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EDITORIAL

Implementation of European Alpha-1 Research Collaboration (EARCO) in Portugal: the future starts now

Characterised over 50 years ago,[1] AATD is considered one of the most common hereditary disorders, but its epidemiology remains unknown in many countries, mainly due to its underdiagnosed state and a lack of registries of patients already identified.[2–4] In recent years, some countries are trying to fill this gap by creating diagnose and management guidelines and national and international patient registries.[5]

The European Respiratory Society (ERS) statement on AATD[6] has highlighted the differences in access to specialised care and specific treatments for patients with this rare disorder in Europe. In addition, there is a lack of prospective, standardised, follow-up data to understand the natural history of the disease in Europe and the influence of the risk factors, other genetic determinants, and augmentation therapy in the prognosis of the disease. Regarding augmentation therapy, the ERS statement summarised the inequalities of access to augmentation therapy in different European countries,[6] which were confirmed in a recent European survey,[7] but even in countries where augmentation is available and reimbursed there are differences in prescribing habits.[8] In Portugal, it is estimated that 1:5249 individuals 2000 individuals have a ZZ genotype, and that 1:281 individuals 37,400 individuals have a SZ genotype. Multiple rare alleles have been identified in Portugal but their frequencies in random populations are still unknown.[9–12] Nonetheless, the real burden of the disease is still unrecognized since there is no national registry. The Portuguese consensus document for the management of AATD was published in 2018.[13]

A study published in 2018 describes the current situation of AATD in Portugal.[14] In a 10 years' time frame, from 2006 to 2015, 417 individuals (almost 25% of tested cases) were confirmed as having severe or very severe AATD. These included 158 ZZ cases, 188 SZ and different combinations of rare and null alleles (n = 71). This study represents the most complete survey of AATD in Portugal so far and discloses a high rate of severe and very severe deficiency cases, attributed not only to ZZ and SZ genotypes but also a large number of rare combinations with other null and deficiency alleles.

Trying to answer fundamental questions about epidemiology, genetics, physiopathology, clinical management and prognosis of lung disease associated with AATD, a group of experienced and new researchers across Europe joined to form the European Alpha-1 Research Collaboration (EARCO).[15]

The EARCO is a Clinical Research Collaboration (CRC)[16] of the European Respiratory Society (ERS) Assembly 5 (airway diseases, asthma and chronic obstructive pulmonary disease) and aims to establish a collaborative effort that brings together multiple stakeholders, including researchers, healthcare providers, patients and industry, with the aim of advancing understanding through clinical and scientific research and improving the quality of life of patients with AATD.

The core project is the pan-European AATD Registry, a collaboration which will offer longitudinal real-world data for patients with AATD. The EARCO registry is modelled in part on the Alpha One International Registry (AIR) group established in 1997, which included representatives from 14 European countries.[17] The AIR group was successful in stimulating international collaborative research and organising and developing clinical trials; however, no real-life, longitudinal data were systematically collected.[5] The EARCO registry will also take advantage of the existing AATD registries that have been developed at the national level. However, these registries differ in terms of inclusion criteria, data collected and follow-up. One of the key tasks of EARCO will be harmonising the data collection and assessing the quality of the data included prospectively.[18]

In addition to the development of the registry, there are other initial objectives of EARCO for the next 3 years. Among these objectives, it is of great importance to build a network of patient representatives, researchers and clinical investigators, to identify informed research needs and establish an

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agenda for AATD research, and to attract young investigators to the area of clinical management and research of AATD for the future. In this respect, two surveys are being conducted, one for patients and the second for healthcare providers, particularly in order to understand the key research needs in the field of AATD in Europe.

Another project of EARCO is the evaluation of laboratory diagnostic methods of AATD in Europe. Developing reliable standards for laboratory diagnosis of AATD is crucial. There are different diagnostic algorithms in different reference laboratories in Europe,[19] which are usually adapted to the demands of the countries or to the needs of the target population for whom diagnosis is required. Although all these algorithms can provide an accurate diagnosis, it is important to establish an external quality control programme that can also be used for new laboratories, in order to ensure reliable test results.[20] The quality control programme of laboratory diagnosis will set the standards for the correct diagnosis of the condition across Europe.[21]

An ongoing international survey, on the initiation and indications of augmentation therapy, will provide insights into the current practice of augmentation therapy in those European countries where it is available.

Over the next 3 years, EARCO will set up the new European-based AATD registry and establish the roadmap for clinical and translational research in the field. It will also make a substantial contribution in advocacy and education in AATD and we appeal to all ERS members to be part of this. EARCO can be contacted through the group members, the national representatives, or directly through the website (www.ersnet.org/research/earco-european-alpha-1-research-collaboration). Portugal has a group of dedicated researchers in the field of AATD that are contributing to the different work-packages of EARCO; it is estimated that approximately 100 patients with severe deficiency could be included in the EARCO registry and some centers are already completing the regulatory process necessary to participate in this important international initiative. We encourage all health care providers involved in the care of patients with AATD to join EARCO by contacting the national or international representatives and start to improve the future of patients with this disease. The collaboration of all stakeholders, and in particular the inclusion of patients as active participants in the development of EARCO, makes it highly likely that EARCO will generate new knowledge with direct impact on patients' quality of life and clinical s care.[15]

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