Interstitial lung disease in Sjögren's disease: the portrait of a national cohort

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Abstract

Introduction: Apart from exocrine glands involvement with sicca symptoms, several extra-glandular manifestations can occur in Sjögren's disease (SjD) such as pulmonary manifestations. Interstitial lung disease (ILD) is the most common lung manifestation in SjD.

We aim to evaluate the presence of ILD in a national cohort of patients with SjD, identify variables associated with its development and progression, as well as describe the treatment used for SjD-ILD and its effectiveness and tolerability.

Methods: We conducted an observational multicenter study of SjD-ILD patients prospectively followed in Reuma.pt. Demographic and clinical data were collected.

We compared patient characteristics between groups using Chi-square or Fisher's exact test, Mann–Whitney or independent samples t-test, as appropriate. Logistic regression analysis was used to identify predictors of SjD- ILD.

A linear mixed model with random intercept was used to compare results from pulmonary function tests (PFTs) before and after immunosuppression initiation.

Results: Of the 1532 patients enrolled in the Reuma.pt-SjD protocol, 1333 (87%) had information on the presence of pulmonary manifestations. Among these, 127 (9.5%) had documented lung involvement, with ILD being the most common manifestation (74%). Ever smoking (OR=2.175; [95%CI:1.214-3.899]; p=0.009) and older age at SjD diagnosis (OR=1.047 per year; [95%CI:1.025-1.069]; p<0.001) were predictors of ILD. Nonspecific interstitial pneumonia was the most frequent ILD pattern (45.7%). Immunosuppression was used in 62 (66%) SjD-ILD patients and antifibrotics in eight patients (in seven of them in association with immunosuppression).

Among the 26 patients with serial PFTs available, 10 (38.5%) showed ILD progression. Progressors had a higher forced vital capacity (FVC 96.8 ± 22.1 vs. 71.1 ± 21.4%; p=0.007) and diffusion capacity for carbon monoxide (DLCO 75.5 ± 12.1 vs. 50.2 ± 16.6%; p=0.002) at baseline and tend to have hypergammaglobulinemia more often (80% vs. 43.8%; p=0.069). Nevertheless,

immunosuppression interrupted the decline of FVC (absolute value) and DLCO (percent predicted).

Conclusion: This work demonstrated that a substantial proportion of SjD-ILD patients present with progressive fibrosis. Immunosuppression seems to delay the progression of lung disease. Therefore, identifying predictors for ILD development and progression is essential for recognizing which patients will require closer monitoring and intervention.

Keywords: Interstitial lung disease; Antifibrotics; Lung fibrosis; Immunosupression; Lung involvement; Sjogren's disease

Introduction

Sjögren's disease (SjD) is a chronic systemic rheumatic disorder[1], characterized by excessive mucosal dryness, fatigue and musculoskeletal pain[1]. Major organ involvement and increased risk of lymphomas[1] can also occur in patients with SjD. This disease has characteristic autoantibodies, glandular histopathology and pattern of systemic involvement, making it a distinct clinical entity [2].

Pulmonary involvement is among the most common extra-glandular manifestations of SjD[3] and includes airway abnormalities, interstitial lung disease (ILD), pleural disease, nodular pulmonary amyloidosis and lymphoproliferative disorders[4]. Although clinically significant lung disease has only been reported in 9–20% of SjD patients[3–5], asymptomatic/subclinical disease can occur in up to 75% of SjD patients[3,5,6]. On the other hand, cough is also frequently reported by SjD patients even without evidence of lung involvement, due to the reduction or absence of respiratory tract glandular secretion[3].

Some factors have been associated with a higher risk of developing ILD in SjD, such as male sex, older age, cigarette smoking, high antinuclear antibodies (ANA) titer, positive rheumatoid factor, presence of anti-Ro52 antibodies, elevated C-reactive protein, hypergammaglobulinemia and other systemic manifestations[7–9]. Early identification of these patients and appropriate screening strategies are crucial for a timely diagnosis.

Regarding treatment, although randomized controlled trials and comparative studies on SjD-ILD are lacking, both the 2020 EULAR recommendations for the management of SjD[10] and the 2021 Consensus Guidelines for Evaluation and Management of Pulmonary Disease in Sjögren's[11] recommend pharmacological treatment for SjD-ILD patients with moderate/severe lung involvement according to the EULAR Sjögren's syndrome disease activity index (ESSDAI)[12]. Steroids are especially indicated for patients with lymphocytic interstitial pneumonia (LIP) and

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organizing pneumonia (OP), with azathioprine (AZA) and mycophenolate mofetil (MMF) being considered second-line agents[10,11]. Cyclophosphamide (CYC) and rituximab (RTX) can be used as rescue therapy[10,11]. More recently, the British Society for Rheumatology guideline on management of adult and juvenile onset Sjögren disease also considered MMF and RTX as alternatives for ILD treatment[1]. Antifibrotics, which include nintedanib and pirfenidone, have shown potential benefit in patients with progressive pulmonary fibrosis, including those associated to SjD [13,14].

Despite growing interest in SjD-ILD, it remains underreported in the literature compared to other rheumatic musculoskeletal diseases (RMDs), although progressive ILD can be as frequent in SjD as in the other RMDs[15,16].

The aim of this study is to evaluate the proportion of patients with ILD in a national cohort of patients with SjD, better characterize these patients and identify variables associated with its development and progression. Additionally, we seek to evaluate the treatments used for treating SjD-ILD, focusing on their effectiveness and tolerability.

Material and Methods

Study design and population

We conducted an observational, retrospective, multicenter study of SjD-ILD patients prospectively followed in the Rheumatic Diseases Portuguese Registry (Reuma.pt). Data were collected until 15th January 2025.

We included patients having i) a diagnosis of SjD by the treating rheumatologist and/or that fulfil the 2002 American-European Consensus Group (AECG) classification criteria, ii) ≥ 18 years old at initial diagnosis, iii) information on the presence/absence of lung involvement, and iiii) at least one registered clinical evaluation. Patients fulfilling classification criteria for both SjD and another inflammatory RMDs were excluded, as well as those with another RMD with only sicca features. Patients with SjD and an unrelated lung disease were also excluded.

ILD was defined by findings in chest high-resolution computed tomography (HRCT scan) suggestive of SjD-related ILD, with or without histopathological documentation.

We assessed demographic data (age, race and sex), smoking habits (categorized as ever smoker or non-smoker), SjD duration, immunological manifestations (ANA, anti-SSA, anti-SSB, rheumatoid factor, cryoglobulinemia, hypergammaglobulinemia), multiorgan involvement based on ESSDAI domains and SjD Damage Index (SSDI) at the last appointment.

Regarding ILD, we collected disease duration, ESSDAI at the time of ILD diagnosis (± 6 months), chest HRCT pattern according to the American Thoracic Society/ European Respiratory Society

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international multidisciplinary classification of idiopathic interstitial pneumonias[17], results from pulmonary function tests (PFTs) at baseline and follow-up. All exams were performed as part of routine clinical practice. Data collected from PFTs included forced vital capacity (FVC; in liters [L] and percent predicted [pp]), and diffusion capacity for carbon monoxide corrected for Hb (DLCO; pp).

Drugs specifically used for ILD, including immunosuppressants and antifibrotics, were also recorded, as well as related adverse drug reactions.

We considered ILD progression when there was an absolute FVC decline >5% or an absolute DLCO decline >10%, within 12 ± 6 months of follow-up, based on the physiological definition of progressive pulmonary fibrosis stated in the 2022 ATS/ERS/JRS/ALAT Guidelines[18].

In patients who died, the cause of death was retrieved.

Statistical analysis

A descriptive analysis was performed. Continuous variables were expressed as mean ± standard deviation (S.D.) or median with interquartile range (IQR). Categorical variables were presented as absolute values and frequencies. Shapiro-Wilk test was used to evaluate the normality of data distribution.

Chi-square or Fisher's exact test, Mann–Whitney or independent samples t-test were used for group comparisons, as appropriate.

To identify predictors of SjD-associated ILD, we performed a binary logistic regression using backward selection and including variables whose bivariate analysis had a p-value <0.1.

Patients having FVC and DLCO results at three time-points (immunosuppression initiation [index date], 12 (± 6) months before and 12 (± 6) months after) were included in a linear mixed-effect model with random intercept. Immunosuppression initiation (time 0) served as the reference point for comparing each variable before and after immunosuppression initiation. Since each patient served as their control, analysis was performed without covariate adjustment.

A significance level of 5% was considered. SPSS version 29.0 (IBM Corp, Armonk NY, USA) was used.

Ethical considerations

This study was conducted according to the Declaration of Helsinki (revised in Helsinki – 2024) and was approved both by the Ethics Committee of Hospital Garcia de Orta and the Reuma.pt Coordinating and Scientific Committee. All patients signed the Reuma.pt informed consent and pseudonymised data was processed in accordance with the EU General Data Protection Regulation.

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Results

General characterization

From a total of 1532 patients enrolled in Reuma.pt-SjD protocol, from 15 national Rheumatology centres, 1333 (87%) had information regarding the presence/absence of lung involvement.

Among these 1333 patients, the majority were females (93.5%), and Caucasian (92.8%; 38 missing information), with a mean age of 61.7±14.0 years at their last appointment. The mean age at SjD diagnosis and symptom onset was 53.6±14.9 and 49.1±14.6 years, respectively.

Smoking habits were reported in 205 (22%; 401 missing data) patients.

Most patients were positive for ANA (90.4%; 29 missing data) and anti-SSA antibodies (83.3%; 29 missing data). Positive anti-SSB antibodies and rheumatoid factor were reported in nearly half of the patients (44.9%; 80 missing data and 47.8%; 170 missing data, respectively), as well as hypergammaglobulinemia (49.4%; 157 missing data). Cryoglobulinemia was uncommon (12.4%), although highly underreported (881 missing data).

Nearly half of the patients had an available minor salivary gland biopsy (MSGB) (n=697, 52.3%), from whom 58.4% documented one or more focus per $4mm^2$ (Chisholm-Mason Grade ≥3), 14.8% a moderate lymphocytic infiltration with a focus score < 1 (Grade 2) and 26.8% had no or only mild changes (Grades 0/1) [19].

Lung involvement

Lung involvement was documented in 127 patients (9.5%) of our cohort. From these, 91 (71.6%) had ILD, 24 (18.9%) airways disease, 3 (2.4%) airways disease and concomitant ILD (bronchiolitis obliterans organizing pneumonia [BOOP]), 3 (2.4%) lung amyloidosis, 1 (0.8%) lung lymphoma and in 5 (3.9%) the type of lung involvement was not specified.

Table I compares the clinical characteristics of patients with and without ILD.

In multivariate analysis, ever smoking (OR=2.175; [95%CI:1.214-3.899]; p=0.009) and older age at SjD diagnosis (OR=1.047 per year; [95%CI:1.025-1.069]; p<0.001) were associated with ILD.

Regarding ILD patients, 50 of them (53.2%) had ESSDAI evaluated at ILD diagnosis (± 6 months), with a median value of 10.5 [IQR 5-15].

Data from HRCT demonstrated that nonspecific interstitial pneumonia (NSIP) was the most frequent ILD pattern, accounting for 45.7% of the cases. LIP was documented in 23.4%, usual interstitial pneumonia (UIP) in 11.7% and BOOP in 3.2% of the patients. Fifteen (16%) patients had an unclassifiable ILD pattern based on HRCT, with one of them having lung biopsy

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performed, although inconclusive. At baseline, mean FVC was 84.9 ± 25.2% (2.1 ± 0.7 L) and DLCO 58.6 ± 15.9%.

Regarding treatment, MMF was used in almost one-third (31.9%; N= 30) of ILD patients, in two of them as maintenance treatment after induction with CYC and in five in association with a biologic drug (three RTX and two abatacept [ABA]). AZA was used in 20 (21.3%) patients, in one of them as maintenance treatment after induction with CYC and in three of them in association with RTX. CYC was used in six (6.4%) patients. Twenty-four (25.5%) patients received a biologic drug (22 RTX and two ABA). Steroids were prescribed to nearly half of the patients (51%).

The number of patients treated with each immunosuppressive drug, according to HRCT pattern, as well as adverse drug reactions reported, are summarized in Supplementary Table I.

Antifibrotics were used in eight patients, in all except one in association with immunosuppression. All patients received nintedanib, with two patients reporting gastrointestinal adverse events. One of them reduced drug dosage with symptom resolution and the other was switched to pirfenidone with tolerability.

In 26 (27.6%) patients it was possible to evaluate ILD progression based on PFTs. Of these, ten (38.5%) had ILD progression. Table II compares patients with and without ILD progression.

We found no statistically significant difference between patients with and without ILD progression regarding the use of immunosuppression (50% of patients with ILD progression vs. 31.3% of patients without ILD progression were under immunosuppression; p=0.339). From 18 patients who received immunosuppression, we had at least one value for FVC and DLCO 12 (± 6) months before and 12 (± 6) months after immunosuppression initiation and comparisons between these variables are shown in Table III.

At the last follow-up appointment, the median SjD duration was 9.8 [IQR 5.8-16.6] years. SSDI data was available for 632 (41.2%) patients. Patients with ILD had significantly higher SSDI scores compared to those without ILD (median 2 (IQR 1-2] vs. 1 [0-2]; p<0.001], primarily driven by differences in the pulmonary domain.

Among patients with SjD-ILD, the median ILD duration at the last appointment was 5.6 [IQR 3.5-8.5]. Nine patients with SjD-ILD died, although the specific causes of death were not reported.

Discussion

ILD was documented in 6.8% of our cohort, being the most common manifestation of lung involvement in SjD. This value is lower than those previously published[3–6], which might be due to differences in the populations studied, disparity of SjD classification criteria used and/or the lack of consensual criteria/methods for diagnosing lung involvement. Besides, there is no

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recommendation for systematic ILD screening in patients with SjD, so unless patients present with respiratory symptoms or have changes on chest x-rays, ILD can remain undiagnosed for a long period of time. On the other hand, symptoms like a dry cough can be attributed to xerotrachea without patients undergoing additional assessments to evaluate the presence of lung involvement.

In our cohort, although SjD was more prevalent among females, patients with ILD were more frequently male. Variables independently associated with ILD development were smoking and older age at SjD diagnosis.

Smoking is a well-recognized risk factor for idiopathic pulmonary fibrosis (IPF)[20] and some RMDs-related ILD, particularly in rheumatoid arthritis (RA)[21]. However, while some studies demonstrated that smoking was associated with a higher risk of developing SjD-ILD[9,22], others found no association between smoking and lung involvement in SjD[23,24]. Nevertheless, smoking is considered a mortality risk factor among patients with SjD-ILD[25].

As far as age is concerned, certain mechanisms that naturally occur with age, such as telomere shortening and epigenetic alterations, are recognized as major contributors to the pathogenesis of IPF and RMDs-related ILD[26–30]. These mechanisms can also be involved in SjD-ILD pathogenesis, making older age an independent risk factor for ILD.

In our cohort, patients with ILD had a moderate ESSDAI at ILD diagnosis. Constitutional and lymphadenopathic involvement were both more common in SjD patients with ILD, denoting that these patients had an important burden of systemic disease. A higher focus score (≥4) on MSGB was also pointed as a potential risk factor for airways disease and ILD in SjD, reflecting a higher lymphoproliferative/inflammatory activity in these patients [31]. However, in our cohort, nearly 50% of the patients had no available MSGB, and among those who had, 40% were negative.

Although LIP is the classic/distinctive SjD-ILD pattern, NSIP was the most prevalent pattern in our cohort, in agreement with previously published data[6].

At baseline, most SjD-ILD patients had a normal FVC with a reduced DLCO, suggesting that DLCO can be more sensitive to predict the presence of ILD than FVC, similar to other RMDs-ILD[32]. However, FVC declined below 80% during follow-up in most ILD patients of our cohort.

In our cohort, when evaluating ILD progression based on lung function (either FVC or DLCO decline), we found that patients who progressed had a higher FVC (96.8 ± 22.1 vs. 71.1 ± 21.4%; p=0.007) and DLCO (75.5 ± 12.1 vs. 50.2 ± 16.6%; p=0.002) at baseline and tend to have hypergammaglobulinemia more often (80% vs. 43.8%; p=0.069). Similar data were also pointed out by Anna-Maria Hoffmann-Vold *et al.*[33], who identified higher values of FVC and DLCO at baseline and increased C-reactive protein as factors associated with ILD progression. This data

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highlights the importance of close monitoring of SjD-ILD patients, particularly those with evidence of persistent inflammation, regardless of FVC and/or DLCO at baseline.

Immunosuppression was used in two-thirds of ILD patients in our cohort, with MMF and RTX being the most frequently used drugs. Although the number of patients receiving immunosuppression was not statistically different between patients with and without ILD progression, these drugs appear to have prevented the decline of FVC (L) and DLCO present before the beginning of immunosuppression. Immunosuppressants were associated with antifibrotics in one patient from each group (progressor vs. non-progressor). Gastrointestinal adverse events and infections were the most common adverse events in patients treated with immunosuppression.

This is a multicenter study, including a nationwide cohort of patients with SjD-related ILD, which illustrates our current national practice in the diagnosis and follow-up of these patients.

Our study has some limitations. Patients with SjD in our cohort did not undergo systematic ILD screening, which may lead to its underreporting and an unreliable assessment of SjD-ILD prevalence. Besides, our work has the inherent biases of any retrospective study, with data missing and inhomogeneous index data. On the other hand, the fact that most of these patients are concomitantly followed by pulmonologists, some data may be missing from Reuma.pt, particularly concerning PFTs.

Despite multicentric recruitment, the sample size is small, decreasing the power to detect significant differences in change in lung function and also limiting the performance of other sub-analyses, namely the comparison between different immunosuppressants.

Other limitations that can be pointed out are the absence of symptomatic and imaging assessment for lung disease progression.

Despite a prevalence that can reach 75% among SjD patients and the fact that it can progress as frequently as in other RMDs, ILD associated with SjD remains undervalued in clinical practice, with the presence of respiratory symptoms often being attributed to dryness of the upper respiratory airways, without considering other causes, namely the presence of pulmonary involvement. However, taking into consideration the wide spectrum of therapies currently available (immunosuppression and antifibrotics) and their potential role in delaying ILD progression, it is essential to ensure a timely diagnosis and an appropriate treatment as early as possible. Identifying predictors for ILD development and patients at greater risk of having progressive pulmonary fibrosis helps to improve the healthcare provided to these patients. In the future, studies with larger sample sizes would be essential to obtain more robust results, particularly regarding the implication that each patient's profile, namely ILD pattern, can have on drug choices.

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Conclusions

Our study demonstrated that a significant proportion of SjD-ILD patients present with progressive fibrosis, although immunosuppression seems to delay disease progression. Since systematic ILD screening of all SjD patients is not part of current clinical recommendations, identifying predictors for ILD development and progression can pinpoint patients who may require diagnostic tests, even in the absence of respiratory symptoms, as well as closer monitoring.

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Tables and Figures

Table I - Comparison of clinical characteristics between patients with and without interstitial lung disease

	ILD (N=94) *	Non-ILD (N=1239)	Percentage of missing data	p-value
Male	17 (18.1%)	69 (5.6%)	0%	**<0.001**
Caucasian	72 (92.3%)	955 (92.8%)	22.8%	0.869
Ever smoking	24 (34.3%)	181 (21%)	34.9%	**0.010**
Age at SjD diagnosis	61.3 ± 12.8	53 ± 14.3	13.8%	**<0.001**
SjD duration at last visit	12.5[5.35-19.35]	9.6 [5.8-16.2]	26.5%	0.140
Positive ANA	87 (92.6%)	1092 (90.2%)	14.9%	0.465
Positive anti-SSA antibodies	78 (84.8%)	1008 (83.2%)	10.1%	0.689
Positive anti-SSB antibiodies	37 (41.1%)	525 (45.1%)	13.7%	0.459
Positive RF	40 (46.5%)	516 (47.9%)	21%	0.803
Hypergammaglobulinemia	40 (57%)	516 (48.9%)	21%	0.164
MSGB with a focus score ≥ 1	34 (58.6%)	373 (58.4%)	52.8%	0.971
Constitutional involvement	27 (30.7%)	206 (16.9%)	13.8%	**0.001**
Lymphadenopathic involvement	16 (18.2%)	131 (10.7%)	14%	**0.032**
Glandular involvement	28 (30.8%)	386 (31.3%)	12.8%	0.923
Articular involvement	36 (39.1%)	532 (43%)	12.3%	0.464
Muscular involvement	2 (2.2%)	17 (1.4%)	13.2%	0.504
Cutaneous involvement	17 (19.1%)	211 (17.1%)	12.9%	0.624
PNS involvement	7 (7.9%)	49 (4%)	13.1%	0.078
CNS involvement	3 (3.4%)	19 (1.5%)	13.3%	0.192
Renal involvement	3 (3.4%)	34 (2.8%)	13.1%	0.732
Gastrointestinal/hepatobiliary involvement	3 (3.3%)	33 (2.7%)	13.1%	0.711
Hematologic involvement	23 (25.6%)	425 (34.5%)	13.1%	0.084
Biologic involvement	53 (58.9%)	672 (54.5%)	12.8%	0.424

*The 3 patients with ILD and concomitant airways disease were also included

SjD- primary Sjögren's disease; ANA – antinuclear antibodies; RF – rheumatoid factor; MSGB – minor salivary gland biopsy; PNS – peripheral nervous system; CNS – central nervous system

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Table II - Comparison between patients with and without interstitial lung disease progression

	Progressor (N=10)	Non-progressor (N=16)	p-value
Male	1 (10%)	1 (6.3%)	0.727
Ever smoking	3 (30%)	2 (12.5%)	0.350
Age at SjD diagnosis	59 ± 15.7	57.4 ± 13.9	0.683
Positive anti-SSA antibodies	10 (100%)	15 (93.8%)	0.420
Positive anti-SSB antibodies	4 (40%)	6 (37.5%)	0.899
Positive RF	6 (60%)	6 (37.5%)	0.327
Hypergammaglobulinemia	8 (80%)	7 (43.8%)	0.069
Baseline FVC (pp)	96.8 ± 22.1	71.1 ± 21.4	**0.007**
Baseline DLCO (pp)	75.5 ± 12.1	50.2 ± 16.6	**0.002**
UIP pattern	1 (10%)	0	0.405
Specific ILD treatment *	5 (50%)	5 (31.3%)	0.339

SjD- primary Sjögren's disease; RF – rheumatoid factor; FVC – forced vital capacity; DLCO - diffusion capacity for carbon monoxide corrected for hemoglobin; pp – precent predicted; UIP – usual interstitial pneumonia; ILD – interstitial lung disease

*1 patient in each group was receiving antifibrotic

Table III – Comparison between mean FVC and DLCO before and after immunosuppression initiation, using a linear mixed-effect model

	12 (±6) months before immunosuppression initiation	**Immunosuppression initiation**	**12 (±6) months after immunosuppression initiation**	p-value
	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.	
FVC (L)	2.09 ± 0.83	2.02 ± 0.57	2.09 ± 0.64	0.962
FVC (pp)	73.3 ± 27.3	74.8 ± 26.6	78.0 ± 27.3	0.895
DLCO (pp)	69.3 ± 15.7	57.45 ± 19.8	59.75 ± 21.3	0.292

FVC – forced vital capacity; DLCO – diffusion capacity for carbon monoxide corrected for hemoglobin; pp – percent predicted

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Supplementary material

Table I – Distribution of immunosuppressive drugs according to underlying interstitial lung disease pattern and reported adverse drug reactions

Drug	ILD pattern	Number of patients	Tolerability
MMF (N=30)	NSIP	16 (53.3%)	- 5 patients suspended MMF due to ADRs (2 specified as gastrointestinal) - 3 patients died
	LIP	5 (16.7%)	
	UIP	6 (20%)	
	BOOP	0	
	Unclassifiable	3 (10%)	
AZA (N=20)	NSIP	8 (40%)	- 4 patients suspended AZA due to unspecified ADRs
	LIP	10 (50%)	
	UIP	0	
	BOOP	0	
	Unclassifiable	2 (10%)	
CYC (N=6)	NSIP	3 (50%)	- No ADRs reported
	LIP	0	
	UIP	1 (16.7%)	
	BOOP	0	
	Unclassifiable	2 (33.3%)	
RTX (N=22)	NSIP	11(50%)	- 5 patients suspended RTX due to ADRs (3 with recurrent infections, 1 with hypogammaglobulinemia and 1 for unspecified ADR) - 1 patient suspended RTX after the diagnosis of lung cancer - 3 patients died
	LIP	3 (14.3%)	
	UIP	5 (23.8%)	
	BOOP	1 (4.8%)	
	Unclassifiable	2 (9.5%)	
ABA (N=2)	NSIP	2 (100%)	- No ADRs reported
	LIP	0	
	UIP	0	
	BOOP	0	
	Unclassifiable	0	

ILD – interstitial lung disease; MMF – mycophenolate mofetil; AZA – azathioprine; CYC – cyclophosphamide; RTX – rituximab; ABA – abatacept; NSIP – nonspecific interstitial pneumonia; LIP – lymphocytic interstitial pneumonia; UIP – usual interstitial pneumonia; BOOP - bronchiolitis obliterans organizing pneumonia; ADR – adverse drug reaction

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