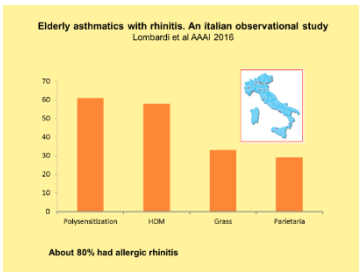
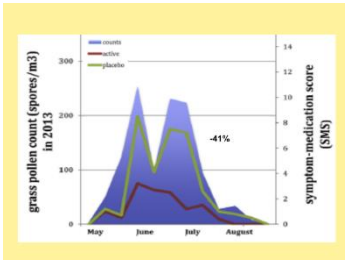
Rhinitis in the elderly



Prof. Milanese from Pietra Ligure (IT), spoke about Rhinitis in the elderly. The speaker went deeper in his talk, by presenting very interesting and impressive data about the increasing burden of the chronic noncommunicable diseases and about the prevalence of rhinitis symptoms in people over 65 years old. In the main part of his lecture Prof. Milanese spoke about the nasal cytology in the elderly characterized by the reduction of the ciliated and goblet cells compared to the ones in young people. More in particular the speaker presented data on the correlation between asthma and allergic rhinitis in the elderly, by highlighting that most asthmatic patients suffer for allergic rhinitis. In the last part of his presentation, Prof. Milani spoke about nonallergic rhinitis, by presenting data on three major forms, like the vasomotor, the gustatory and the hormonal induced rhinitis. Finally, the speaker presented very interesting data on the treatment of the allergic rhinitis in the elderly.





- What are the main medications that can cause or contribute to rhinitis?
- What are the major types of rhinitis seen in the elderly based on the data presented by the speaker?
- What's about the duration of asthma and rhinitis in the elderly?
- What is the frequency of positive skin test results in elderly rhinitic subjects?
- What is the prevalence of elderly asthmatics with rhinitis based on the data presented by the speaker?
- What's about the correlation between olfactory scoring and age?
- What is the main difference in nasal cytology between elderly and young people?

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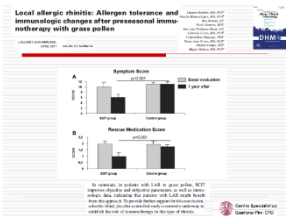
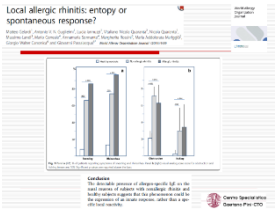
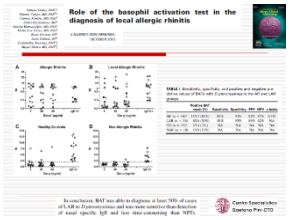
Local allergic rhinitis: which evidence?



The evidence of the local allergic rhinitis was the topic Prof. Incorvaia spoke about in her lecture. The speaker coming from Milan (IT), started his talk, by highlighting that the discovery of the IgE role in the rhinitis pathophysiology was done in 1975 and starting from that time the studies on the IgE functions in the rhinitis pathogenesis are exponentially increased. Going deeper in his lecture, Prof. Incorvaia presented many data derived from clinical studies on the role played by the IgE in the rhinitis etiopathogenesis and, more in particular on the affordability of the nasal provocation test (NPT), by highlighting that there is a poor evidence of the real effectiveness of this test for the diagnosis of the local rhinitis. In conclusion, the speaker pointed out that the local allergic rhinitis does exist, but neither NPT nor the detection of the local IgE production can establish a firm diagnosis.





- What is the role of the basophil activation test in the diagnosis of the local allergic rhinitis?
- Is the local allergic rhinitis an entopy or a spontaneous response?
- What are the main allergen-specific IgEs in the skin and nasal mucosa of symptomatic and asymptomatic children sensitized to aeroallergens?
- What's about the evidence of the diagnostic performance of the nasal provocation test?

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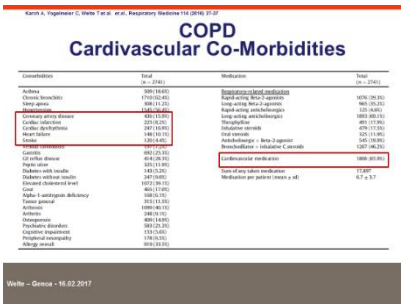
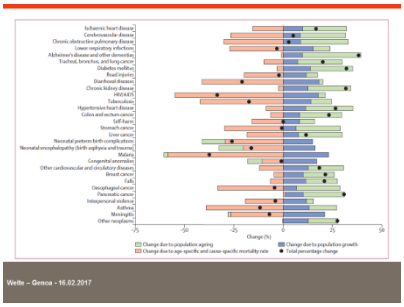
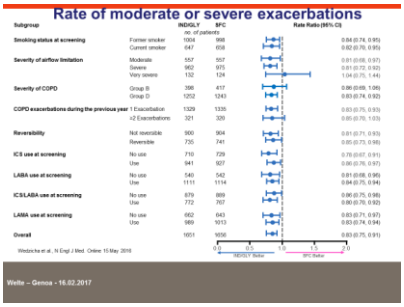
Epidemiology of COPD development and evolution



The Epidemiology of COPD development and evolution was the topic at the core of the lecture discussed by Prof. Welte. At the beginning of his talk the speaker, coming from Hannover (Germany) presented very interesting data derived from many epidemiologic and registries studies, by highlighting that the major COPD co-morbidities are the cardiovascular diseases. Speaking about prevalence, Prof. Welte presented data given by epidemiologic studies, by highlighting that in Italy there are 2-2.5 million people affected by COPD. In the main part of his lecture, Prof. Welte spoke about the nonpharmacological and the pharmacological treatment of COPD, by highlighting that the drugs developed for COPD are very old. The speaker presented many data given by clinical trials, on the effects of corticosteroids, bronchodilators and other drugs. In conclusion, Prof. Welte pointed out that the progress in COPD therapy is only marginal, because COPD is an umbrella term for different diseases, and it is necessary to improve in phenotyping or better in clustering the patients for the development of biomarkers able to divide them in more homogeneous groups for a better development of new very effective drugs.





- What's about the new drugs for the COPD treatment?
- What is the modern pharmacotherapy of the obstructive lung disease?
- What are the mayor abnormal ECG findings discovered by the speaker with his ECG screening project?
- What's about the effects of the non-pharmacological treatment of COPD?
- What's about the prevalence of COPD in the world?
- What are the main COPD co-morbidities presented by the speaker?

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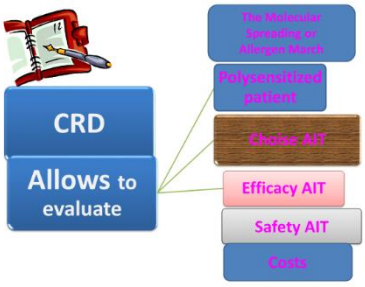
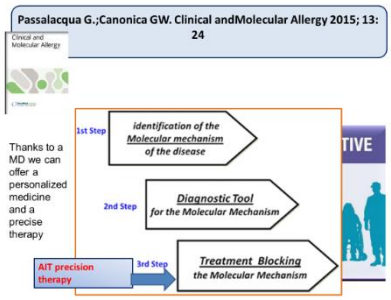
Molecular diagnosis of Rhinitis



The molecular diagnosis of rhinitis was the topic at the core of the lecture discussed by Prof. Savi. The speaker, coming from Piacenza (IT), introduced her talk by presenting data on the WAO ARIA GA2LEN consensus document on molecular-based allergy diagnosis, by highlighting that the diagnostic approach to allergic rhinitis can be performed with the molecular diagnosis before the execution of the prick test. Going deeper in her lecture, Prof. Savi spoke about CRD for the evaluation of the polysensitized patients, the choice and the efficacy of the immune therapy and finally for the evaluation of the allergic march. In the main part of her speech Prof. Savi presented many data on the CRD application in the diagnosis and prognosis of the pet allergy. In the last part of her presentation the speaker talked about the efficacy of the molecular diagnosis for the choice of the more suitable immunotherapy, by highlighting that CRD can allow a personalized treatment for any single patient. Finally, Prof. Savi talked about the CRD cost-effect evaluation, by highlighting that the use of the molecular diagnosis may be a cost-effective way to a better selection of patients for immunotherapy.



- What's about the economic analysis and the costs related to CRD from the speaker point of view?
- What's about CRD for the efficacy AIT evaluation?
- What is the relationship between CRD and precision medicine based on the data presented by the patients?
- What's about the application of CRD in the PET allergy?

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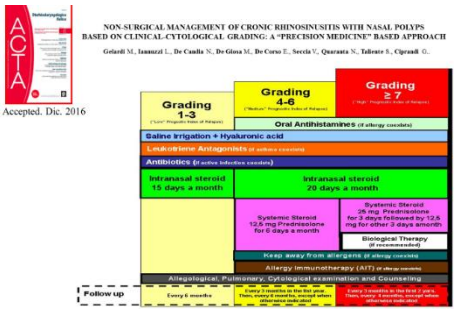
The role of nasal cytology

The role of nasal cytology was the topic of Prof. Gelardi presentation. The speaker, coming from Bari (IT), started his lecture, by highlighting that only in the last times have been published many scientific articles on the nasal cytology. Going deeper in his lecture the speaker talked about the role of the nasal cytology in the diagnosis of the muco-ciliary system alterations leading to the onset of the allergic rhinitis. Prof. Gelardi pointed out that the nasal cytology is very helpful in the correct diagnosis of all the types of rhinitis. In the main part of his lecture, the speaker presented very interesting data on the application of the nasal cytology for the prognostic evaluation of the patients affected by nasal polyposis and allergic rhinitis, by highlighting the importance of a correct phenotyping of these patients. In conclusion, Prof. Gelardi pointed out that the movement of the nasal ciliary system is at the basis of our life.



- What is the role of the nasal cytology in the treatment's choice?
- What's about the relationship between phenotyping and nasal cytology?
- What are the main clinical aspects of the nasal polyposis presented by the speaker?
- How to evaluate the chronic nasal symptoms from the speaker point of view?
- What's about the general classification of rhinitis and its relationship with the nasal cytology?

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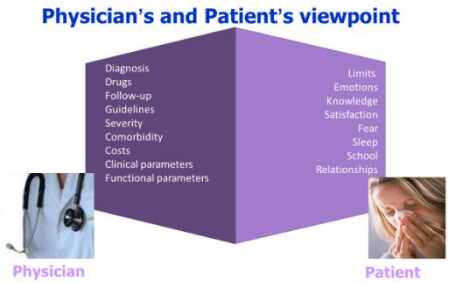
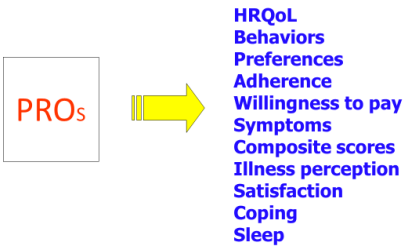
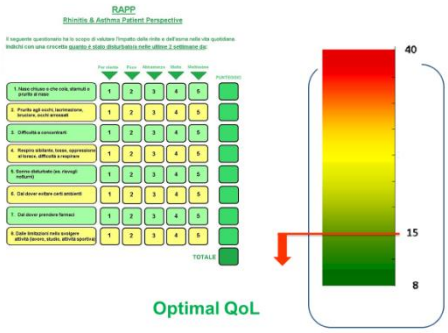
Patients reported outcomes in Rhinitis



Patients reported outcomes in Rhinitis was the topic of Prof. Baiardini presentation. The speaker, coming from Genova (IT), at the beginning of her lecture, talked about the physician and the patients' point of view of the disease. Going deeper in her lecture, Prof. Baiardini pointed out that the patient reported outcomes (PRO) refers to "any report coming from patients about a health condition and its treatment" and its importance is growing also for the Regulatory processes evaluation. More in particular the speaker highlighted that the patients' point of view must be measured directly from the patients, thanks to the application of validated tools.





Prof. Baiardini presented very interesting data on the relationship between the quality of life perception and the patients reported outcomes, by highlighting that PRO may help in the assessment of the possible reasons of uncontrolled asthma and in modifying the treatment plan. Finally, Prof. Baiardini spoke about RAPP (rhinitis and & asthma patient perspective) as a new short questionnaire for the daily asthma and rhinitis QoL assessment, developed by her team of research with the aim to facilitate the clinical application of PAR.

- What are the main barriers for the use of the current PRO questionnaires in daily practice?
- What are the main characteristics of the relationship between illness optimal control and optimal QoL from the patients point of view?
- What are the main coping strategies presented by the speaker?
- What's about the PROs evaluations?
- What are the key points referring to the Patient reporting outcomes presented by the speaker?

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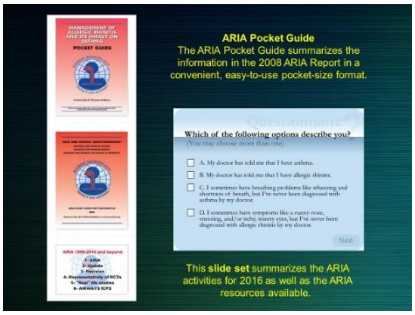
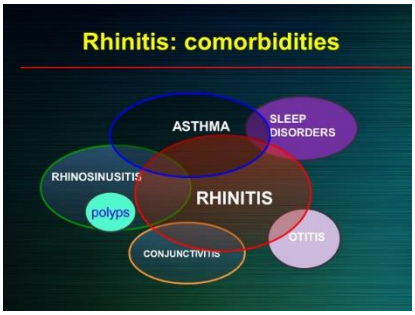
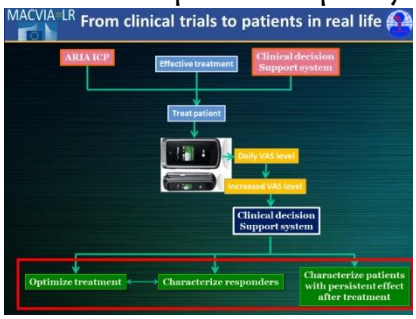
The Italian ARIA Guidelines



Prof. Lombardi, coming from Brescia (IT) spoke about the Italian ARIA guidelines, by presenting very interesting data on allergic rhinitis and its impact on Asthma and on the GRADE approach. GRADE stands for grading of recommendations assessment, developing and evaluation and it is characterized by the presence of very strong recommendations inside the guidelines themselves. Going deeper in his lecture Prof. Lombardi spoke about the ARIA pocket Guide and the ARIA pharmacist's guide. In the main part of his presentation, the speaker talked about the Italian project and more in particular on the MASK study that provides for the use of the mobile technology for a better involvement of patients in the asthma control. In the second part of his talk, Prof. Lombardi, presented data on the rhinitis comorbidities, highlighting that the respiratory symptoms and diseases are still increasing in Italy as in all the world. The speaker presented also data on rhinitis pathogenesis, diagnosis and on the patients' quality of life. Finally, Prof. Lombardi spoke about treatment, by presenting data on the educational approach of patients, on the environmental intervention for the selection and the removal of any specific allergen, on pharmacotherapy and immunotherapy for a personalized approach to any patient. In conclusion, the speaker pointed out that allergic rhinitis and its comorbidities are a worldwide spread illness having an important impact on social life, sleep quality, school and work productivity.





- What are the unmet needs of the patients affected by rhinitis?
- What are the main outcomes of immunotherapy in allergic rhinitis and lower airway diseases?
- What are the key points of the allergic rhinitis ARIA classification?
- What's about the rhinitis pathogenesis based on the data presented by the speaker?
- What is the trend of the allergic rhinitis prevalence in Italy?
- What are the key points of the GRADE classification?
- What's about the app developed in the context of the MASK project?

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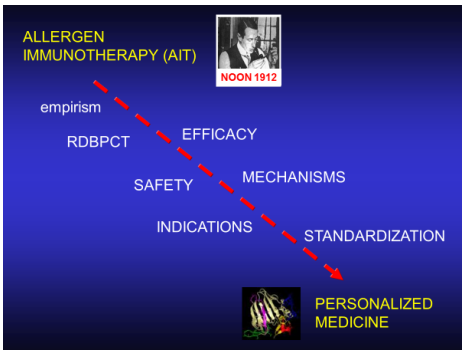
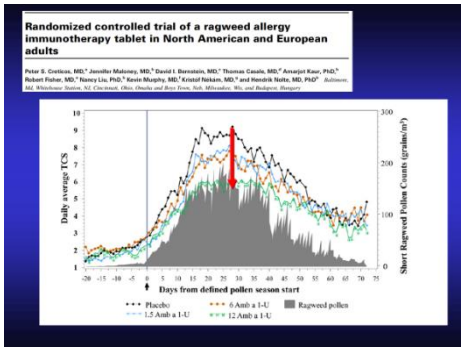
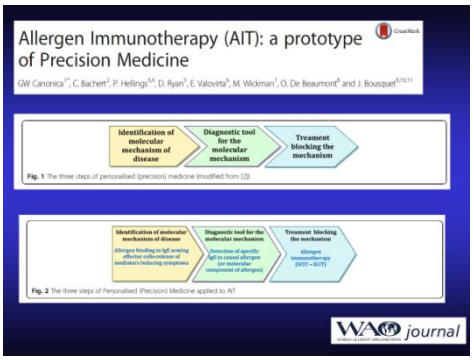
Immunotherapy as precision medicine



Immunotherapy as precision medicine was the topic at the core of Prof. Passalacqua presentation. The speaker, coming from Genova (IT), at the beginning of his talk, addressed the audience with this question: what is precision medicine and what is AIT? In order to find a very comprehensive answer, Prof. Passalacqua went deeper in his speech and presented very interesting data on the new biological drugs for the personalised treatment of Asthma. Talking about immunotherapy, the speaker pointed out that in the past, this approach was quite far from the concept of the precision medicine, but now after the IgE introduction, the story is dramatically changed. In the main part of his lecture, the speaker talked about the sublingual immunotherapy discovered for the first time in Italy and on its dose dependent effect in asthma and rhinitis patients. Prof. Lombardi presented data on the dose-finding studies and spoke about safety, by highlighting that the only one contraindication for the sublingual immunotherapy is characterized by the uncontrolled asthma. In the last part of his presentation the speaker talked about the allergic rhinitis pathophysiology, the related immunotherapy mechanisms and finally on the molecular diagnosis of these patients. In conclusion, Prof. Passalacqua pointed out that the knowledge of the pathogenesis and the specific allergens involved in the disease manifestation can lead to a very detailed diagnosis, that is the first very important step toward the wide application of the precision medicine in AIT.





- How the molecular diagnosis can change the allergen-specific immunotherapy prescription?
- What are the main problems for a wide precision medicine application in allergic rhinitis patients?
- What are the main recombinant allergens for specific immunotherapy?
- Where does IT preferentially work?
- What's about the application of specific biomarkers in allergic rhinitis patients' selection?
- What's about the monoclonal therapy in allergic rhinitis patients?

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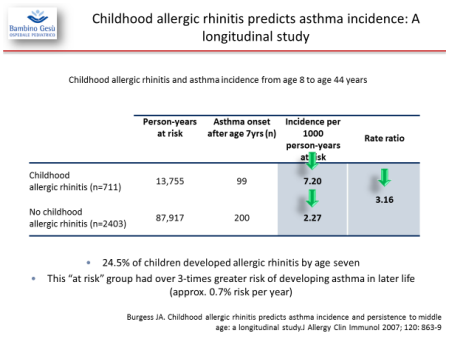
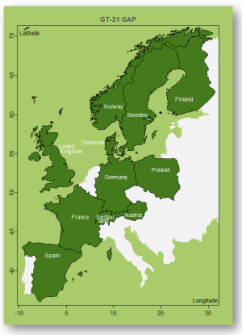
The preventive role of allergen immunotherapy in children

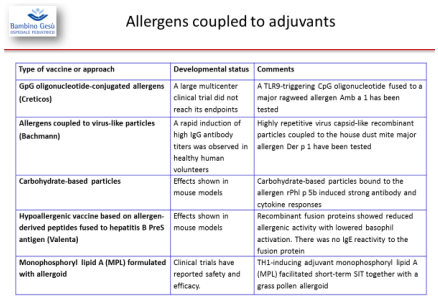


The allergen immunotherapy in children and its preventive role was the topic discussed by Dr. Fiocchi. The speaker, coming from Vatican City, presented very interesting data about the immunotherapy in children affected by allergic rhinitis for the secondary prevention of asthma. More in particular Dr. Fiocchi pointed out that AIT is very important in these patients for the high risk to develop asthma in the adult life. In the main part of his lecture, the speaker presented data about the GAO trial, a very interesting study running in children affected by allergic rhinitis for testing the effect of the immunotherapy for the prevention of asthma. Prof. Fiocchi presented other very interesting data on the AIT effect in allergy primary prevention, by highlighting the importance of the early intervention in children affected by allergic rhinitis. In the second part of his talk the speaker presented data given by the LEAP study, on the oral immunotherapy for the primary prevention of allergy. Finally, Dr. Fiocchi spoke about AIT and immunomodulators, by presenting data on the allergen exposure in early life as a protective procedure against the onset of allergic diseases in the future. In this view the speaker highlighted that the use of probiotics in pregnant women at high risk for allergy in their children is highly recommended. In conclusion, Dr. Fiocchi pointed out that AIT presents a very useful potential approach for the modulation of the sensitization and of the allergy risk in children.

GAP **Trial Centres**

Austria:	2 sites
Denmark:	7 sites
Finland:	3 sites
France:	12 sites
Germany:	20 sites
Norway:	6 sites
Poland:	12 sites
Spain:	12 sites
Sweden:	8 sites
Switzerland:	3 sites
UK:	4 sites

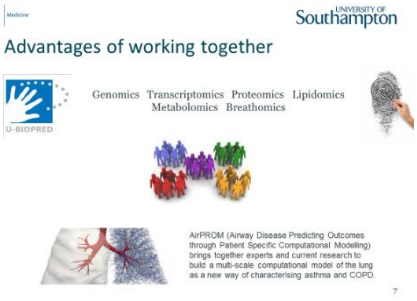




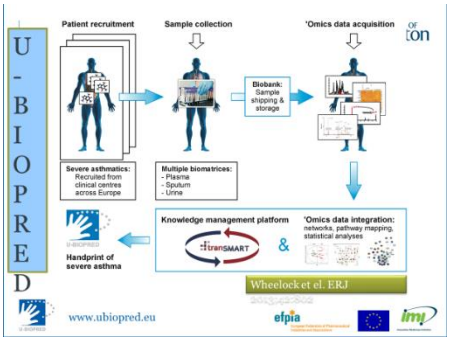
- Is allergen exposure in early life protective?
- Why the early AIT intervention in children is effective from the speaker point of view?
- What's about serology in the diagnosis of the viral myocarditis?
- What are the main key points of the effects of the allergic sensitization in children?
- What are the main results of the GAP trial presented by the speaker?

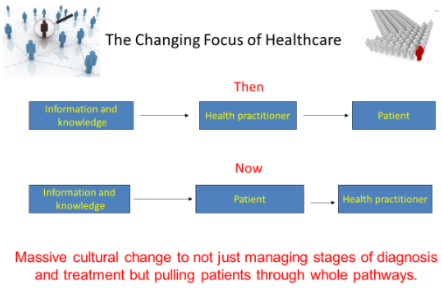
To follow the presentations of this congress, click on the link below: http://www.fondazione-menarini.it/Archivio-Eventi/2017/FIRST-INTERNATIONAL-MEETING-FOCUS-on-UPPER-LOWER-AIRWAYS-DISEASES/Materiale-Multimediale … and, after having logged in, enter in the multimedia area.

The future of research in asthma & COPD



Prof. Djukanovic, talked about the future of the research in asthma and COPD. The speaker coming from Southampton (UK), presented very interesting data on the new models for working together in this research field, by highlighting the advantages of working in such a way in order to improve in genomics, transcriptomics, proteomics, lipidomics, metabolomics and breathomics asthma research. More in particular Prof. Djukanovic spoke about the U-BIOPRED project, its stakeholders, characterized by a huge amount of people and its key topics starting from the patients' recruitment to the omics data acquisition and integration. The speaker presented the main Universities involved in this translational research project and the related clinical studies, running thanks to this wide collaboration between Academy and Industry. In the last part of his presentation, Prof Djukanovic spoke about the other national networks working on asthma and more in particular about SHARP (Severe Heterogeneous Asthma Research cllaboration Patient-centred project) its objectives, composition and structure involving experts and people affected by asthma and its performance indicators. Finally, the speaker presented data on the new biologics launch timeline.

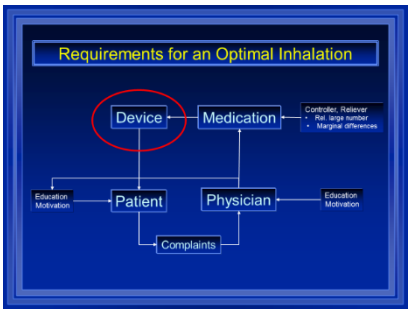




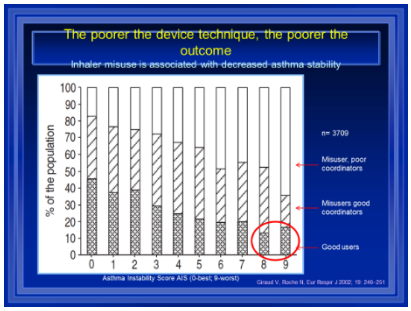
- What is the consequence of the rapid developmental evolution of omics technology platforms from the speaker point of view?
- What's about the new biological agents launch timeline?
- What is the SHARP structure and composition?
- What are the specific aims of the SHARP project?
  What is the TRPs portfolio presented by the speaker?

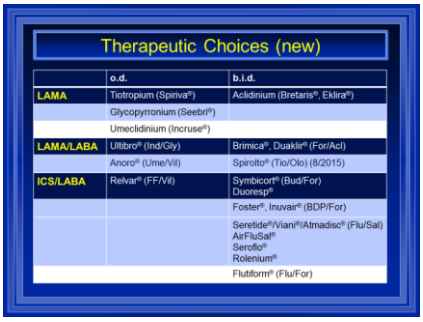
To follow the presentations of this congress, click on the link below: http://www.fondazione-menarini.it/Archivio-Eventi/2017/FIRST-INTERNATIONAL-MEETING-FOCUS-on-UPPER-LOWER-AIRWAYS-DISEASES/Materiale-Multimediale … and, after having logged in, enter in the multimedia area.

Innovation of inhalers for COPD



The innovation of the inhalers developed for COPD treatment and control, was the topic discussed by Prof. Virchow. The speaker coming from Rostock (Germany) talked about the role of the inhaler devices in asthma and COPD and about the impact of the poor inhaler training/technique on the disease control and on the health care system. Prof. Virchow presented also very interesting data on the approaches for an intuitive identification of the easy-to-use inhalers. Going deeper in his lecture, Prof. Virchow spoke about the requirements for an optimal inhalation, by highlighting the central role played by the device, the patient, his adherence to therapy and his inhaler training technique. More in particular the speaker spoke about the main characteristics of an ideal device, by highlighting that a poor inhalation technique is highly prevalent in patients and this problem leads to worse outcomes. In the second part of his presentation the speaker talked about the requirements for an optimal inhalation and on the strategies for the improvement of the inhaler effectiveness. In conclusion, Prof. Virchow pointed out that an innovative device is more likely to have a significant impact on the treatment success than an innovative drug.





- What are the economic advantages of correct inhaler use?
- What is the impact of the devices on the adherence?
- What are the main characteristics of an ideal device?
- What are the main requirements for an optimal inhalation?
- What are the main reasons for the poor asthma control?
- What's about the inhalation therapy and the role of the inhaler devices from the speaker point of view?

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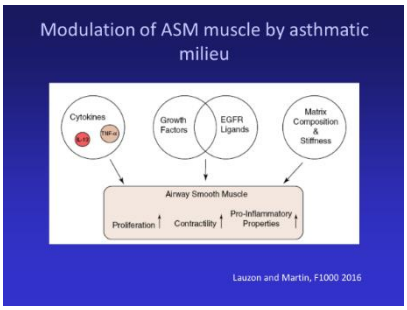
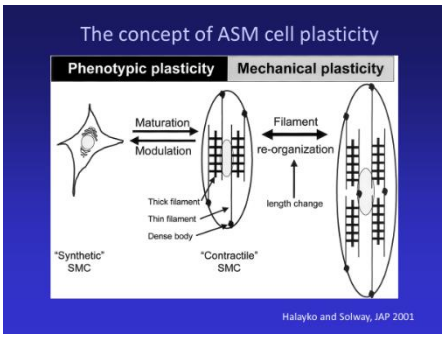
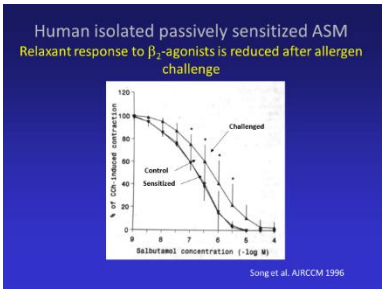
The role of smooth muscle in asthma



Prof. Brusasco from Genoa (IT), spoke about the role of the smooth muscle cells in asthma, by presenting very interesting data on the relationship between the airways smooth muscle (ASM) and the asthmatic milieu, by highlighting that the airways smooth muscle cells from asthmatic subjects proliferate more rapidly than those from non-asthmatic subjects. Going deeper in his lecture, Prof. Brusasco spoke about the concept of the ASM cell plasticity, by highlighting that in the asthmatic patients there is a re-organization of the filaments of the airways smooth muscle cells leading to their greatest length. The speaker presented very interesting data given by clinical studies running in asthmatic patients, by highlighting that their smooth muscle cells present an increased velocity of shortening in comparison to normal subjects. Prof. Brusasco discussed also about the reduced sensitivity to mechanical stress in asthmatic patients due to their limited strain. In conclusion, Prof. Brusasco pointed out that the airways smooth muscle is the principal actor in the airway hyper responsiveness of the asthmatic patients.





- What are the main mechanical determinants of the airway hyper responsiveness in asthmatic patients?
- What are the key points of the ASM modulation due to the asthmatic milieu?
- What are the main effects of bronchoconstriction and unloading on airway distensibility?
- What's about the length adaptation of airway smooth muscle based on the data presented by the speaker?
- What are the hypothetical mechanisms for increased ASM tone in obesity?

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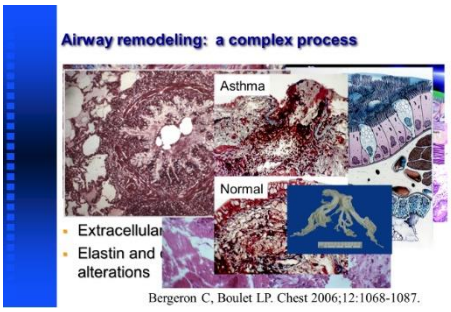
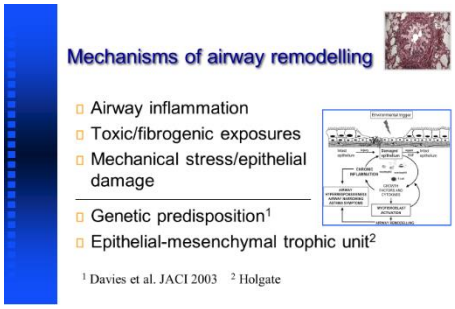
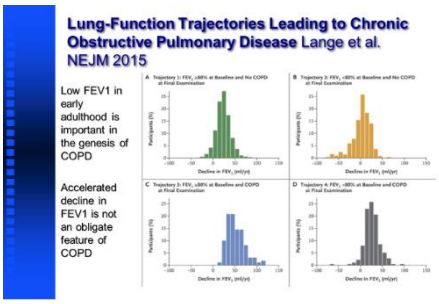
Airways remodelling and its role in respiratory decline



The airways remodelling and its role in the respiratory decline was the topic discussed by Prof. Boulet in his lecture. The speaker coming from Quebec (Canada), talked about the airways structural changes in asthma, the relationship with clinical and physiological parameters of clinical relevance, the relationship between remodelling and the lung function decline and finally about the influence of treatment on the structural changes. Going deeper in his lecture, Prof. Boulet presented data on the changes in the composition, quantity and organization of the bronchial structural elements, by highlighting that remodelling is a complex process involving the epithelial damage, the mucous glands hyperplasia, the subepithelial collagen deposition and the angiogenesis. In the main part of his lecture, the speaker talked about the mechanical effects of remodelling on the airways epithelial cells and the its potential influences on the onset of asthma, by presenting very interesting data on all the factors associated with the progressive development of airway obstruction like smoking, obesity, occupational exposure, eosinophilic airways inflammation and polymorphisms of the ADAM33 gene. In the last part of his speech, Prof Boulet presented data on the influence of the medications and the monoclonal antibodies on the airways remodelling. In conclusion, the speaker pointed out that the airways remodelling is a distinct feature of asthma, it begins before the onset of the symptomatology and the asthma medications have minimal effects on its key components.





- What's about the future research in airway remodelling from the speaker point of view?
- What are the effects of thermoplasty on the airways smooth muscle cells?
- What are the beneficial effects of the airways remodelling presented by the speaker?
- What's about the genetic and behavioural influences on lung function decline in asthma?
- What are the major changes in lung physiology with age, from the speaker point of view?
- What's about the relationship between smoking and asthma, based on the data presented by the speaker?

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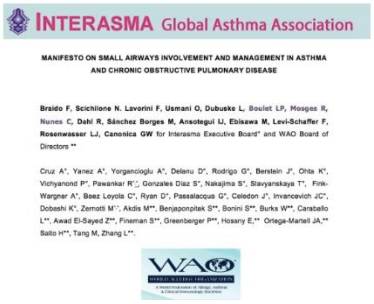
Manifesto Small Airways


INTERASMA Global Asthma Association

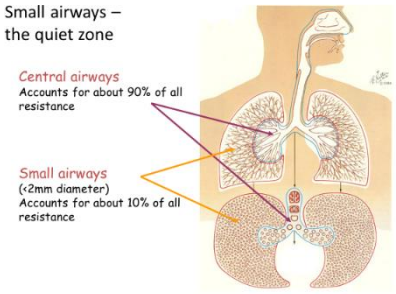
MANIFESTO ON SMALL AIRWAYS INVOLVEMENT AND MANAGEMENT IN ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

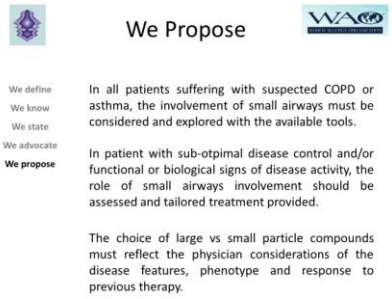
Braido F, Scichilone N, Lavorini F, Usmani O, Dubuske L, Boulet LP, Mosges R, Nunes C, Dahl R, Sánchez Borges M, Ansotegui IJ, Ebisawa M, Levi-Schaffer F, Rosenwasser LJ, Canonica GW for Interasma Executive Board* and WAO Board of Directors **

Cruz A*, Yanez A*, Yorgancioglu A*, Delanu D*, Rodrigo G*, Berstein J*, Ohta K*, Vichyanond P*, Pawankar R*,, Gonzales Diaz S*, Nakajima S*, Slavyanskaya T*, Fink-Wargner A*, Baez Loyola C*, Ryan D*, Passalacqua G*, Celedon J*, Invancevich JC*, Dobashi K*, Zernotti M*; Akdis M**, Benjaponpitak S**, Bonini S**, Burks W**, Caraballo L**, Awad El-Sayed Z**, Fineman S**, Greenberger P**, Hossny E,** Ortega-Martell JA,** Saito H**, Tang M, Zhang L**.

WAO

Prof. Scichilone from Palermo (IT), presented very interesting data on this manifesto published by Interasma the Global Asthma Association, with the aim to take a position on the small airways - the so called "silent zone"- in the light of the available evidence. Going deeper in his lecture, Prof Scichilone spoke about the form and the structure of this manifesto, based on previously published opinions and public consensus, by presenting its main topics on definition, knowledge, stating, advocating and proposing. More in particular the speaker talked about the role played by the small airways as a major determinant of the airflow obstruction in COPD and asthma patients and the available tests for their assessment. Speaking about what the manifesto states, Prof. Scichilone pointed out that the small airways in asthma and in COPD represent one of the targets in order to achieve the disease control and better outcomes. The speaker talked also about the need for functional and biological tools for the improvement of the patient's phenotyping process. In conclusion, Prof. Scichilone pointed out that the choice of large vs small particle compounds must reflect the physician's considerations of the disease features, phenotype and response to previous therapy.





- What is the topic of the Manifesto Small Airways?
- What are the main definitions of the Manifesto?
- How to assess the small airways changes based on the Manifesto declarations?
- What's about knowledge of asthma and COPD based on the Manifesto declarations?
- What do the Manifesto state?
- What do the Manifesto propose in all patients suffering from suspected asthma or COPD?

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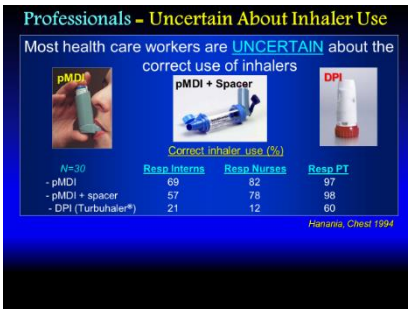
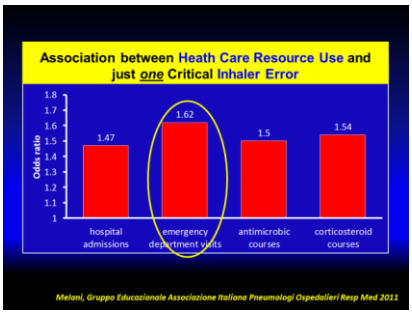
the role of devices and adherence monitoring



The main topic at the core of Prof. Usmani presentation, was the role of devices and adherence monitoring. The speaker, coming from London (UK), presented very interesting and shocking data on the heterogeneity of devices and the patients' adherence and knowledge, by highlighting that even professionals as doctors and pharmacists do not sufficiently know the correct inhaler use. Going deeper in his lecture, Prof. Usmani highlighted that patients, without any affordable guide, do not have a sufficient knowledge on the correct use of these devices. In the second part of his lecture the speaker presented data on the major critical errors performed in the inhaler use and their correlation with the burden of costs charged on the health care system resources. Finally, Prof Usmani highlighted that one possible solution is linked with the improvement of digital technology and the e-health application for all those patients affected by chronic diseases like COPD and asthma. In conclusion, Prof. Usmani pointed out that using digital health applications may be beneficial in promoting health awareness and empowering patients for self-management.



- What are the main applications of e-health in asthma control presented by the speaker?
- What are the main components of the digital health system based on the data presented by the speaker?
- What's about the economic burden of Asthma and COPD based on the data presented by the speaker?
- What is the prevalence of the critical errors in the inhaler use?
- What's about the knowledge of the correct use of devices by physicians and pharmacists?

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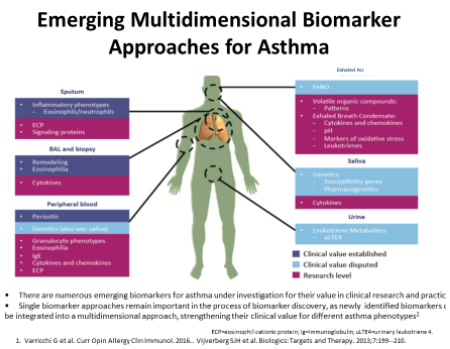
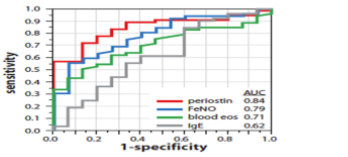
Biomarkers in severe asthma



The main topics at the core of Prof. Hanania presentation, were the biomarkers in severe asthma. The speaker, coming from Huston (USA), presented very interesting data, starting from the description of the main pathways leading to airways inflammation and remodeling in patients affected by asthma. Going deeper in his lecture, Prof. Hanania presented very interesting data on the utility of biomarkers in the diagnosis and prognosis of patients affected by severe asthma. More in particular the speaker spoke about the emerging multidimensional biomarker approaches for asthma, from sputum to urine, passing through BAL and biopsy, peripheral blood, exhaled air and saliva. Prof. Hanania presented a huge amount of data on these topics in order to identify the major applications of biomarkers in asthma management. In the main part of his lecture, the speaker pointed out that more than one biomarker may be needed in asthma diagnosis and prognosis due to the heterogeneity of this disease and presented very interesting data on eosinophil-high, FeNO-high and Periostin-high biomarkers. Finally, the speaker talked about the ongoing biomarkers studies and more in particular about the UK Refractory Asthma Stratification Programme, that is a randomized, pragmatic, multicenter, parallel-group trial addressing whether these biomarkers can guide corticosteroid therapy compared to the standard of care management. In conclusion, Prof Hanania pointed out that the evolving biomarkers may be helpful in defining phenotypes and predicting prognosis and response to novel targets of therapy in severe asthma.

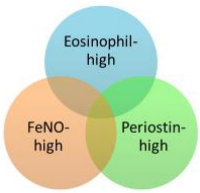
Periostin

Receiver operating characteristic curve analysis of the sensitivity and specificity of serum periostin, FeNO, and serum IgE levels and blood eosinophil numbers for composite airway eosinophil status (sputum and tissue biopsy).



Jia et al. J Allergy Clin Immunol. 2012

Overlap of Biomarkers



- What are main clinical applicability of Periostin?
- What's about the role of FeNO for guiding treatment in Chronic Asthma?
- What are the clinically significant cut points of FeNO?
- What is the correlation between blood eosinophils and future risk?
- What are the emerging multidimensional biomarker approaches for asthma presented by the speaker?
- What are the main characteristics of an ideal biomarker?

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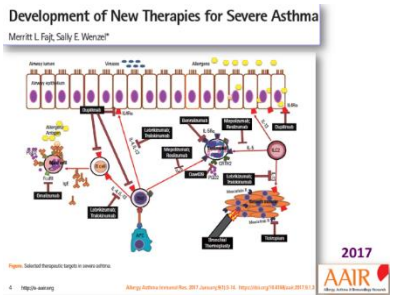
Personalized medicine in asthma: treatment with biologics



Prof. Canonica, chairman of this symposium, spoke about biologics, as the treatment of choice for a personalized medicine in patients affected by asthma, by presenting a huge amount of data on the new biologics actually studied in the ongoing clinical trials. Going deeper in his lecture, Prof. Canonica presented very interesting data on the main monoclonal agents acting at different interleukin levels like Brodalumab, Mepolizumab, Reslizumab, Benralizumab, Dupilumab, Lebrikizumab, Tralokinumab, Omalizumab and Reslizumab. In the main part of his presentation, Prof. Canonica, discussed the major results of the studies running in these monoclonal antibodies, by highlighting successes and failures of any of these agents. In the last part of his lecture, the speaker presented the PROXIMA study design and discussed the first confidential non-published data, by highlighting the role played by Galactin 3 in the typing of patients affected by nasal polyposis. Finally, Prof Canonica spoke about the need for networking, by presenting data on the main teams of research working in Italy and in Europe, like the SANI network and the European Respiratory Society Network. In conclusion, the speaker pointed out that this is the era of Biologics and also of their biosimilars for the treatment of patients affected by asthma.

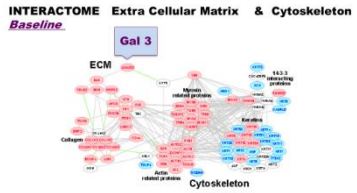


Figure 4 - Nodes and Network involved the **main R vs NR differences**.
Red= upregulated in R;
Blue: upregulated in NR;
White: undifferentiated

Mauri et al 2014

- What are the main biologics developed for the asthma treatment and on the market from the 2016?
- What are the main Italian centers taking part of the SANI network?
- What's about the effects of mepolizumab in the treatment of the Nasal Polyposis?
- What is the PROXIMA study design presented by the speaker?
- What's about Galactin 3 as a predictor of airway remodelling based on the data presented by the speaker?
- What is the role of Interleukin 5 in asthma, from the speaker point of view?

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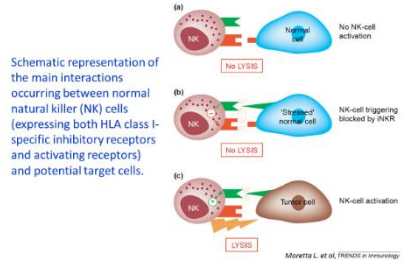
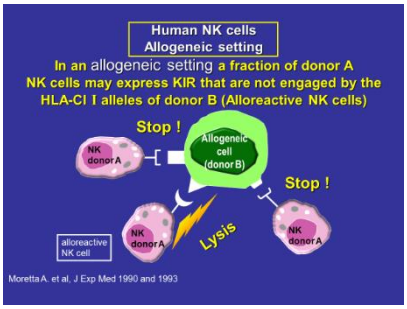
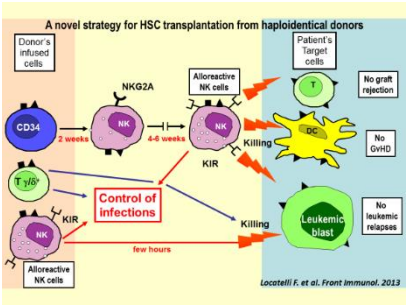
Advances in innate immune response



Schematic representation of the main interactions occurring between normal natural killer (NK) cells (expressing both HLA class I-specific inhibitory receptors and activating receptors) and potential target cells.

The advances in innate immune response, was the topic at the core of Prof. Moretta presentation. The speaker coming from Rome, at the beginning of his presentation talked about the innate and adaptive immunity and more in particular on the innate lymphoid cells (ILC) and the signals leading to their activation. Going deeper in his presentation, Prof. Moretta talked about the ILC lymphoid precursors, their presence in the mucosal tissues and their allergic responses induced by ILC2. In the main part of his lecture, the speaker presented very interesting data on the natural killer cells, one of the major player of the innate immunity, speaking about their major functions like cytotoxicity, the cytokine production and about their proliferation memory. More in particular Prof. Moretta presented very impressive data on the role played by the NK cells in the haemopoietic stem cell transplantation for the therapy of high risk leukemias patients and on the linked criteria for the donor selection. Finally, the speaker talked about a new strategy for the HSC transplantation from haploidentical donors, by highlighting the success in term of long term leukemia free survival.





- What is the evolution of the T-cell depletion strategy for the identification of haploidentical donors?
- What's about the main criteria for the donor selection, based on the data presented by the speaker?
- What is the main therapeutic role of the NK cells in the haploidentical haemopoietic stem cell transplantation?
- What is the model of the human PB NK cell differentiation?

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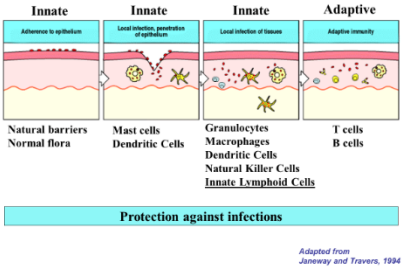
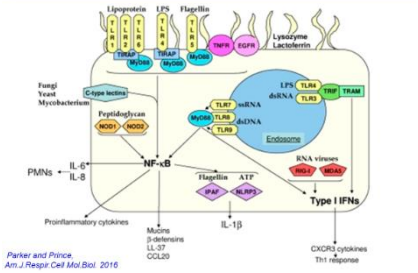
Natural immunity and infections

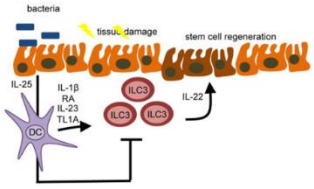


The natural immunity and the infections was the topic at the core of Prof. Ferlazzo presentation. The speaker coming from Messina (IT), at the beginning of his presentation talked about the innate system leading to the protections against infections, by highlighting the role played by the natural barriers and the innate lymphoid cells. Going deeper in his presentation, the speaker talked about the innate immunity at the respiratory epithelium level, by presenting the main activities of the antimicrobial peptides. Speaking about the innate lymphoid cells, Prof. Ferlazzo presented very interesting data on their origins and on the signals coming from injured or infected tissues which activate the NK cells, ILC1s, ILC2s and ILC3s. In the main part of his lecture, the speaker talked about the ILC2 and ILC3 main activities in promoting the inflammation resolution and the tissue repair. In the last part of his talk, Prof. Ferlazzo addressed the audience with this question: do dendritic cells interact with ILC3? and in order to find a very comprehensive answer he presented very interesting and unpublished data on the strong relationship between dendritic cells (DCs), cytokines and ILC3. In conclusion, the speaker pointed out that the DCs/ILC3 cross-talk during the infections, plays a pivotal role both in the earliest phases of the innate immune response and in the following adaptive immune response.

Innate immunity in the respiratory epithelium



ILC2 and ILC3 promote resolution of inflammation and tissue repair



- Do dendritic cells interact with ILC3?
- What are the main mechanisms leading to the resolution of inflammation and the tissue repair stating from ILC2 and ILC3 activation?
- What are the main signals coming from injured or infected tissues and activating NK cells, ILC1s, ILC2s and ILC3s?
- What are the main members of the ILCs family presented by the speaker?
- What's about the innate immunity in the respiratory epithelium based on the data presented by the speaker?
- What are the main host defence mechanisms of the respiratory epithelium based on the data presented by the speaker?

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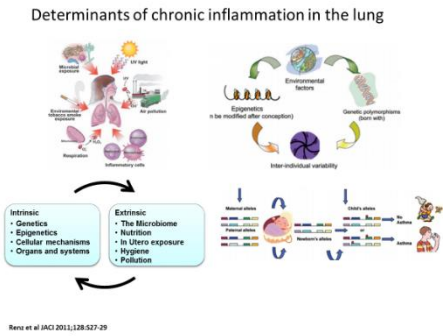
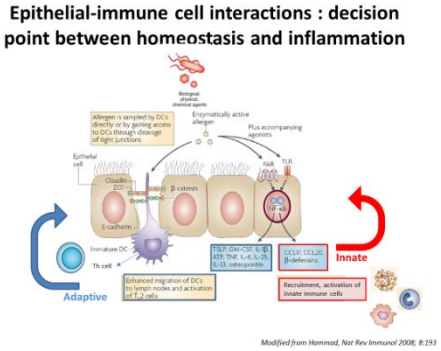
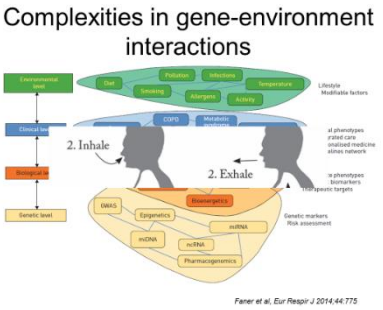
Airways inflammations



The airways inflammations were the topic Prof. Stellato talked about. The speaker coming from Salerno (IT), presented very interesting data on the relationship between Asthma and COPD characterized by inflammatory processes associated with environmental and nutritional conditions like high-calorie nutrients, low-level physical activity, exposure to pollutants and toxic compounds. In the main part of her presentation, the speaker talked about the consequences of the chronic state of the inflammatory processes, leading to the increased oxidative burden as a common denominator of the maladaptive inflammatory responses in the lung. More in particular Prof. Stellato highlighted that the adaptive mechanisms start from the genetic networks till the phenotypic traits and these processes open the road for asthma and COPD. The speaker talked also about the main epigenetic modifications which regulate the genetic expression in the mammalian cells leading to the cellular oxidative stress as one of major steps at the basis of the chronic inflammatory processes. In the last part of her presentation, the speaker talked about the microbiome as an extrinsic determinant of the chronic inflammation in the lung. In conclusion, Prof. Stellato pointed out that the complexities of the gene-environment interactions are at the basis of the chronic inflammatory diseases like asthma and COPD.





- What are the main gene-environment interactions presented by the speaker?
- What are the links between lung and systemic inflammation induced by atmospheric pollution?
- What's about the modulation of the adaptive immune responses mediated by the microbiota?
- What are the main intrinsic and extrinsic determinants of chronic inflammation in the lung presented by the speaker?
- What are the main epithelial-immune cell interactions based on the data presented by the speaker?

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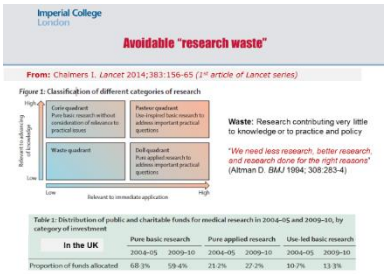
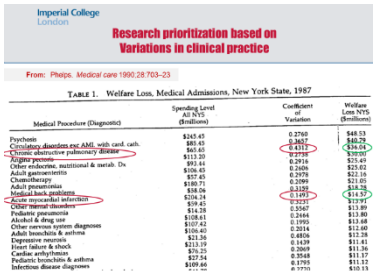
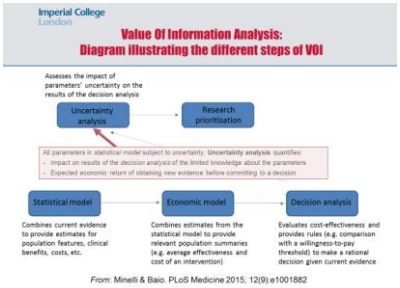
Value of information: a tool to improve research prioritization and reduce waste



The value of information as a tool for improving the research prioritization and reducing the waste, was the topic at the core of Prof. Minelli presentation. The speaker coming from London (UK), at the beginning of her talk presented very interesting data on the need for the prioritization of the research by focusing on the avoidable waste or the inefficiency in biomedical research. Going deeper in her presentation, Prof. Minelli discussed on the 4 quadrants for the classification of different categories of research based on the balance between the relevance of the immediate application and the relevance of the advancing knowledge. In the main part of her presentation the speaker talked about the applied methods used for setting the priorities in health research like the burden disease approach, the variations in clinical practice and the value of information (VOI) analysis. Finally, Prof. Minelli presented the aim and the design of a study implemented by her team of research named ALEC (ageing lungs in european cohorts), by highlighting the general challenges in applying VOI to ALEC.





- What methods are most commonly used for a consensus-based approach in clinical research?
- What's about the research prioritization based on the burden of disease approach?
- Why do we need for the research prioritization application, based on the data presented by the speaker?
- What's about the avoidable "research waste"?
- How is the research prioritization done in practice?
- Which methods are most commonly used for a consensus-based approach?
- What are the key points of the Value of information analysis based on the data presented by the speaker?

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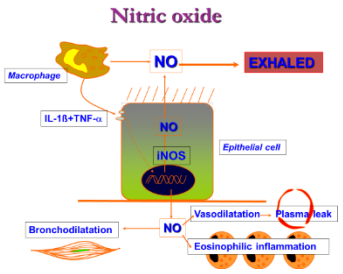
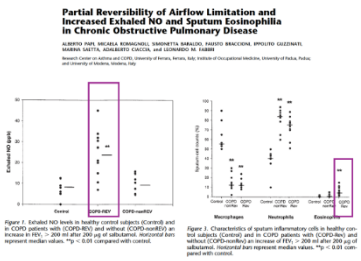
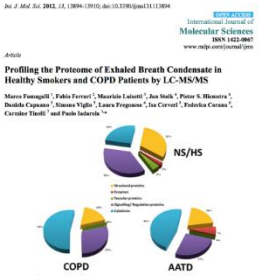
Non-invasive methods and results



Prof. Carpagnano talked about the non-invasive methods and the related results. The speaker coming from Foggia (IT), presented very interesting data on the exhaled nitric oxide, the induced sputum, the exhaled breath condensate, the enose and on the exhaled breath temperature. Going deeper in her presentation Prof. Carpagnano pointed out that these methods are well accepted and useful in clinical practice, in children, in diagnosis and follow-up and finally in the therapeutic approach, thanks to their non-invasive nature. In the main part of her lecture, the speaker presented very interesting data on any single method given by clinical studies and guidelines recommendations and talked about their utility and application in the clinical setting. Speaking about the induced sputum, Prof. Carpagnato highlighted its utility in the phenotyping of the obstructive lung diseases. The exhaled breath condensate analysis presents a lack in the reproducibility and this is the main reason for its application only in the clinical research setting, the speaker pointed out. One of the main applications of this method is the study of the DNA. Finally, the speaker talked also about the electronic nose and the exhaled breath temperature as a sign of the inflammations at the airways level. In conclusion, Prof. Carpagnano pointed out that the exhaled NO and the induced sputum are the only two non-invasive techniques actually applicable to COPD in clinical practice.





- What are the main characteristics of the exhaled breath temperature?
- What's about the e-nose based on the data presented by the speaker?
- What are the main genomic markers in the exhaled breath condensate?
- What's about the RNA finding in the exhaled breath condensate?
- What is the reproducibility of the exhaled breath condensate?
- What are the main clinical applications of the induced sputum?
- What are the main applications of the exhaled gas (NO) analysis?

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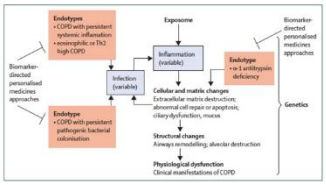
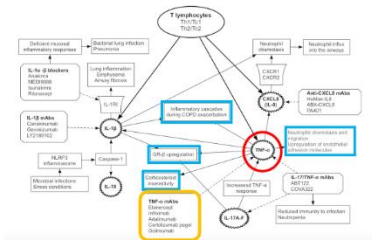
Biologics and COPD treatment



Prof. Braido talked about the Biologics and the COPD treatment. The speaker coming from Genoa (IT), presented very interesting data on biologics applied to COPD and the problems linked with the biological drug research. Going deeper in his presentation, Prof. Braido spoke about the so called biomarker-direct personalised medicine approach, by highlighting the role played by the innate and the adaptive immune cells in the activation of specific molecular pathways and factors target for the monoclonal antibodies. In the main part of his talk, the speaker presented very interesting and innovative data on the main therapeutic effects of the monoclonal antibodies in clinical development. More in particular Prof. Braido spoke about the Anti-TNFα monoclonal, the Anti-IL-1RI, the Anti TGF-β, the Anti-IL-8, IL-33, IL-6 and IL-5 antibodies, by presenting their main results in the clinical setting. In conclusion, Prof. Braido pointed out that the therapeutic impact of the monoclonal antibodies in the COPD patients are very far from to be well defined, many studies are ongoing and others are to be implemented in order to find an affordable role for these agents in the treatment of the patients with COPD.

Molecular pathways of TNFα, CXCL8, IL-1b and relative targets for monoclonal antibodies or biologics



Therapeutic impact of monoclonal antibodies in COPD

Biological target	Biological agent	Impact in COPD
TNFα	Etanercept	Reduction in the rate of COPD hospitalization (evidence from a retrospective, observational, non-randomized, administrative database study)
		Not more effective than prednisone for the treatment of acute exacerbations of COPD (evidence from a proof-of-concept RCT)
	Infliximab	No beneficial effects on various clinical parameters (evidence from a phase II RCT)
IL-1	Canakinumab	Ineffective in the treatment of stable COPD (evidence from a phase I/II RCT)
	MEDI8968	No effect in moderate-to-very-severe COPD (evidence from a phase II RCT)
IL-4	NA	Not tested
IL-5	Mepolizumab	No improvement in lung function and exacerbation rates after 6-months of treatment in patients with current moderate-to-severe COPD with sputum eosinophilia. Clinically meaningful (>0.5 units) improvement of CRQ mean dyspnoea domain score (evidence from a phase III RCT)
		Ongoing phase III RCTs
	Benralizumab	No influence on the rate of acute exacerbations of COPD in patients with moderate-to-severe COPD, having had at least one acute exacerbation of COPD, and a sputum eosinophil count ≥3 % within the previous year. Reduction of COPD exacerbations and improved lung function, as well as disease-specific health status in patients with higher baseline levels of blood eosinophils (>200 cells/μl) (evidence from a phase II RCT)
		Ongoing phase III RCTs
IL-6	NA	Not tested
CXCL8 (IL-8)	ABX-CXCL8	Improved the transition dyspnoea index (evidence from a pilot RCT)
IL-13	Lebrikizumab	Ongoing phase II RCT
IL-17	CNTO6785	Completed phase II RCT, no results available
IL-23	NA	Not tested
IL-33	AMG 282	Headed into phase II RCT
TGF-β	NA	Not tested

- What are the molecular pathways of the IL-17/IL-23 axis and the relative targets for monoclonal antibodies?
- What is the Anti-IL5R COPD exacerbation rate presented by the speaker?
- What is the Anti-IL5R lung function?
- What is the main composition of the Eosinophilic COPD Microbiome?
- What are the main results of the WISDOM study?
- What is the relationship between the sputum eosinophilia and the response to corticosteroid in COPD patients?

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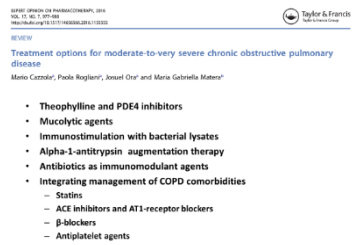
Beyond dual and triple therapy


Taylor & Francis

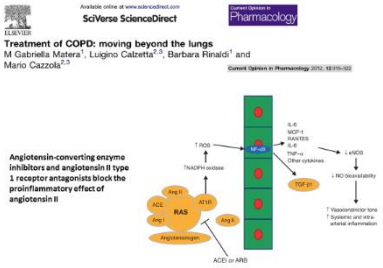
REVIEW

Treatment options for moderate-to-very severe chronic obstructive pulmonary disease

Mario Cazzola[a], Paola Rogliani[a], Josuel Ora[a] and Maria Gabriella Matera[b]

- Theophylline and PDE4 inhibitors
- Mucolytic agents
- Immunostimulation with bacterial lysates
- Alpha-1-antitrypsin augmentation therapy
- Antibiotics as immunomodulant agents
- Integrating management of COPD comorbidities
  - Statins
  - ACE inhibitors and AT1-receptor blockers
  - β-blockers
  - Antiplatelet agents

Beyond the dual and triple therapy was the topic Prof. Cazzola talked about. The speaker coming from Rome (IT), presented very interesting data on the treatment options for the moderate-to-severe COPD. More in particular Prof. Cazzola spoke about the efficacy and the safety of many drugs like Theophylline, the PDE4 inhibitors and the mucolytic agents. The speaker talked also about the immunostimulation with bacterial lysates, the Alpha-1-antitrypsin augmentation therapy, the use of the antibiotics as immunomodulant agents and finally about the integrating management of the COPD comorbidities with statins, ACE-inhibitors, β-blockers and antiplatelet agents. In the main part of his lecture, Prof. Cazzola presented very innovative data on the use of the bifunctional drugs for the treatment of patients affected by asthma and COPD and finally on the effects of the monoclonal antibodies. In conclusion, Prof. Cazzola pointed out that the evolution of the therapy is oriented toward the personalized therapy in order to improve the outcome and the quality of life of the patients affected by COPD.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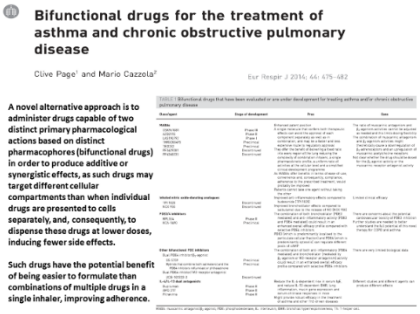
Current Opinion in Pharmacology

Treatment of COPD: moving beyond the lungs

M Gabriella Matera[1], Lugino Calzetta[2,3], Barbara Rinaldi[1] and Mario Cazzola[2,3]

Current Opinion in Pharmacology 2012, 12:315–322

Angiotensin-converting enzyme inhibitors and angiotensin II type 1 receptor antagonists block the proinflammatory effect of angiotensin II


Bifunctional drugs for the treatment of asthma and chronic obstructive pulmonary disease

Clive Page[1] and Mario Cazzola[2]

Eur Respir J 2016; 44: 475–482

A novel alternative approach is to administer drugs capable of two distinct primary pharmacological actions based on distinct pharmacophores (bifunctional drugs) in order to produce additive or synergistic effects, as such drugs may target different cellular compartments than when individual drugs are presented to cells separately, and, consequently, to dispense these drugs at lower doses, inducing fewer side effects.

Such drugs have the potential benefit of being easier to formulate than combinations of multiple drugs in a single inhaler, improving adherence.

- What's is the efficacy and the safety of RPL554 in patients with asthma or COPD?
- What are the main characteristics of the bifunctional drugs for the treatment of patients affected by asthma and COPD presented by the speaker?
- What are the main effects of the β-blockers on the COPD exacerbations?
- What's about the effects of the statins in COPD patients?
- What is the role played by the ACE-inhibitors in the treatment of the patients affected by COPD?

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These are only some of the topics addressed in the congress's sections

For a deeper knowledge on these topics, please visit the International Menarini Foundation web site where You can find all the speeches in their full version.

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