Current Pharmaceutical Treatment Landscape of Pulmonary Arterial Hypertension (PAH) Patients in Germany – A Claims Data Analysis

Acceptance Code: HSD67

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Objectives

- Pulmonary arterial hypertension (PAH) is a rare, life-threatening, and progressive disease characterized by remodeling and progressive narrowing of the pulmonary vessels.[1]
- The current treatment strategies for PAH, depending on disease severity and treatment response, include therapy with high-dose calcium channel blockers (in vasoreactive patients) or PAH-specific agents (in non-vasoreactive patients) where treatment choice is individually at physician's decision.[2-4]
- The study aimed to describe treatment patterns with PAH-specific agents from the German payer's perspective.

Methods

Study design

- A retrospective analysis using anonymized German Statutory Health Insurance (SHI) data was conducted.
- The study covered a time period from 2016 to 2021 to include the latest available data in the database at the start of the study.

Data source

- Data from the Institute for Applied Health Research Berlin GmbH (InGef) research database was used.
- The database includes approximately 4 million insured individuals (~ 5% of the German population[5]) and is representative for the German population in terms of age, gender, and region of residence.[6]

Study population

- The study population comprised patients with a documented diagnosis of PAH who were treated with eligible PAH-specific agents in 2021.
- Patients needed to have ≥ 1 inpatient (primary or secondary discharge diagnosis) and/or ≥ 2 outpatient (verified) diagnosis codes for PAH (ICD-10-GM I27.0) in 2021.
- At least one prescription of pre-defined eligible PAH-specific agents in 2021 (identified by 7 digit ATC codes) was required **(see Table 1)**.

Table 1 ATC codes for identification of patients with PAH-related agents[4]

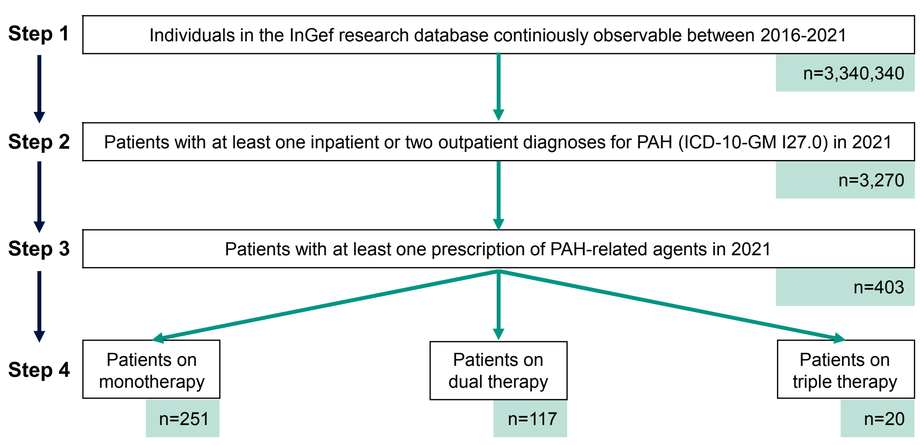
Agent	ATC codes
Riociguat	C02KX05
Macitentan	C02KX04
Ambrisentan	C02KX02
Bosentan	C02KX01
Sildenafil	C02KX06
Tadalafil	C02KX07
Iloprost	C02KX08
Selexipag	C02KX09
Treprostinil	B01AC21
Epoprostenol	B01AC09

- Patients were categorized into three subgroups: patients on monotherapy, dual therapy, or triple therapy for PAH.
- Patients were characterized in terms of age and gender distribution as well as co-morbidities.

Results

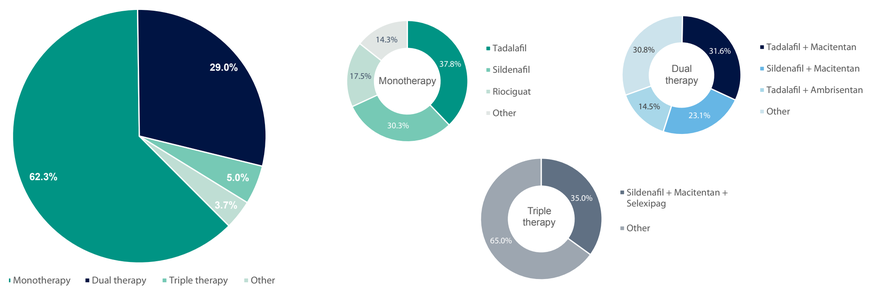
- Among the continuously observable individuals in the InGef research database (2016-2021), 3,270 patients had ≥ 1 inpatient and/or ≥ 2 outpatient diagnosis codes for PAH in 2021 **(see Figure 1)**.
- Thereof, 403 patients (12.1 per 100,000 individuals) received PAH-specific treatment in 2021.
- Identified patients were, on average, 71.0 (SD: 14.8) years old, with patients aged 80 and above accounting for approximately one third of the total.
- Most of the patients were female (63.8%).
- About 62.3% (n=251), 29.0% (n=117) and 5.0% (n=20) received monotherapy, dual or triple therapy, respectively. The remaining 3.7% had a prescription of ≥ 2 of the eligible PAH-related agents in 2021 but none of the pre-defined combinations.

Figure 1: Patient selection steps



- As monotherapy, the following agents were most frequently prescribed: tadalafil (37.8%), sildenafil (30.3%) and riociguat (17.5%).
- The combinations of tadalafil+macitentan (31.6%), sildenafil+macitentan (23.1%) and tadalafil+ambrisentan (14.5%) were the most commonly prescribed dual therapies.
- Sildenafil+macitentan+selexipag was the most prevalent triple therapy (35.0%).
- The distribution of PAH-related agents into three subgroups is shown in **Figure 2.**

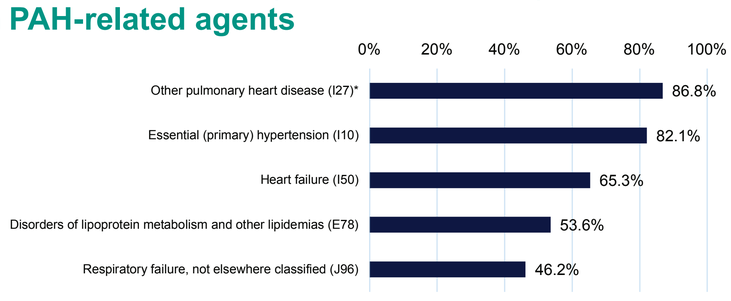
Figure 2: Distribution of PAH-related agents



Note: Due to data protection regulations, results for n<5 patients cannot be shown.

- Top 5 co-morbidities of patients treated with PAH-related agents are shown in **Figure 3**. Other pulmonary heart disease (ICD-10-GM I27) and essential (primary) hypertension (ICD-10-GM I10) were recorded in 86.8% and 82.1% of patients, respectively.

Figure 3 Top 5 co-morbidities (ICD-10-GM codes) of identified PAH patients treated with PAH-related agents



**In this figure, 3-digit ICD-10-GM are presented. ICD-10-GM I27 only includes the 4-digit codes I27.1 "Kyphoscoliotic heart disease", I27.2 "Other secondary pulmonary hypertension", I27.8 "Other specified pulmonary heart diseases", and I27.9 "Pulmonary heart disease, unspecified", as I27.0 "Primary pulmonary hypertension" was used for the patient identification. Note: In 88.6% of patients ICD-10-GM "Z"-code Z01 and in 58.8% of patients "Z"-code Z92 was recorded. "Z" codes are technically no co-morbidities but represent factors that influence health status and lead to healthcare utilization. Further, ICD-10-GM U11 "Need for vaccination against COVID-19" was documented in 63.0% of patients, which is technical no co-morbidity but encounter with the healthcare system.*

Discussion

- The results from our study on the distribution of the PAH-related agents are in line with published literature (e.g., German COMPERA registry).[7,8]
- However, our study has some uncertainties concerning the identification of patients within the study population:

(1) Since there is no dedicated diagnosis code for PAH, the ICD-10-GM code I27.0 ("Primary pulmonary hypertension") was utilized in the analysis, which may lack specificity. Consequently, the number of identified patients could be overestimated.

(2) Despite claims data being collected for reimbursement, they can still be prone to coding inaccuracies, including variations in coding practices by treating physicians (e.g., due to the absence of precise diagnosis codes).

(3) Health insurance data do not allow conclusions to be drawn about the indication for which a drug has been prescribed (e.g., riociguat is also indicated for treatment of adult patients with chronic thromboembolic pulmonary hypertension (CTEPH which is also part of the I27.0)).

- Therefore, an overestimation of the number of patients cannot be ruled out.

Conclusion

- This study showed that in Germany almost two-thirds (62.3%) of PAH patients treated with PAH-specific agents in 2021 received monotherapy, 29% received dual therapy and 5% triple therapy.
- The treatment decision is multifactorial and must be made on a patient-individual basis, especially taking severity of disease and previous PAH-specific therapies into account.

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