Incidence of Acute Exacerbation Among Patients with Fibrotic Interstitial Lung Disease in the United States

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Introduction

- Acute Exacerbation (AEx) in the context of interstitial lung disease (ILD) is a rapid deterioration of pulmonary functions, characterized by an increase in respiratory symptoms (eg, dyspnea and cough).[1]
- AEx is unpredictable, and its exact etiology is unknown.
- While it is estimated that the risk of AEx is higher in patients with IPF compared to other ILD types, AEx in ILD is associated with a high mortality rate and a poor prognosis, regardless of the underlying ILD types.[2, 3]
- Currently, there is a lack of robust incidence estimates of AEx among the ILD population in the US.

Objectives

To examine the incidence of AEx and characterize the precursors to AEx episodes among patients with different types of fibrosing ILD.

Methods

- This analysis is a retrospective cohort study leveraging the Optum® Market Clarity database (Figure 1).
- The study population comprised adult patients newly diagnosed with fibrosing ILD.
- The index date was set as the initial fibrosing ILD diagnosis date, and patients were followed until the earliest of the following: disenrollment from the plan, death, or end of study period.

Figure 1. Study Schematics

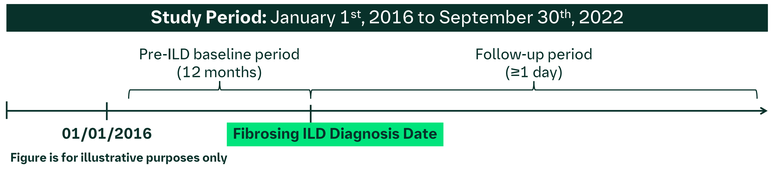


Figure is for illustrative purposes only

Patients were assigned to the following cohorts based on known underlying fibrosing ILD types:

- Autoimmune ILD
- Hypersensitivity Pneumonitis (HP)
- IPF
- Sarcoidosis
- Unclassified Idiopathic Interstitial Pneumonia (IIP)
- Multiple

Diagnostic criteria for AEx episodes*

- Previously diagnosed with fibrosing ILD, **and**
- ≥1 claim with procedure code for imaging procedures (eg, Chest CT scans, HRCT, and chest X-ray), **and**
- ≥1 claim with dyspnea and/or other acute worsening (eg, acute and chronic respiratory failure) within 30 days prior to date of imaging procedures, **and**
- No claims for alternative causes, including a diagnosis for heart failure, pulmonary embolism, pneumothorax, and pleural effusion within 30 days prior to date of imaging procedures, **and**
- Evidence of high-dose steroid pulse therapy, defined as ≥3 consecutive days with IV corticosteroid or oral corticosteroid dosage equivalent to ≥60 mg/day of prednisone, within 15 days before or 15 days after the date of the imaging procedures.

*Diagnostic criteria for AEx episodes for both IPF and other fibrosing ILD types were developed based on the International Working Group (IWG) criteria for AEx in IPF and the need for high-dose steroid therapy.[4]

Results

- The study cohort comprised of 215,214 patients newly diagnosed with fibrosing ILD, of which 8,734 (4.1%) had IPF and 206,480 (95.9%) had non-IPF ILD.
- The mean age of the study cohort was 67.5 years, and 45.1% were male.
- The incidence rate of AEx for the study cohort was 2,538 cases per 100,000 person-years (PY) (Table 1).
- The incidence rate of AEx was 25% higher in patients with IPF compared to patients with non-IPF ILD (Table 1).
- Among non-IPF ILD types, the incidence rate was the highest among patients with multiple ILD types, followed by HP and sarcoidosis (Table 1).
- The incidence rate of AEx was the highest in the first year after the ILD diagnosis. The incidence rate of AEx remained consistently higher across the follow-up years in patients with IPF vs non-IPF ILD (Table 2).
- Among all observed AEx episodes following ILD diagnosis, 69.8% and 30.2% were considered triggered and idiopathic, respectively (Figure 2).

Table 1. Incidence rates of AEx

	Incidence Rate per 100,000 PY (95% CI)
Total (n=215,214)	2,538 (2,489 – 2,588)
IPF (n=8,734)	3,144 (2,890 – 3,414)
Non-IPF ILD (n=206,480)	2,508 (2,458 – 2,560)
Autoimmune ILD (n=41,150)	2,681 (2,575 – 2,791)
HP (n=15,932)	4,670 (4,420 – 4,931)
Sarcoidosis (n=8,628)	2,978 (2,730 – 3,242)
Unclassified IIP (n=133,211)	1,890 (1,832 – 1,949)
Multiple (n=7,559)	5,924 (5,578 – 6,285)

AEx=acute exacerbation; CI=confidence interval; ; IIP=idiopathic interstitial pneumonia; ILD=interstitial lung disease; IPF=idiopathic pulmonary fibrosis; PY=person-years

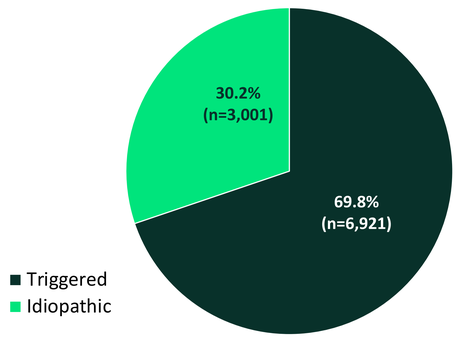
Notes: Incidence rate was calculated by the total number of AEx episodes, following ILD diagnosis divided by the sum of follow-up time at risk in person-years for all eligible study population.

Table 2. Annual incidence rates of AEx

	Incidence Rate per 100,000 PY		
Year (days) after the initial fibrosing ILD diagnosis	**Total (n=215,214)**	**IPF (n=8,734)**	**Non-IPF ILD (n=206,480)**
0 (Day 1 - 365)	2,994	3,419	2,975
1 (Day 366 - 730)	2,259	3,117	2,217
2 (Day 731 - 1096)	2,251	2,820	2,221
3 (Day 1097 - 1461)	2,017	2,572	1,986

Note: Incidence rate was calculated by the total number of AEx episodes following ILD diagnosis divided by the sum of follow-up time at risk in person-years for all eligible study population for each year after the initial ILD diagnosis.

Figure 2. Potential underlying causes of AEx episodes



Note: Each AEx episode was categorized into either triggered or idiopathic based on the following definitions: triggered=presence of ≥1 claim for pulmonary infection and/or aspiration during the acute exacerbation episode period (ie, 30 days before or 15 days after the date of the imaging procedure); idiopathic=all other acute exacerbation episodes.

Limitations

- There is no validated algorithm to accurately identify AEx in a claims database, which may introduce misclassification bias. However, we have operationalized the AEx criteria in accordance with the IWG's criteria and added a corticosteroid requirement to improve the accuracy.
- This study is subject to the inherent limitations of a claims database, such as coding errors, that may result in inaccurate or incomplete data.

Conclusions

- The incidence of AEx was estimated among patients with ILD, and the incidence rate was notably higher in patients with IPF vs non-IPF ILD.
- The incidence rate of AEx was the highest in the first year following ILD diagnosis, highlighting the need for attention and proactive management to mitigate the risk of AEx after ILD diagnosis.
- A significant proportion of AEx episodes were considered triggered. Further research is warranted to understand these triggers and develop effective preventive measures.
- Lastly, a future assessment of the impact of AEx on clinical and economic outcomes is warranted to understand the burden of AEx.

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Disclosure and Acknowledgment: This study was funded by Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI). The author(s) met criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). Joseph Yang, Josh Ide, and Amy Olson are employees of Boehringer Ingelheim.