# DARWIN EU® - Drug utilisation study in individuals with cystic fibrosis in Europe

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## BACKGROUND

Cystic fibrosis (CF) is a rare genetic disorder caused by mutations in the *CFTR* gene, leading to multi-organ dysfunction.[1,2] The introduction of CFTR modulators has transformed CF management, yet real-world evidence (RWE) on utilisation and patient characteristics across Europe remains limited.[3]

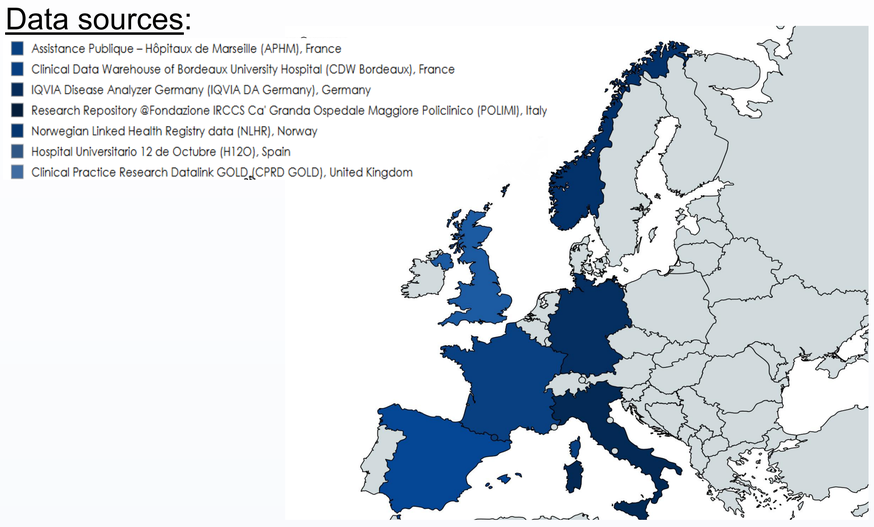
## OBJECTIVES

This study aimed to describe CFTR modulator treatment patterns and patient-level characteristics across multiple European data sources mapped to the OMOP Common Data Model (CDM), while assessing the current capability of the DARWIN EU® network to generate evidence in a rare disease population.

## MATERIALS AND METHODS

Study design: A retrospective cohort study.

Data sources:




All data sources previously mapped their data to the OMOP CDM.

Study population: All individuals with first recorded CFTR modulator prescription during the study period after their CF diagnosis, with at least one year of data visibility prior to the date of first recorded CFTR modulator prescription and no prior use of CFTR modulators. To ensure adequate follow-up, only individuals with the first recorded CFTR modulator at least 180 days prior to the end of data availability in each data source were included.

Study period: 2015 – 2024.

Drugs of interest: CFTR modulators (ivacaftor, ivacaftor/lumacaftor, ivacaftor/tezacaftor, ivacaftor/tezacaftor/elexacaftor) and supportive CF therapies.

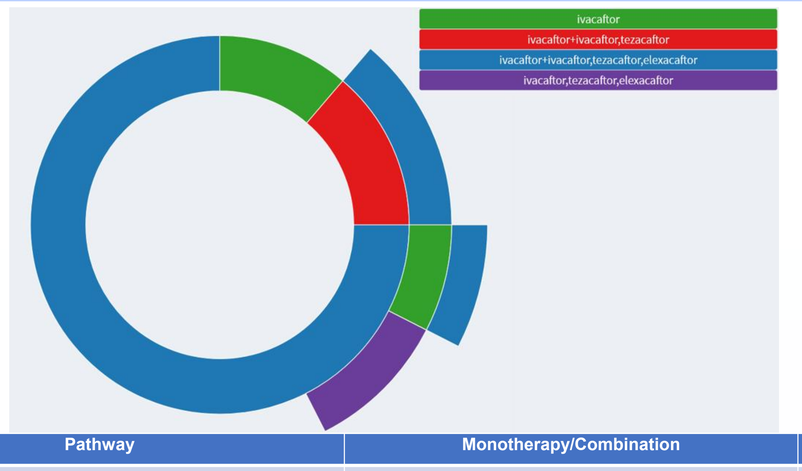
Condition of interest: Cystic fibrosis.

Data analysis: Patient-level characterisation, including demographics and supportive therapy use, was presented overall and stratified by paediatric and adult populations. The number and percentage of individuals treated with each of the CFTR modulators after diagnosis of CF were described, including treatment sequence over time and the use of treatment combinations. Analyses were restricted to treatments observable within each source as several data sources capture only part of the CF care pathway (e.g., hospital only or outpatient only data) and linkage between settings was generally not available.

## RESULTS

A total of 801 individuals with a prescription record for any CFTR modulator were included, with the largest contributions from NLHR (34.1%) and IQVIA DA Germany (21.4%). The most frequently used therapies were ivacaftor (n=506), the fixed-dose combination of ivacaftor/tezacaftor/elexacaftor (n=398), and ivacaftor/lumacaftor (n=229). Median age at treatment initiation ranged from 16 years in APHM to 34 years in CPRD GOLD. Paediatric prescriptions predominated in hospital-based sources (CDW Bordeaux and APHM), while adult prescriptions predominated in registry and primary care sources. Female predominance was observed in most data sources (>52.3%), except for NLHR (53.9% males). Supportive therapy use (e.g., mucolytics, salbutamol, pancreatic enzymes) showed distinct trends over time.

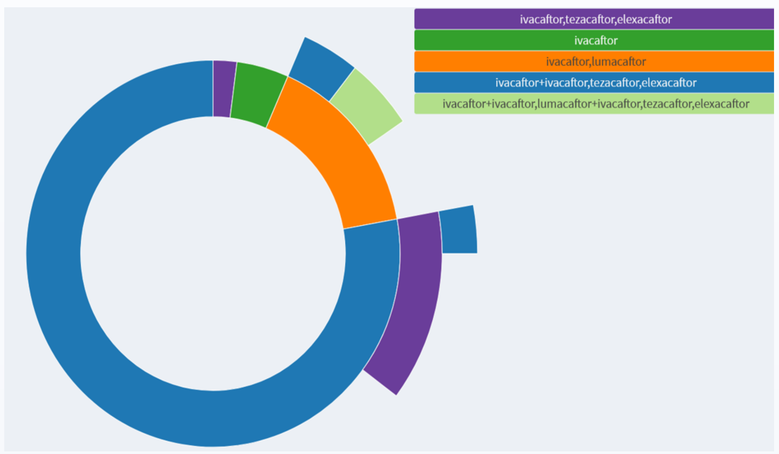
Treatment pattern analyses were performed in IQVIA DA Germany, NLHR, and CPRD GOLD. CPRD GOLD results were not reported due to low sample sizes and data suppression. The most common first-line CFTR modulator was ivacaftor with a fixed-dose combination product of ivacaftor/tezacaftor/elexacaftor, corresponding to the recommended triple therapy for CF (**Figure 1**, **Figure 2**). This treatment pattern was consistently predominant in NLHR (77.87%) and IQVIA DA Germany (75.00%). Other first-line treatments varied by data source. Switching between CFTR modulator therapies was infrequent.




| ID | Pathway | Monotherapy/Combination | Line | Percentage |
|---|---|---|---|---|
| 1 | ivacaftor+ivacaftor,tezacaftor,elexacaftor | ivacaftor+ivacaftor,tezacaftor,elexacaftor | 1 | 75.00% |
| 2 | ivacaftor+ivacaftor,tezacaftor-ivacaftor+ivacaftor,tezacaftor,elexacaftor | ivacaftor+ivacaftor,tezacaftor | 1 | 13.75% |
| 2 | ivacaftor+ivacaftor,tezacaftor-ivacaftor+ivacaftor,tezacaftor,elexacaftor | ivacaftor+ivacaftor,tezacaftor,elexacaftor | 2 | 13.75% |
| 3 | ivacaftor | ivacaftor | 1 | 11.25% |
| 4 | ivacaftor+ivacaftor,tezacaftor,elexacaftor-ivacaftor,tezacaftor,elexacaftor | ivacaftor,tezacaftor,elexacaftor | 2 | 10.00% |
| 5 | ivacaftor+ivacaftor,tezacaftor,elexacaftor-ivacaftor-ivacaftor+ivacaftor,tezacaftor,elexacaftor | ivacaftor | 2 | 7.50% |
| 5 | ivacaftor+ivacaftor,tezacaftor,elexacaftor-ivacaftor-ivacaftor+ivacaftor,tezacaftor,elexacaftor | ivacaftor+ivacaftor,tezacaftor,elexacaftor | 3 | 7.50% |

**Figure 1**. Sunburst plot of CFTR modulator use among individuals with cystic fibrosis in IQVIA DA Germany.

The sunburst plot displays treatment sequences, with the inner ring representing first-line therapy and outer rings representing subsequent lines. Segment size reflects the number of individuals following each treatment, and colours correspond to specific CFTR modulator regimens. A '+' denotes concurrent prescriptions within the same episode (combination therapy), whereas a '–' denotes a switch. The accompanying table reports percentages for each monotherapy/combination treatment.




| ID | Pathway | Monotherapy/Combination | Line | Percentage |
|---|---|---|---|---|
| 1 | ivacaftor+ivacaftor,tezacaftor,elexacaftor | ivacaftor+ivacaftor,tezacaftor,elexacaftor | 1 | 77.87% |
| 2 | ivacaftor+ivacaftor,tezacaftor,elexacaftor-ivacaftor,tezacaftor,elexacaftor | ivacaftor,tezacaftor,elexacaftor | 2 | 13.11% |
| 3 | ivacaftor,lumacaftor | ivacaftor,lumacaftor | 1 | 15.57% |
| 4 | ivacaftor,lumacaftor-ivacaftor+ivacaftor,lumacaftor+ivacaftor,tezacaftor,elexacaftor | ivacaftor+ivacaftor,lumacaftor+ivacaftor,tezacaftor,elexacaftor | 2 | 4.92% |
| 5 | ivacaftor | ivacaftor | 1 | 4.51% |
| 6 | ivacaftor,lumacaftor-ivacaftor+ivacaftor,tezacaftor,elexacaftor | ivacaftor+ivacaftor,tezacaftor,elexacaftor | 2 | 4.10% |
| 7 | ivacaftor+ivacaftor,tezacaftor,elexacaftor-ivacaftor,tezacaftor,elexacaftor-ivacaftor+ivacaftor,tezacaftor,elexacaftor | ivacaftor+ivacaftor,tezacaftor,elexacaftor | 3 | 2.87% |
| 8 | ivacaftor,tezacaftor,elexacaftor | ivacaftor,tezacaftor,elexacaftor | 1 | 2.05% |

**Figure 2**. Sunburst plot of CFTR modulator use among individuals with cystic fibrosis in NLHR.

The sunburst plot displays treatment sequences, with the inner ring representing first-line therapy and outer rings representing subsequent lines. Segment size reflects the number of individuals following each treatment, and colours correspond to specific CFTR modulator regimens. A '+' denotes concurrent prescriptions within the same episode (combination therapy), whereas a '–' denotes a switch. The accompanying table reports percentages for each monotherapy/combination treatment.

## CONCLUSIONS

This study provides an exploratory description of CFTR modulator use across multiple European data sources. While the findings illustrate the potential of routinely collected healthcare data to inform real-world treatment patterns in CF, the lack of linkage across care settings (hospital vs. outpatient), partial visibility of specialist prescribing, and variability in data completeness and population coverage impose important constraints on the interpretability of the results. These results should therefore be interpreted as exploratory rather than confirmatory. Continued improvements in data completeness, longitudinal depth, and harmonisation across care settings will be essential to strengthen future RWE generation for CF.

## REFERENCES

1. Parisi, G.F., et al., *Cutting-Edge Advances in Cystic Fibrosis: From Gene Therapy to Personalized Medicine and Holistic Management.* Genes, 2025. **16**(4): p. 402.
2. Han, X., et al., *Recommended Tool Compounds for Modifying the Cystic Fibrosis Transmembrane Conductance Regulator Channel Variants.* ACS Pharmacol Transl Sci, 2024. **7**(4): p. 933-950.
3. Rafeeq, M.M. and H.A.S. Murad, *Cystic fibrosis: current therapeutic targets and future approaches.* J Transl Med, 2017. **15**(1): p. 84.

## DISCLOSURE

This study was funded by the European Medicines Agency (EMA) and performed via DARWIN EU® (EUPAS1000000708). EMA was involved in conceiving the research, objectives, and reviewing the study protocol and the study report including the results. Data partners do not have an investigator role. They execute analytical code at their respective data sources, review, and approve their results. This communication represents the DARWIN EU® Coordination Centre only and cannot be interpreted as reflecting those of the EMA or the European Medicines Regulatory Network.

## CONTACT

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