Prevalence of Immunosuppressant and Antifibrotic Use in Patients with Connective Tissue Disease-related Interstitial Lung Disease

Joseph Yang, PharmD, MS[1]; Katy Sadowski, BS[1]; Amy Olson, MD, MSPH[1]; Tejaswini Kulkarni, MD, MPH[2]

[1]Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, US; [2]University of Alabama at Birmingham, Birmingham, AL, US

Introduction

- Connective tissue diseases (CTDs) are a group of autoimmune diseases characterized by abnormal immune responses directed against the body's own tissues.[1]
- Interstitial lung disease (ILD) is a group of disorders characterized by chronic inflammation and fibrosis of the lung interstitium.[2]
  - ILD is one of the most serious pulmonary complications associated with CTDs, and this is often referred to as CTD-ILD.
- Immunosuppressants (IS) have been the cornerstone of therapy for patients with CTD-ILD, despite limited evidence supporting their effectiveness in slowing lung function decline.[1]
- Recent findings from the INBUILD and SENSCIS trials have shed light on the potential benefits of antifibrotics (AF) in patients with CTD-ILD. However, the literature describing the use of antifibrotics in patients with CTD-ILD remains sparse.[3,4]

Objective

To understand the prevalence of patients with CTD-ILD who have received IS and/or AF therapies, as well as their demographics and clinical characteristics.

Methods

Study Design

This retrospective cohort study used Optum Clinformatics® US claims data from 01/01/2017 through 12/31/2022.

Figure 1. Study Schematics

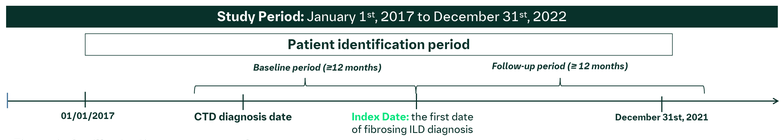

Figure is for illustrative purposes only

Study Cohorts

1. **ILD-treating IS only:*** Patients with ≥1 prescription for an immunosuppressive drug and no prescription for antifibrotics
2. **AF only:** Patients with ≥1 prescription for antifibrotics and no prescription for immunosuppressants
3. **Both IS and AF:** Patients with ≥1 prescription for any drug classified as IS and AF
4. **Neither IS nor AF:** Patients without any prescriptions for any drug classified as IS and AF

*Biologic DMARD (tocilizumab, rituximab), other immunosuppressants (azathioprine, cyclophosphamide, mycophenolate mofetil, and tacrolimus), and corticosteroids.

Study Outcomes

- Prevalence of treatment during the first 12 months of follow-up
- Medication use during the first 12 months of follow-up
- Time-to-treatment initiation from CTD-ILD diagnosis (days)
- Specialty of the initial AF prescribing provider

Statistical Analysis

All study measures were analyzed descriptively and reported as total and stratified treatment groups. No inferential statistics were generated for the study cohort.

Results

Study Cohort Characteristics

- The study included 6,070 CTD-ILD patients, with a mean age of 70.9 years and 4,597 (75.7%) female patients (Table 1).

Table 1. Patient demographics and clinic characteristics

	Total (n= 6,070)	IS only (n= 4,134)	AF only (n= 11)	Both IS + AF (n= 70)	Neither IS nor AF (n= 1,855)
Demographics					
Age, mean (SD)	70.93 (11.25)	69.78 (11.58)	74.27 (6.18)	68.99 (9.9)	73.56 (10.06)
Gender, n (%)					
Female	4,597 (75.73%)	3,136 (75.86%)	7 (63.64%)	53 (75.71%)	1,401 (75.53%)
Male	1,473 (24.27%)	998 (24.14%)	4 (36.36%)	17 (24.29%)	454 (24.47%)
Race/Ethnicity, n (%)					
White	3,852 (63.46%)	2,659 (64.32%)	4 (36.36%)	39 (55.71%)	1,150 (61.99%)
African American	734 (12.09%)	512 (12.39%)	4 (36.36%)	14 (20%)	204 (11%)
Asian	171 (2.82%)	106 (2.56%)	1 (9.09%)	1 (1.43%)	63 (3.4%)
Hispanic	1,045 (17.22%)	680 (16.45%)	1 (9.09%)	14 (20%)	350 (18.87%)
Unknown	268 (4.42%)	177 (4.28%)	1 (9.09%)	2 (2.86%)	88 (4.74%)
Clinical Characteristics					
Underlying CTD (mutually exclusive)*, n (%)					
ANCA-associated vasculitis	84 (1.38%)	67 (1.62%)	0 (0%)	0 (0%)	17 (0.92%)
Dermatomyositis/Polymyositis	58 (0.96%)	39 (0.94%)	0 (0%)	1 (1.43%)	18 (0.97%)
Mixed connective tissue disease	88 (1.45%)	47 (1.14%)	1 (9.09%)	1 (1.43%)	39 (2.10%)
Rheumatoid arthritis	3,137 (51.68%)	2,128 (51.48%)	6 (54.55%)	29 (41.43%)	974 (52.51%)
Sjögren's syndrome	262 (4.32%)	143 (3.46%)	0 (0%)	1 (1.43%)	118 (6.36%)
Systemic lupus erythematosus	208 (3.43%)	132 (3.19%)	0 (0%)	1 (1.43%)	75 (4.04%)
Systemic sclerosis	169 (2.78%)	79 (1.91%)	2 (18.18%)	2 (2.86%)	86 (4.64%)
Multiple known types	2,064 (34.00%)	1,499 (36.26%)	2 (18.18%)	35 (50.00%)	528 (28.46%)
Baseline Quan-Charlson comorbidity index, mean (SD)	4 (2.65)	4 (2.63)	3 (2.39)	3 (2.47)	4 (2.7)
Select Respiratory comorbidities, n (%)†					
Asthma	1,193 (19.65%)	900 (21.77%)	2 (18.18%)	14 (20%)	277 (14.93%)
COPD	2,433 (40.08%)	1,741 (42.11%)	4 (36.36%)	26 (37.14%)	662 (35.69%)
Lung cancer	132 (2.17%)	96 (2.32%)	0 (0%)	1 (1.43%)	35 (1.89%)
Pneumonia	1,829 (30.13%)	1,376 (33.28%)	4 (36.36%)	27 (38.57%)	422 (22.75%)
Pulmonary hypertension	848 (13.97%)	580 (14.03%)	2 (18.18%)	13 (18.57%)	253 (13.64%)
Respiratory Tract Infection	2,331 (38.40%)	1,745 (42.21%)	4 (36.36%)	32 (45.71%)	550 (29.65%)
Smoking status, n (%)	2,383 (39.26%)	1,732 (41.9%)	5 (45.45%)	28 (40%)	618 (33.32%)
Pulmonary rehabilitation, n (%)	35 (0.58%)	27 (0.65%)	0 (0%)	1 (1.43%)	7 (0.38%)

AF=antifibrotics; COPD=chronic obstructive pulmonary disease; CTD=connective tissue disease; IS=immunosuppressants; SD=standard deviation.
*defined as having ≥ 2 diagnoses of the same CTD condition during the study period.
†Other respiratory comorbidity assessed during the baseline period include cystic fibrosis, hypersensitivity pneumonitis, and pulmonary embolism.

Medication Use

- The prevalence of patients receiving ILD-treating IS only, AF only, both, and neither, were 4,134 (68.11%), 11 (0.18%), 70 (1.15%), and 1,855 (30.56%), respectively.
- Among patients who received any ILD-treating IS (ie, 'IS only' and 'Both IS+AF' cohorts), corticosteroids were the most prescribed drug class, followed by other immunosuppressants and biologic DMARD (Table 2).
- Among the ILD-treating IS, mycophenolate mofetil, azathioprine, and rituximab were the most prescribed medications (Table 2).

Table 2. Medication use during the first 12 months following ILD diagnosis‡

	Total (n= 6,070)	IS only (n= 4,134)	AF only (n= 11)	Both IS + AF (n= 70)
Antifibrotic, n (%)	81 (1.33%)	-	11 (100%)	70 (100%)
ILD-treating Biologic DMARDs, n (%)	295 (4.86%)	292 (7.06%)	-	3 (4.29%)
Tocilizumab, n (%)	73 (1.20%)	72 (1.74%)	-	1 (1.43%)
Rituximab, n (%)	225 (3.71%)	223 (5.39%)	-	2 (2.86%)
Other Immunosuppressant, n (%)	762 (12.55%)	737 (17.83%)	-	25 (35.71%)
Azathioprine, n (%)	298 (4.91%)	291 (7.04%)	-	7 (10%)
Cyclophosphamide, n (%)	29 (0.48%)	28 (0.68%)	-	1 (1.43%)
Mycophenolate mofetil, n (%)	476 (7.842%)	457 (11.05%)	-	19 (27.14%)
Tacrolimus, n (%)	28 (0.46%)	28 (0.68%)	-	0 (0%)
Corticosteroids*, n (%)	4,068 (67.02%)	4,000 (96.76%)	-	68 (97.14%)

AF=antifibrotics; IS=immunosuppressants; SD=standard deviation.
*Including betamethasone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, and prednisone
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Time-to-treatment[1]

- The mean (SD) time from ILD diagnosis to the first biologic DMARD, other immunosuppressants, and corticosteroids was 148 (109.1), 113 (102.8), and 118 (112.1) days, respectively.

Initial AF Prescriber's Specialty

- Pulmonology was the provider specialty most frequently associated with the initial antifibrotic prescription (56.8%), followed by others/unknown (37.0%) and primary care (4.9%).

Limitations

- Potential misidentification of newly diagnosed CTD-ILD patients due to reliance on a claims-based algorithm.
- Survival bias could have been introduced as patients must survive and continuously enroll in the health plan for ≥12 months after the diagnosis to be included.

Conclusions

- The study findings demonstrate a high prevalence of corticosteroid use in patients with CTD-ILD within the first 12 months following the ILD diagnosis, but a low utilization of steroid-sparing immunosuppressants.
- The limited use of AF and the significant number of patients receiving neither treatment (ie, IS nor AF) indicate potential gaps in current treatment strategies.
- While disease severity was not captured in this current study, a future study utilizing disease progression proxies to further understand treatment practices and outcomes in patients with CTD-ILD is planned.

References: 1. Mathai SC, et al. *BMJ.* 2016;352:h6819. **2.** Podolanczuk AJ, et al. *Am J Respir Crit Care Med.* 2021;203(11):1343-1352. **3.** Flaherty KR, et al. *Eur Respir J.* 2022;59(3):2004538. **4.** Highland KB, et al. *Lancet Respir Med.* 2021;9(1):96-106.
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