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DSVR 2022

14e Colloque Données de Santé en Vie Réelle
21 juin 2022 Paris (France)

Treatment sequences in patients with Fabry disease in France,
using the SNDS database and a clustering methodology

Introduction

Fabry Disease (FD) is a rare lysosomal storage disorder caused by alpha-galactosidase A deficiency. Fabry disease incidence is generally known to be between 1/60 000 to 1/35 000 new births, but recent studies show that when including late onset Fabry variant, incidence is up to 1/10 000[1].

Currently, 3 treatments are available in France. (agalsidase beta, **agalsidase alfa**, and migalastat). Within the timeframe of this analysis, between 2009 and 2016, only agalsidase beta and alfa were available.

A shortage of agalsidase beta occured between 2009 and 2013. Few real-wolrd data is available in France.

Objective: describe the treatment sequences of patients with FD

Methods

Cohorts

It is a **retrospective cohort** using the **SNDS [2] database**, composed of patients who received **at least one FD treatment** over 2009-2016.

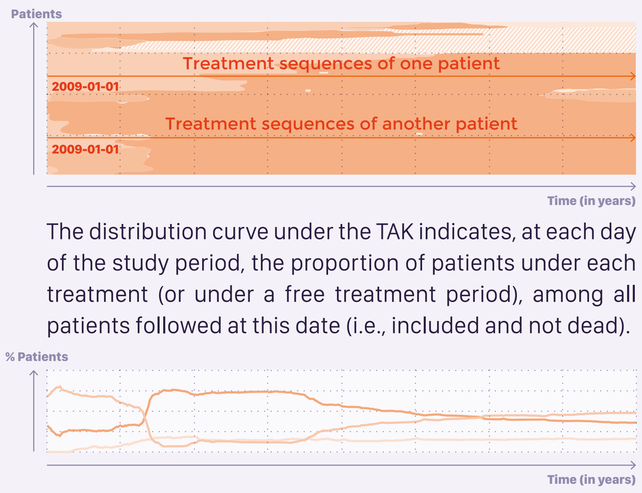
Four complementary sub-cohorts are defined:
- Male / female,
- Patients with / without cardiac variant of FD.

Patients with cardiac variant have diagnosis codes for cardiovascular disease [3], no renal impairment, no cornea verticillata (H180) and no angiokeratoma (D239, I780).

All **FD therapies** delivered to these patients over 2009-2016 are extracted and the **TAK [4]** methodology is used to describe the treatment sequences of the cohort.

How to read a TAK?

The TAK represents the treatment sequences of each patient in a linear graph. Each patient is aligned on the 1st of January 2009 on the left vertical axis of the graph. Then it moves horizontally to the right over the course of the study period, until the end of 2016. Patients are clustered into disjoint groups, so that each group is composed of similar treatment sequences.



The distribution curve under the TAK indicates, at each day of the study period, the proportion of patients under each treatment (or under a free treatment period), among all patients followed at this date (i.e., included and not dead).

Conclusion

The SNDS gives real-world evidence on FD and its management.

The TAK allows easy visualization of complex treatment patterns by eliminating noise and extracting the great trends to provide a simplified way to understand phyisician's prescribing practices.

We observed the agalsidase beta shortage and its effects on patients' management. Some differences in term of treatment sequences can be observed for patients with a cardiac variant: more usage of agalsidase alfa and more treatment discontinuation, possibly due to clinical trial.

References

[1] Newborn Screening for Fabry Disease in Northeastern Italy: Results of Five Years of Experience Gragnanaillo et al. Biomolecules. 2021

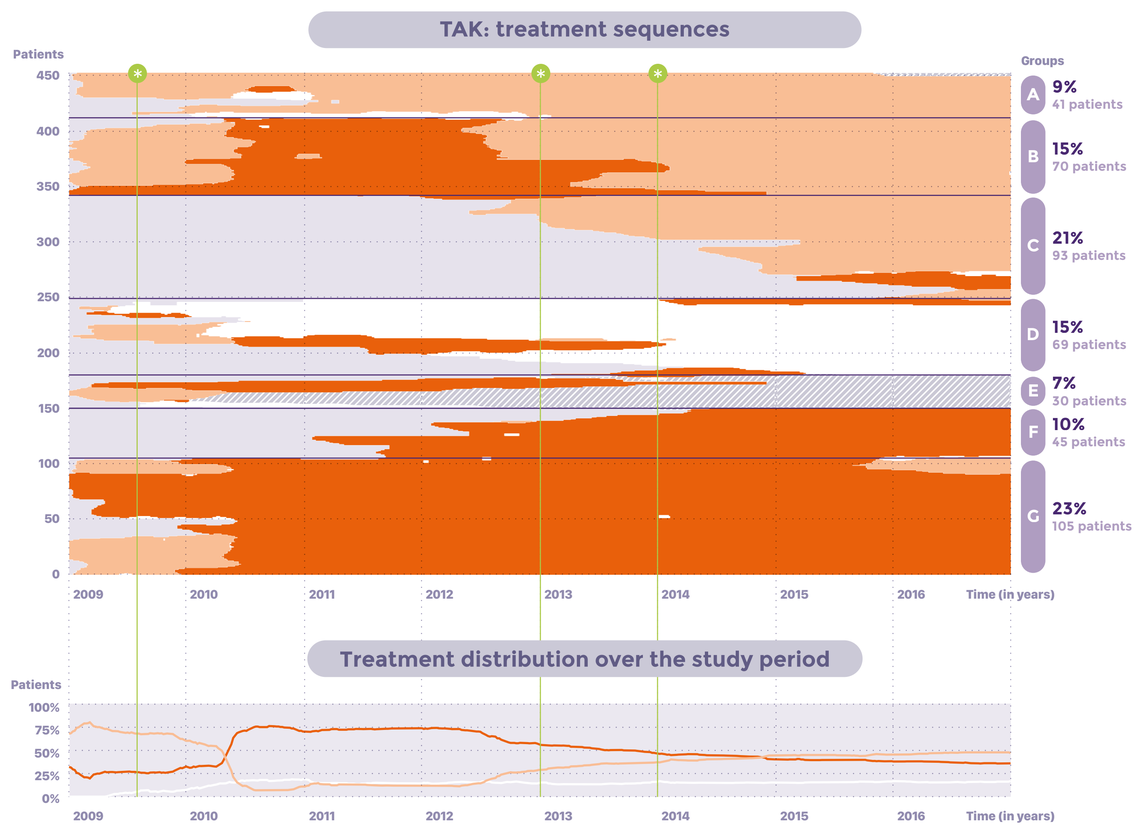
[2] French National Health Data System, including primary and secondary care data from 98% of the French population

[3] Hypertension cardiac insufficiency, cardiomegaly, pacemaker, rhythm disorders, angina pectoris, myocardial infarction

[4] Time-Sequence Analysis through K-clustering
Machine Learning–Based Analysis of Treatment Sequences Typology in Advanced Non–Small-Cell Lung Cancer Long-Term Survivors Treated With Nivolumab C. Chouaïd et al. JCO Clinical Cancer Informatics 2022 :6

Results

Global cohort: 453 patients



The shortage in 2010 marks a switch from agalsidase beta to agalsidase alfa.
In 2015, an equal number of patients is treated by the 2 treatments.

Legends

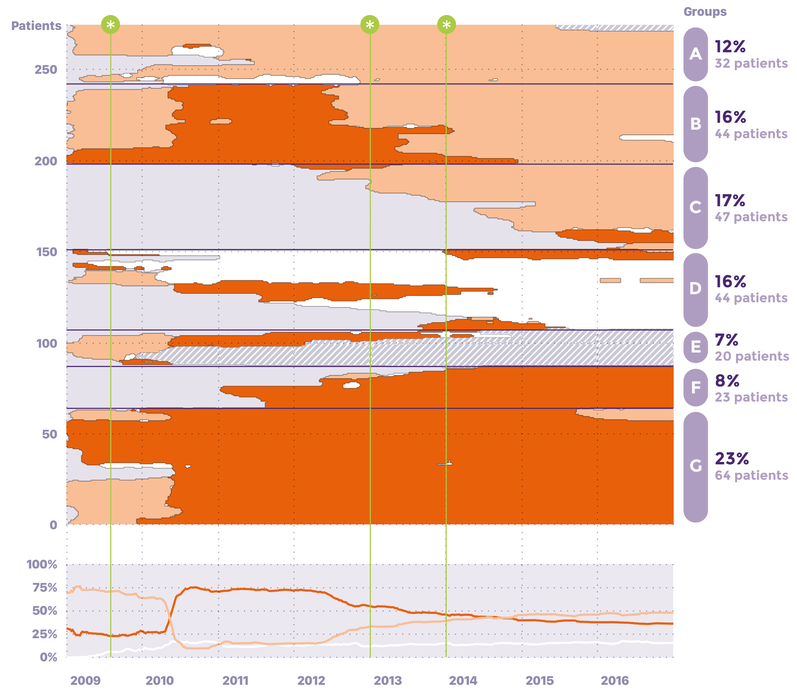
- Agalsidase beta
- Agalsidase alfa
- Before inclusion
- Death
- Not treated

Key dates:
August 1st, 2009: shortage start
January 1st, 2013: shortage end
January 1st, 2014: end of the post-shortage period

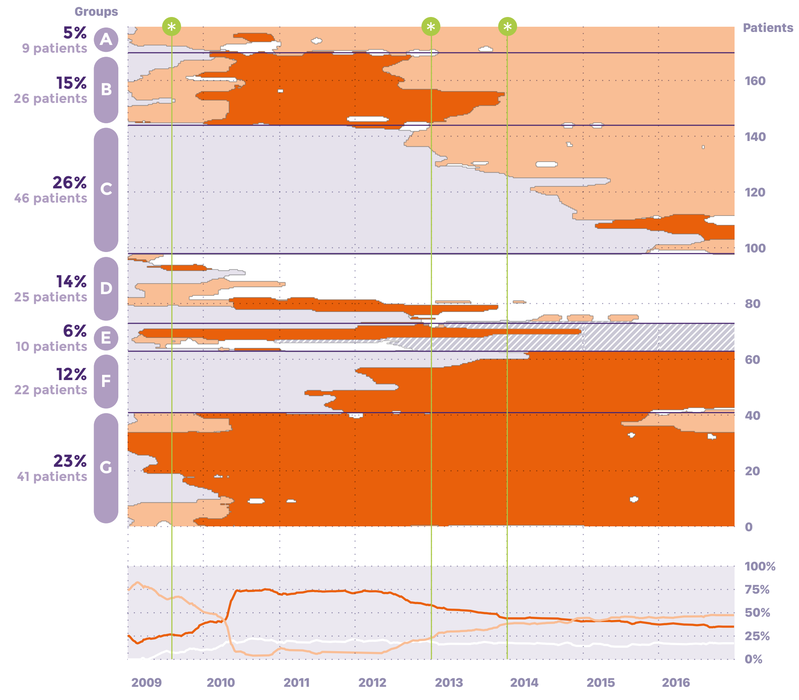
Groups

- **A** Patients treated by agalsidase beta in the long term
- **B** Patients treated by agalsidase alfa during the shortage, but changing to agalsidase bêta after
- **C** Patients starting their treatment after 2012, mainly without treatment changes and under agalsidase beta
- **D** Patients with several years of discontinued treatment (median: 4.5 years of discontinuation could be caused by inclusion in clinical trial, not captured here)
- **E** Patients who died during the study period (2009-2016)
- **F** Patients who started treatment during the shortage on Agalsidase alfa
- **G** Patients treated mostly with agalsidase alfa, since 2010

Male: 274 patients

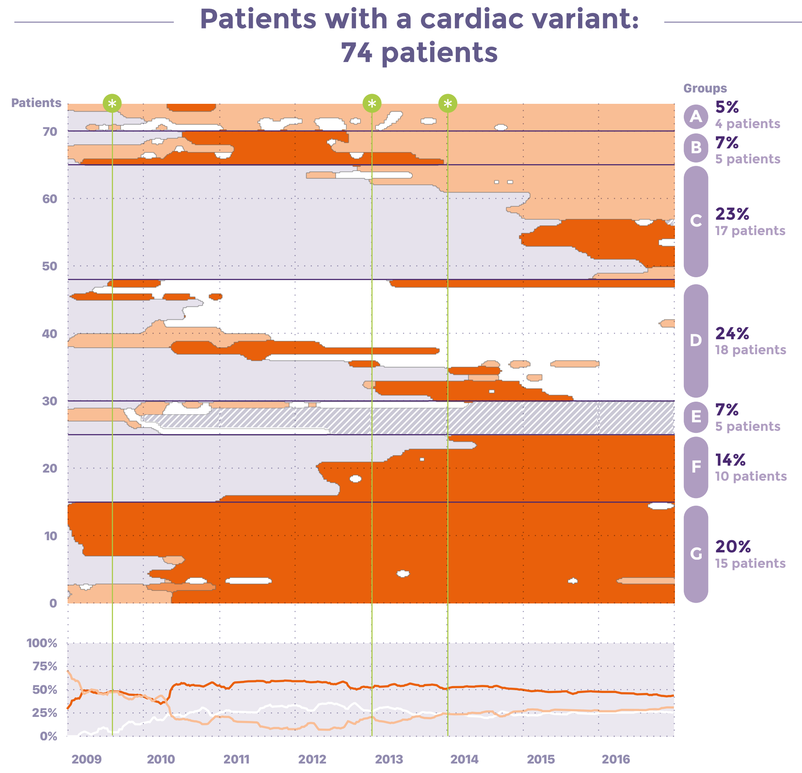


Female: 179 patients

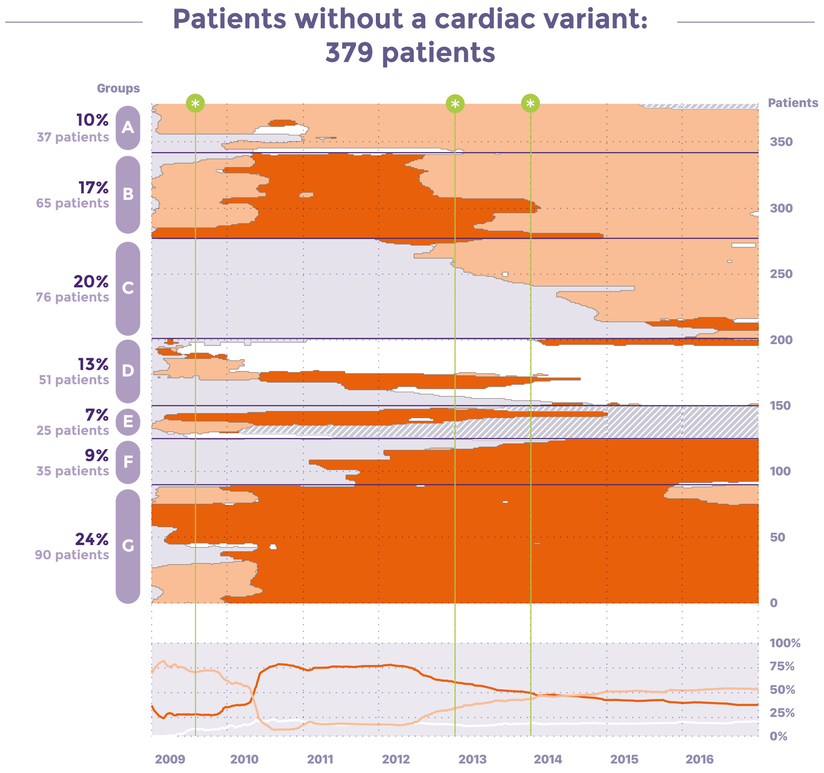


Incident treatment C & F groups (treatment started in 2010 or after) were more represented in women.
There was no other difference in the treatment sequences of men and women.

Patients with a cardiac variant: 74 patients



Patients without a cardiac variant: 379 patients



Patients with cardiac variant were more likely to stop treatment (group D), possibly due to inclusion in a clinical trial.
In 2016, a proportionally higher number of these patients were being treated with agalsidase alfa.

Disclosure/Funding: FR, GC, ML are full time employees at HEVA. FF, NA, MM, LC are full time employees at TAKEDA. This study was financed by TAKEDA France. Heva was responsible for the medical writing of this poster.

SNIIRAM study registered with the INDS on 12/09/2017 and authorised by the CNIL on 04/12/2017. (DR-2017-368 (request 917202)) - CNAM agreement signed on 02/07/2018.