



Rare (pulmonary) disease day: “feeding the breath, energy for life!”

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Broadly speaking, a rare disease is any disease that affects a small percentage of people in a population. Although there is no more specific, widely accepted definition of a rare disease, the European Commission on Public Health defines rare diseases as “life-threatening or chronically debilitating diseases, which are of such low prevalence that special combined efforts are needed to address them” [1]. The term “low prevalence” is defined as generally meaning fewer than one in 2000 people [1, 2]. With a conservative estimate that primary or secondary lung involvement occurs in ~5% of rare diseases (>6000 types), approximately 1–2 million people in the European Union are likely to be affected by rare pulmonary diseases. Therefore, cumulatively, rare pulmonary diseases represent a significant burden of disease, with many of these being severe conditions that result in premature death or major morbidity.

Patients with rare diseases have traditionally lived a lonely existence. Rare diseases are often poorly studied, attract little attention from researchers and clinicians alike, and specific therapy may not be available, thus leading to the term “orphan diseases” being used synonymously to describe these conditions. In order to advance our knowledge and improve outcomes in rare diseases, collective efforts are required not just at a national level but also encompassing international collaboration.

To provide a voice for rare disease patients in Europe, Rare Disease Day (fig. 1) was first launched in 2008 by the European Organisation for Rare Diseases (EURORDIS), a nongovernment alliance of >600 rare disease patient organisations in >50 countries, covering >4000 diseases [3]. Rare Disease Day takes place on the last day of February each year, and thus is held on the 29th, a rare day, in leap years (and on the 28th in other years). Even though this campaign started as a European event, it is now held in many countries around the world. It has progressively gathered momentum and has now become a world phenomenon, with the USA joining in 2009. Participation in 2014 included a record-breaking 84 countries around the world.

The main objective of EURORDIS and Rare Disease Day is to improve the quality of life of people living with rare diseases through advocacy, support for research and medicine development, facilitating

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FIGURE 1 The Rare Disease Day logo.

networking among patient groups, raising awareness, and many other actions designed to reduce the impact of rare diseases on the lives of patients and family [3].

Partly due to greater awareness in the medical community and advancement of diagnostic techniques, registry data indicated that the incidence and prevalence of rare pulmonary diseases appear to be increasing. For instance, the incidence of pure idiopathic pulmonary arterial hypertension (PAH) has increased from 0.7 to 1.1 cases per million persons during the first decade of the 21st century in the UK and Ireland, and PAH (as a collective group) has a minimum prevalence and incidence of 15 per million adult inhabitants and 2.4 cases per million adult inhabitants per year in France, respectively [4, 5]. Similarly, the estimated prevalence of lymphangioleiomyomatosis (LAM) in 2011 was one case per million people, while in 2013 the prevalence was reported to be 5.6 cases per million [6]. In the last 20 years, the knowledge of some rare pulmonary conditions has markedly improved and new therapies are now available that may be effective in changing the clinical course of several illness, such as PAH [7], chronic thromboembolic pulmonary hypertension [8–12], pulmonary vasculitis [13], bronchiolitis [14–16], LAM [17–20], pulmonary alveolar proteinosis [21, 22], α_1 -antitrypsin deficiency [23], pulmonary Langerhans cell histiocytosis [24, 25] and, more recently (and after several negative trials), idiopathic pulmonary fibrosis (IPF) [26–30]. New horizons of hope are now offered to patients suffering from rare pulmonary diseases.

With the organisation of courses and dedicated symposiums during the European Respiratory Society (ERS) International Congress, and the publication of articles in all ERS publications, our society plays a key role in the process of advancing medical research in this field. Moreover, the ERS also promotes and supports guidelines and statements, funds fellowship programmes and many others activities (some in partnership with patients' associations), and coordinates actions against rare pulmonary diseases with European health authorities. In recent years, the *European Respiratory Journal (ERJ)* has focussed particular attention on rare pulmonary diseases and orphan drugs [26, 31–35]. Several important articles dealing with everything from basic science to clinical research have been published in the field of rare pulmonary diseases such as IPF, LAM, PAH or pulmonary Langerhans cell histiocytosis [14–17, 21–24, 26, 36].

The critical role of patient associations has been clearly recognised in recent years. A strong partnership with medical societies like the ERS is crucial to establishing successful political actions, and to improving communication with healthcare professionals, patients suffering from rare diseases and their relatives. Strong action is needed at the European level to overcome all the differences in the national health systems that can discriminate against patients with rare conditions and limit their access to treatment. It is also important to identify uniform criteria to be adopted by referral centres in the various European countries; moreover, in the spirit of the “free circulation of patients within the European member states”, it is also important to create, for selected cases, some dedicated European referral centres and networks that can manage patients and, therefore, accumulate enough experience to maximise the skills in the management of particularly rare diseases.

In February 2015, the ERS will endorse the Sixth International Meeting on Pulmonary Rare Diseases and Orphan Drugs, which will take place on Rare Disease Day in Milan, Italy. This international conference, the first of which was held 10 years ago, is entirely dedicated to the management of rare pulmonary parenchymal and vascular diseases, and rare variants of more common pulmonary conditions (such as severe refractory asthma and α_1 -antitrypsin deficiency emphysema).

This conference is the only European event dedicated to these challenging tasks, and it highlights that rare pulmonary diseases represent an important field of medicine not only for selected pulmonologists who are skilled in diagnosing and treating particular groups of these diseases, but also for all respiratory physicians. Dissemination among experts in different areas of clinical and basic research in respiratory medicine is part of the stimulating challenge of providing new insights, helping patients and supporting healthcare professionals. Topics that will be discussed during the conference include basic science, new genetic studies, molecular advances, and issues related to trial design and surrogate end-points in rare diseases studies; moreover, findings that will facilitate the development of new therapeutic options for patients affected by these conditions will be presented.

The Sixth International Meeting on Pulmonary Rare Diseases and Orphan Drugs will take place in Milan on the February 27–28, 2015, just a few weeks before this city will play host to the World Expo 2015. Expo 2015 will explore the theme “feeding the planet, energy for life”, a topic of great importance for the future of our lives and for world health: this world exposition is expected to attract >20 million visitors from all over the world.

Proceedings from past annual meetings and several selected reports from the 2013 meeting have previously been published in the *European Respiratory Review (ERR)* [37, 38]. Some manuscripts from the 2015 conference will be published in the *ERR*. In addition, later this year, the *ERJ* will publish a series of articles from the 2015 conference that will discuss rare pulmonary diseases and orphan drugs, and cover various topics (e.g. IPF, LAM, PAH and pulmonary veno-occlusive disease).

Crucial issues in research on rare diseases include solid and transparent collaborations with the pharmaceutical industry, fostered by orphan drug legislation, and development of independent and unsponsored investigations, supported by national, European and international funding. In this sense, PAH represents an important example with an outstanding international network of PAH clinicians and researchers, ranging from basic science to clinical studies, working in close partnership with pharmaceutical companies. In the near future, several programmes, including Horizon 2020, which is supported by the European Union, will offer important opportunities to promote research in the whole field of pulmonary medicine.

We hope that this conference and related articles will help our readers understand the main purposes of the discussions arising during the Milan conference and will increase awareness of rare pulmonary diseases. The International Meetings on Pulmonary Rare Diseases and Orphan Drugs are scheduled every other year because this area of medicine is growing rapidly and attracts increasing attention from the entire medical community. For the upcoming Sixth International Meeting on Pulmonary Rare Diseases and Orphan Drugs, we have decided to paraphrase the Expo motto and adopt our own: “feeding the breath, energy for life!”.

References

- 1 Cordier JF, ed. Orphan lung diseases. *Eur Respir Monogr* 2011; 54.
- 2 Spagnolo P, du Bois RM, Cottin V. Rare lung disease and orphan drug development. *Lancet Respir Med* 2013; 1: 479–487.
- 3 Rare Disease Day. What is Rare Disease Day? www.rarediseaseday.org/article/what-is-rare-disease-day Date accessed: November 23, 2014.
- 4 Humbert M, Sitbon O, Chaouat A, et al. Pulmonary arterial hypertension in France: results from a national registry. *Am J Respir Crit Care Med* 2006; 173: 1023–1030.
- 5 Ling Y, Johnson MK, Kiely DG, et al. Changing demographics, epidemiology, and survival of incident pulmonary arterial hypertension: results from the pulmonary hypertension registry of the United Kingdom and Ireland. *Am J Respir Crit Care Med* 2012; 186: 790–796.
- 6 Orphanet. About rare diseases. http://www.orpha.net/consor/cgi-bin/Education_AboutRareDiseases.php?lng=EN Date accessed: November 23, 2014. Date last updated: October 25, 2012.
- 7 Humbert M, Lau EMT, Montani D, et al. Advances in therapeutic interventions for patients with pulmonary arterial hypertension. *Circulation* 2014; 130: 2189–2208.
- 8 Hoepfer MM. Chronic thromboembolic pulmonary hypertension at the crossroad. *Eur Respir J* 2014; 43: 1230–1232.
- 9 Jenkins DP, Madani M, Mayer E, et al. Surgical treatment of chronic thromboembolic pulmonary hypertension. *Eur Respir J* 2013; 41: 735–742.
- 10 Taboada D, Pepke-Zaba J, Jenkins DP, et al. Outcome of pulmonary endarterectomy in symptomatic chronic thromboembolic disease. *Eur Respir J* 2014; 44: 1635–1645.

- 11 Pepke-Zaba J, Jansa P, Kim NH, *et al.* Chronic thromboembolic pulmonary hypertension: role of medical therapy. *Eur Respir J* 2013; 41: 985–990.
- 12 Ghofrani HA, D'Armini AM, Grimminger F, *et al.* CHEST-1 Study Group. Riociguat for the treatment of chronic thromboembolic pulmonary hypertension. *N Engl J Med* 2013; 369: 319–329.
- 13 Cordier JF, Cottin V, Guillemin L, *et al.* Eosinophilic granulomatosis with polyangiitis (Churg-Strauss). *Presse Med* 2013; 42: 507–510.
- 14 Cordier JF, Cottin V, Khouatra C, *et al.* Hypereosinophilic obliterative bronchiolitis: a distinct, unrecognised syndrome. *Eur Respir J* 2013; 41: 1126–1134.
- 15 Poletti V. Eosinophilic bronchiolitis: is it a new syndrome? *Eur Respir J* 2013; 41: 1012–1013.
- 16 Meyer KC, Raghu G, Verleden GM, *et al.* An international ISHLT/ATS/ERS clinical practice guideline: diagnosis and management of bronchiolitis obliterans syndrome. *Eur Respir J* 2014; 44: 1479–1503.
- 17 Chang WY, Cane JL, Kumaran M, *et al.* A 2-year randomised placebo-controlled trial of doxycycline for lymphangioleiomyomatosis. *Eur Respir J* 2014; 43: 1114–1123.
- 18 Cottin V, Harari S, Humbert M, *et al.* Pulmonary hypertension in lymphangioleiomyomatosis: characteristics in 20 patients. *Eur Respir J* 2012; 40: 630–640.
- 19 McCormack FX, Inoue Y, Moss J, *et al.* Efficacy and safety of sirolimus in lymphangioleiomyomatosis. *N Engl J Med* 2011; 364: 1595–1606.
- 20 Cottin V. Treatment of lymphangioleiomyomatosis: building evidence in orphan diseases. *Eur Respir J* 2014; 43: 966–999.
- 21 Borie R, Danel C, Debray MP, *et al.* Pulmonary alveolar proteinosis. *Eur Respir Rev* 2011; 20: 98–107.
- 22 Bonella F, Bauer PC, Griese M, *et al.* Wash-out kinetics and efficacy of a modified lavage technique for alveolar proteinosis. *Eur Respir J* 2012; 40: 1468–1474.
- 23 Piras B, Ferrarotti I, Lara B, *et al.* Clinical phenotypes of Italian and Spanish patients with α_1 -antitrypsin deficiency. *Eur Respir J* 2013; 42: 54–64.
- 24 Wei P, Lu HW, Jiang S, *et al.* Pulmonary Langerhans cell histiocytosis: case series and literature review. *Medicine (Baltimore)* 2014; 93: e141.
- 25 Caminati A, Cavazza A, Sverzellati N, *et al.* An integrated approach in the diagnosis of smoking-related interstitial lung diseases. *Eur Respir Rev* 2012; 21: 207–217.
- 26 Taniguchi H, Ebina M, Kondoh Y, *et al.* Pirfenidone in idiopathic pulmonary fibrosis. *Eur Respir J* 2010; 35: 821–829.
- 27 Noble PW, Albera C, Bradford WZ, *et al.* Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomised trials. *Lancet* 2011; 377: 1760–1769.
- 28 King TE Jr, Bradford WZ, Castro-Bernardini S, *et al.* A phase 3 trial of pirfenidone in patients with idiopathic pulmonary fibrosis. *N Engl J Med* 2014; 370: 2083–2092.
- 29 Richeldi L, Costabel U, Selman M, *et al.* Efficacy of a tyrosine kinase inhibitor in idiopathic pulmonary fibrosis. *N Engl J Med* 2011; 365: 1079–1087.
- 30 Richeldi L, du Bois RM, Raghu G, *et al.* Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. *N Engl J Med* 2014; 370: 2071–2082.
- 31 Sitbon O, Jaïs X, Savare L, *et al.* Upfront triple combination therapy in pulmonary arterial hypertension: a pilot study. *Eur Respir J* 2014; 43: 1691–1697.
- 32 Simonneau G, D'Armini AM, Ghofrani HA, *et al.* Riociguat for the treatment of chronic thromboembolic pulmonary hypertension: a long-term extension study (CHEST-2). *Eur Respir J* 2014 [In press DOI: 10.1183/09031936.00087114].
- 33 Simonneau G, Torbicki A, Hoeper MM, *et al.* Selexipag: an oral, selective prostacyclin receptor agonist for the treatment of pulmonary arterial hypertension. *Eur Respir J* 2012; 40: 874–880.
- 34 Epaud R, Ducou Le Pointe H, Fasola S, *et al.* Cladribine improves lung cysts and pulmonary function in a child with histiocytosis. *Eur Respir J* 2014 [In press DOI: 10.1183/09031936.00146114].
- 35 Ortega H, Chupp G, Bardin P, *et al.* The role of mepolizumab in atopic and nonatopic severe asthma with persistent eosinophilia. *Eur Respir J* 2014; 44: 239–241.
- 36 Caminati A, Cassandro R, Harari S. Pulmonary hypertension in chronic interstitial lung diseases. *Eur Respir Rev* 2013; 22: 292–301.
- 37 Harari S, Cottin V, Humbert M. Global effort against rare and orphan diseases. *Eur Respir Rev* 2012; 21: 171–172.
- 38 Harari S, Humbert M, Cottin V. Future perspectives on rare pulmonary diseases and rare presentations of common disorders. *Eur Respir Rev* 2013; 22: 199–201.