Preliminary Data Analysis

Treatment patterns in pulmonary arterial hypertension

Administrative details of the data analysis	
Condition/ADR(s)	Pulmonary arterial hypertension
Short title of topic	Treatment patterns in patients with pulmonary arterial hypertension
TDA-DAT lead analyst (and reviewer)	Karin Hedenmalm (Rob Flynn)

1. Rationale and Background

Pulmonary arterial hypertension is a rare type of pulmonary hypertension characterized by increased mean pulmonary arterial pressure and can be idiopathic, heritable, drug-induced, or secondary to other chronic diseases as HIV infection, congenital heart diseases, portal hypertension [1]. The median survival is about 7 years from the time of diagnostic catheterization.

The therapeutic management differs based on type and severity and usually involves a mono or combination therapy from the following agents: endothelin receptor antagonist (ERA) plus phosphodiesterase-5 inhibitor (PDE5i) and calcium channel blockers (CCB).

In order to evaluate the feasibility of an RCT in PAH patients, it is suggested to conduct an analysis of RWD to describe the actual treatment patterns for patients with PAH in Germany and UK.

2. Research questions

The following research questions will be investigated:

- What is the first line treatment for patients diagnosed with PAH focusing on ERA and PDE5i classes (monotherapy or combined)?
- After how long patients initiating single therapy receive a second drug (combination therapy)?

3. Research methods

3.1. Study design

This will be a cohort descriptive study in which a cohort of patients with a history of PAH (both idiopathic, secondary) will be created, with follow-up starting at the date of diagnosis.

3.2. Setting and study population

The study population will be the general population (UK) and patients visiting general practices (Germany).

3.3. Data sources

The following databases will be used: IQVIA™ Medical Research Data (IMRD) UK, IQVIA™ Disease Analyser Germany Brief descriptions of both databases are provided in Annex 1.

Study period was between January 2006 and June 2021 in IQVIA™ Disease Analyser Germany and between 1998 and 2021 in IQVIA™ Medical Research Data (IMRD) UK.

3.4. Variables

Patients with a history of PAH will be followed since their first incident prescription of either ERA and PDE5i (incident use) and treatment patterns will be reported. Other therapies will not be captured.

A patient is considered to have started directly on combination therapy if a substance from both classes was initiated within 30 days (sensitivity analysis: 60 days).

Since PDE5I's are also indicated for treatment of erectile dysfunction, the analysis in IQVIA™ Disease Analyser Germany will be restricted to the EphMRA ATC code for treatment of PAH (as inclusion of the EphMRA ATC code for treatment of erectile dysfunction in a feasibility assessment resulted in a markedly higher proportion of male patients). For IMRD (UK) prescriptions for sildenafil will be excluded if the quantity prescribed is 2, 4, 8, or 16 (pack sizes used almost exclusively for erectile dysfunction). Prescriptions for tadalafil will be excluded if the quantity supplied is 4 or 8, or if the tablet strength is 2.5mg or 5mg (both used exclusively for erectile dysfunction).

3.5. Statistical analysis

The following variables will be calculated and reported:

- Number of PAH patients
- Number of PAH patients that initiated incident treatment with ERA or PDE5i
- Treatment initiation patterns over time in PAH patients
- Number of patients initially treated with monotherapy which progressed to combination therapy, (assuming that they stayed on the initial therapy), within 1 year and respectively 2 years since start of treatment

3.6. Limitations

- In IQVIA™ Disease Analyser Germany there is a risk that patients might visit another practice to receive prescriptions for PAH. However, it would seem unlikely that such behaviour would depend on the treatment prescribed
- The distinction between switching to the other treatment versus actual combined treatment is to be taken with caution. However, most patients with 'combined' treatment during the first 60 days (after initiating treatment with either therapy) initiated both treatments on the same day, which indicates that they were intended to be taken together
- Some of the treatment with PDE5-I's may relate to treatment of erectile dysfunction, so in the analysis we will try to minimise this bias by including only PDE5-I's that are indicated for treatment of pulmonary hypertension, building on information available on different strengths or pack sizes usually used for the different indications. For both data sources used, a more sensitive approach to identifying PDE5-Is used for erectile dysfunction could have been developed if more time was available.

4. References

1. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, Williams PG, Souza R. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019 Jan 24;53(1):1801913. doi: 10.1183/13993003.01913-2018. PMID: 30545968; PMCID: PMC6351336.

Annexes

Annex 1 - Information on Databases and Healthcare systems included

IQVIA™ Medical Research Data (IMRD) UK

IQVIA™ Medical Research Data (IMRD) UK is a primary care database from the UK. GPs play a gatekeeper role in the healthcare system in the UK, as they are responsible for delivering primary health care and specialist referrals. Over 98% of the UK-resident population is registered with a GP, so that GP patient records are broadly representative of the UK population in general. Patients are affiliated to a practice, which centralizes the medical information from GPs, specialist referrals, hospitalizations, and tests.

IQVIA™ Disease Analyzer Germany

IQVIA™ Disease Analyzer Germany collects computerised information from specialised and general primary care practices throughout Germany since 1992. Around 3% of general practitioners (GP) practices are included, which covers all patients consulting a practice. Data from IQVIA™ Disease Analyzer Germany have been shown to be reasonably representative of German healthcare statistics for demographics and certain diseases and is considered one of the largest national medical databases worldwide. IQVIA™ Disease Analyzer Germany includes more than 2,500 practices and 3,100 physicians (13 speciality groups) representing over 15,000,000 patients. This database used to be named IMS® Disease Analyzer Germany and some use of this terminology may persist.

The quality of IQVIA™ Disease Analyzer data is ensured by a series of continuous QA controls and data refinement. These include checking incoming data for criteria such as completeness and correctness, (e.g. linkage between diagnoses and prescriptions), and standardizing certain data values such as laboratory test results in order to enable reliable analysis.

Annex 2 –Sensitivity analysis with minimum follow up time

Time period after first incident prescription	Minimum follow-up time after first incident prescription	All PAH patients with incident treatment	Incident treatment with endothelin receptor antagonist alone	Incident treatment with PDE5 inhibitor alone	Combined treatment (cumulative)
0-1 days	≥0 days				
0-30 days	≥30 days				
0-60 days	≥60 days				