The European Cystic Fibrosis Society Patient Registry: a platform for pharmacovigilance.

On behalf of the European Cystic Fibrosis Society Patient Registry: Jacqui van Rens[1], Ed McKone[2]
[1] Dept. of Paediatrics, University Hospital Leuven, Belgium, [2] Dept. of Respiratory Medicine, St. Vincent's University Hospital, Dublin, Ireland.

INTRODUCTION

Multiple new medicines for cystic fibrosis (CF) are in the pipeline to come onto the market. Post-authorisation safety surveillance (PASS) and efficacy (PAES) studies need to be carried out in order to support regulatory decision making for these new drugs.

In October 2016 the European Medicine Agency (EMA) set up a Registry Initiative to discuss using existing patient registries to carry out pharmaco-epidemiological studies. They expressed their interest to use the European Cystic Fibrosis Society Patient Registry (ECFSPR) as a model registry for these type of studies.

OBJECTIVE

To describe the EMA qualification process for the assessment of the ECFSPR as a suitable registry to perform PASS and PAES studies, thereby providing clear guidelines on data collection, and how it is to be shared with the EMA and Industry.

METHOD

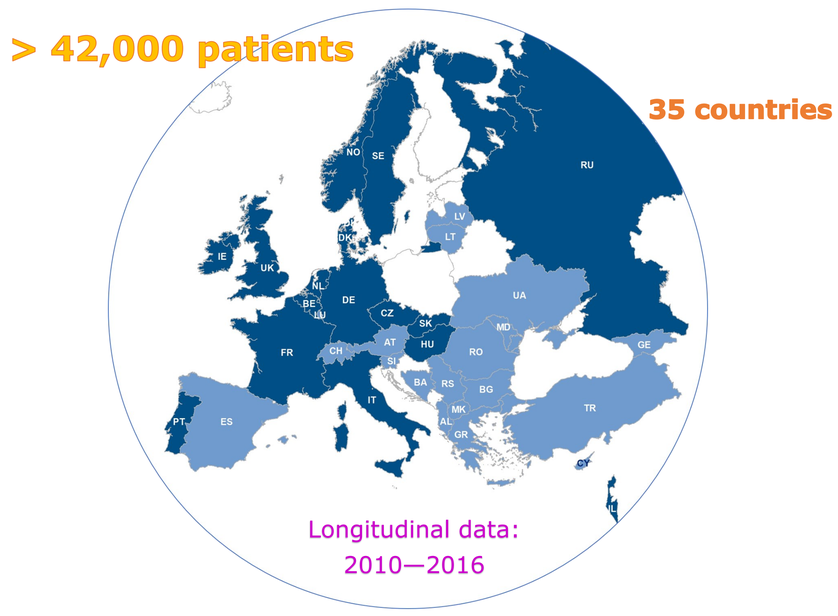
A scientific consortium was set-up consisting of representatives from the ECSPR, larger national registries (such as France, Germany and UK), ECFS Clinical Trial Network, and the ECSPR data-controller. The consortium submitted a proposal to the EMA that CF registries be adopted as a tool for EMA PASS and PAES studies. The proposal included elements on data-completeness, data-quality, data delivery (raw data versus summary data) and governance.

A multi-disciplinary qualification team of regulators was constituted with of representatives from EMA, the Clinical Trial Facilitation Group, health technology assessment bodies, and patients.

In two meetings, in June and September 2017, the proposal was discussed at EMA's offices.

ECFSPR

The ECFSPR is an established disease registry that collects, measures and compares anonymised demographic and clinical data from consenting people with cystic fibrosis (Cystic Fibrosis) in Europe and neighbouring countries. The information is used to improve our understanding of the disease, encourage new European standards of CF care, conduct epidemiological research, provide data for pharmacovigilance, and inform public health-planning.



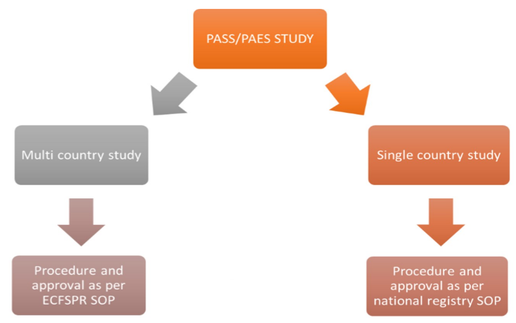
RESULT

As a result of successful collaboration with national CF registries and extensive interaction with the EMA, the ECFSPR has received a qualification opinion from the EMA. This provides a detailed road map for the eventual use of the ECFSPR as an appropriate platform for the collection of CF data for Post Authorisation Safety Studies and Post Authorisation Efficacy studies.

A Context of Use document is available on the EMA website for public consultation. The document presents a model that can be used by other disease registries when applying for EMA qualification to carry out PASS and PAES studies.

www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2018/02/WC500243542.pdf

Contact for PASS/PAES studies — flowchart



RESULT

Specific issues regarding the use of data from CF Registries in PASS and PAES studies of new CF medications were discussed during the qualification procedure:

1. The **target population** will be limited to countries with similar CF outcomes and coverage of the patient population. The **variables** collected will be those that are routinely collected in CF clinical trials and routine clinical practice. Additional variables, for collection of retrospective or prospective data, can be added in specific cases depending on EMA/HTA/Industry requirements. This may require re-consent, unless the additional variable is considered essential to understand the course of the disease.
2. Registries can be used to **monitor** identified or potential **adverse events** (AE), but do not have a signaling function regarding the occurrence of AEs.
   Registries can be adapted to collect specific, additional drug-related AEs depending on EMA/Industry requirements, which will require re-consent.
   To distinguish between complications related to the disease progression and those related to the medication used, a matched control group with patients not on the drug will be involved.
3. **Collection and submission of** efficacy and safety **data** to Industry/EMA/HTA will be done on an annual basis.
4. **Summary data**, rather than patient-level raw data, is considered sufficient for robust PASS/PAES studies. Data-analyses and reporting will be done by the ECFSPR statisticians. In case independent re-assessment of the data is required, a neutral academic institution with no link to the Industry may be involved.
5. The existing standardized approach of data collection, definition, and quality control mechanisms established and implemented by the CF registries are considered sufficient to ensure the **data quality**. The ongoing work to improve the quality and validity of the data, and decrease the missing data will be continued.
6. The most appropriate **statistical method** to analyse the information for PASS and PAES studies will be defined and tailored on a case-by-case basis to specifically address the scientific questions of interest.

CONTACT ecfs-pr@uzleuven.be +32 484 443 435
www.ecfs.eu/ecfspr