Rica Zinsky[1],
Anne Olland[2],
Anders Bjerg[3],
Andras Bikov[4],
Szymon Skoczyński[5]

[1]Institute of Pathology and Cytology, Dr.-Horst-Schmidt-Clinics Wiesbaden, Academic Hospital of University of Mainz, Wiesbaden, Germany
[2]Lung Transplantation Group, Thoracic Surgery Department, Nouvel Hôpital Civil, University Hospital Strasbourg, Strasbourg, France
[3]Krefting Research Centre, Department of Internal Medicine and Clinical Nutrition, University of Gothenburg, Gothenburg, Sweden
[4]Department of Pulmonology, Semmelweis University, Budapest, Hungary
[5]Department of Pulmonology in Katowice SP CSK, The Medical University of Silesia, Katowice, Poland

S. Skoczyński, Department of Pulmonology in Katowice SP CSK, The Medical University of Silesia, ul. Medykow 14, Katowice, Silesia 40-752, Poland

simon.mds@poczta.fm

News from the Underground: What were the most important scientific/clinical take-home messages for juniors?

The ERS International Congress has traditionally been a splendid opportunity to present current updates in clinical respiratory medicine and new research findings. This year's programme was packed, making it impossible to attend all sessions, but juniors interested in specific fields were there for you to highlight the most important take home messages from the 2014 ERS International Congress in Munich.

Amongst the most important news for the clinicians was the publication of a Global Initiative for Asthma (GINA) guidelines update [1]. In the updated guidelines, the heterogeneity of asthma is emphasised, suggesting the need of "4P" (Personalised, Predictive, Preventive and Participatory) treatment regimes. Another clinically important issue recognised in GINA and the Global Initiative for Obstructive Lung Disease (GOLD) guidelines [2], is asthma–chronic obstructive pulmonary disease overlap syndrome (ACOS). ACOS has a special pathophysiological and clinical characteristic and large-scale studies have been initiated to investigate it. In the future of individualised medicine, validated biomarkers are urgently required that can assist in the correct phenotyping of lung diseases and may help to predict treatment responsiveness. A huge number of novel molecules has been introduced for the treatment of airway disorders. The presented studies clearly highlighted the priorities of future research topics, namely the need to investigate methodological and physiological factors and to cross-validate biomarker studies between different centres in large cohorts of subjects.

A number of sessions at Munich showed that epidemiology and environmental exposure are vital factors in translational research. The biggest buzz was surrounding the Sunday Grand Round session "Chemicals made to harm". New data show long-lasting health effects of tear gas and pepper spray, which, in recent years, have been used indiscriminately against non-violent protesters in a number of countries including Bahrain, Egypt and Turkey, but also during the civil unrest in Ferguson, MO, USA. Another important topic was international trends in asthma prevalence. The rise in asthma continues in large parts of the world, while some countries see a plateau in the number of children with asthma. The observations depend much on the definition of

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asthma used, and the importance of clinically validated questionnaires was stressed. The old foe, tobacco, was discussed in a new context: e-cigarettes. It was underlined that high nicotine levels used in these devices may lead users to also start smoking ordinary cigarettes. Moreover inhaled nicotine directly affects the airway epithelium and remodelling. The tobacco industry is a strong lobby and, regrettably, the newly approved EU Tobacco Products Directive revision was less strictly worded than the original. Importantly, it was pleasing to see epidemiological research not only on COPD and asthma, but also on lung cancer and restrictive lung diseases, which is promising for next year's Congress.

ERS offers education in common respiratory disorders but individualised treatments were also extensively addressed. It was underlined again that, COPD is the main indication worldwide for lung transplantation. It was understood that, especially in sophisticated and not widely available treatment modalities, patients' case histories are of great importance. As an example, a 62-year-old man, Dieter Willms, was invited to present a testimony on his experience with lung transplantation. He had suffered from severe allergic asthma since 4 years of age. In time, the disease progressed to emphysema and bronchiectasis leading to his retirement at the age of 47. At the end stage of respiratory insufficiency, long-term oxygen therapy was started. He was placed on lung transplantation waiting list and finally had bilateral lung transplantation 6 years ago. Since then, he has been all around the world and has a new lease of life. However, it was emphasised that, due to organ shortage, not all the patients with such indications can be transplanted.

At Congress, there was indication of a future wherein human lungs can routinely be harvested from non-heart beating cadaveric donors. They can be decellularised and brought to the form of a lung scaffold. In the future, cells will be harvested from recipient and brought back to the induced pluripotent stem cell state. These can then be cultured and the scaffold recellularised. It may take 10–15 years, possibly less, to finalise this technique and make it available for the daily clinical practice. Hopefully, it will enable transplantation for larger number of patients, without organ shortage, and will avoid immunosuppressive therapy.

Another hot topic was lung cancer. In non-small cell lung cancer (NSCLC) patients, EGFR (epidermal growth factor receptor) and EML4-ALK (echinoderm microtubule-associated protein-like 4–anaplastic lymphoma kinase) are the only routinely treated targets for tyrosine kinase inhibitor (TKI) therapy. Even after success with initial treatment, patients can develop resistance; a big issue at Congress was identifying the molecular mechanisms behind that resistance and what new therapeutics and strategies can be used to overcome it.

Inhibition of EGFR was the first targeted therapy in NSCLC. The most frequently occuring resistance to gefitinib or erlotinib treatment is the T790M mutation [3]. Different strategies were presented to overcome this resistance, one of which was afatinib, a second-generation TKI, in combination with cetuximab [4], a third generation TKI, to target T790M [5]. Another option could be to use combined treatments to target more than one pathway [6]. Crizotinib has an overall response rate of >60% [7] and is the treatment of choice for EML4-ALK+ patients. Given mechanisms for crizotinib resistances are amplifications of ALK, ALK mutations, EGFR mutation and c-KIT amplification [8]. For ALK inhibition, new compounds are currently being tested, ceritinib, a 2nd generation ALK inhibitor [7] shows efficiency in ALK+ patients with and without crizotinib treatment before [8] and alectinib, also a second-generation ALK inhibitor showed efficiency in preclinical studies [9] as well as in a phase I trial [10]. Next to crizotinib and pemetrexed [7], heat shock protein 90 inhibition showed efficiency in ALK+ patients and 17AAG was even shown to overcome Crizotinib resistance [11]. Dealing with crizotinib resistance will be crucial for ALK+ patients in the upcoming years.

Another important clinical message presented during Congress was an update to the guidelines on the diagnosis and management of acute pulmonary embolism [12]. Especially important for clinical practise is the new classification of patients with acute pulmonary embolism based on early mortality risk classification. Intermediate risk group was divided for the first time into intermediate–high risk and intermediate–low risk. The former can be diagnosed when pulmonary embolism severity index (PESI) reaches class III–V, or simplified PESI >1 coexists with

echocardiographic pattern of right ventricular dysfunction or elevated concentration of N-terminal pro-brain natriuretic peptide and elevated plasma markers of myocardial injury: high-sensitivity troponin-T concentrations or heart-type fatty acid-binding protein [12]. It was concluded that, in this group, thrombolysis should be postponed but patients should be carefully observed to rule out signs of clinical haemodynamic decompensation. If available, rescue reperfusion therapy should be started on the basis of local accessibility, medical team experience and patients bleeding risk. Finally, a wide group of non-vitamin K-dependent new oral anticoagulants (NOACs) (dabigatran, rivaroxaban and apixaban) was presented as an expensive but clinically useful and widely accepted treatment option.

Another extremely important message was evidence that, in patients treated with noninvasive ventilation (NIV), in whom substantial decrease of carbon dioxide tension was achieved, home NIV in stable COPD can prolong a patient's life [13].

To conclude, The ERS International Congress programme was of high quality. All important respiratory topics were covered, proving once again that all medical specialists and trainees interested in respiratory medicine should attend ERS International Congresses. We are looking forward to seeing you next year in Amsterdam.

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