

Supplementary materials

Invasive fungal diseases in patients with autoimmune diseases: a case series from the French RESSIF network

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Table S1. Species responsible for fungemia in patients with autoimmune disease (France, 2012-2018)

Species	n	%
<i>Candida albicans</i>	81	48.5
<i>Candida glabrata</i>	28	16.8
<i>Candida parapsilosis</i>	20	12.0
<i>Candida tropicalis</i>	12	7.2
<i>Saccharomyces cerevisiae</i>	4	2.4
<i>Candida krusei</i>	3	1.8
<i>Candida orthopsilosis</i>	3	1.8
<i>Clavispora lusitanae</i>	3	1.8
<i>Candida dubliniensis</i>	1	0.6
<i>Candida inconspicua</i>	1	0.6
<i>Fusarium oxysporum</i>	1	0.6
<i>Kodamaea ohmeri</i>	1	0.6
<i>Malassezia furfur</i>	1	0.6
<i>Pichia guilliermondii</i>	1	0.6
<i>Trichosporon spp.</i>	1	0.6
Co-infections		
<i>Candida albicans</i> and <i>Candida glabrata</i>	5	3.0
<i>Candida albicans</i> and <i>Candida krusei</i>	1	0.6

Table S2: Population description, underlying conditions, associated autoimmune disease, treatment in patients with fungemia broken down by *Candida spp.* vs. non-*Candida spp.* fungemia (France, 2012-2018)

	<i>Candida spp.</i> fungemia (n=155)	Non- <i>Candida spp.</i> fungemia (n=12)
Age (years) (median [IQR])	64 (51-74)	62 (57.5-72)
Female sex	80 (51.6)	6 (50)
Solid cancer	30 (19.4)	3 (25)
Hematological malignancy	18 (11.6)	3 (25)
Solid organ transplantation	8 (5.2)	0 (0)
Diabetes mellitus	24 (15.5)	3 (25)
Central catheter	102 (65.8)	9 (75)
Neutropenia	8 (5.2)	2 (17)
Chronic renal failure	29 (18.7)	3 (25)
Chronic respiratory failure	19 (12.3)	2 (17)
Cirrhosis	6 (3.9)	0 (0)
Recent surgery	51 (32.9)	4 (33)
Intensive care unit	68 (43.9)	4 (33)
Mortality at 30 days	62/141 (44.0)	4/10 (40)
Mortality at 90 days	68/130 (52.3)	5/10 (50)
Autoimmune disease^a		
Crohn's disease	28 (18.1)	1 (8.3)
Ulcerative colitis	6 (3.9)	0 (0)
Unclassified inflammatory bowel disease	1 (0.7)	0 (0)
Rheumatoid arthritis	25 (16.1)	3 (25)
Systemic sclerosis	12 (7.8)	0 (0)
Systemic lupus erythematosus	10 (6.5)	2 (17)
Sarcoidosis	9 (5.8)	1 (8)
Dermatomyositis	6 (3.9)	1 (8)
Multiple sclerosis	6 (3.9)	1 (8)
Other	52 (33.5)	3 (25)
Glucocorticoids	82 (52.9)	7 (58)
High-dose ^b	58 (37.4)	5 (42)
Median daily dose (IQR) ^c	25 (10-45)	30 (15-40)
Immunosuppressant	63 (40.7)	4 (33)
Methotrexate	14 (9.0)	1 (8)
Azathioprine	11 (7.1)	0 (0)
Cyclophosphamide	1 (0.6)	1 (8)
Mycophenolate	5 (3.2)	0 (0)
Other	32 (20.6)	2 (17)
TNF-α blocker	11 (7.1)	0 (0)
Infliximab	4 (2.6)	0 (0)
Adalimumab	4 (2.6)	0 (0)
Other ^d	2 (1.3)	0 (0)
Other biologic	19 (12.3)	1 (8)
Rituximab	8 (5.2)	1 (8)
Chemotherapy	7 (4.5)	2 (17)

Legend: results are presented as n (%); a: only one AID per patient reported; b: high-dose: over 0.3 mg/kg/day prednisone-equivalent dose for at least month; c: prednisone-equivalent dose among those on glucocorticoids, missing data for the detailed dose: 26/82 (12.2%) among *Candida spp.* fungemia, and 1/7 (14%) among non-*Candida spp.* fungemia; d: missing detail on type of TNF- α blocker in one patient with *Candida spp.* fungemia.

Table S3. Infectious sites and species responsible for non-candidemia invasive deep-tissue candidiasis in patients with autoimmune disease (France, 2012-2018)

Infectious site	Species	n
Bone and joint	<i>Candida albicans</i>	6
	<i>Candida parapsilosis</i>	2
	<i>Candida glabrata</i>	1
Pleural	<i>Candida albicans</i>	1
	<i>Candida glabrata</i>	1
	<i>Candida pararugosa</i>	1
Liver	<i>Candida albicans</i>	1
	<i>Candida krusei</i> and <i>Candida tropicalis</i>	1
Eye	<i>Candida albicans</i>	2
Heart	<i>Candida parapsilosis</i>	1
Ileocecal	<i>Candida albicans</i>	1
Urine	<i>Candida glabrata</i>	1

Table S4. Infectious site and species responsible for other invasive fungal diseases (other than *Pneumocystis pneumonia*, fungemia, invasive aspergillosis, deep-tissue candidiasis, or cryptococcosis) in patients with autoimmune disease (France, 2012-2018)

Infectious site	Species	n
Skin	<i>Alternaria infectoria</i>	3
	<i>Alternaria spp.</i>	1
Lung	<i>Chaetomium funicola</i>	1
	<i>Coccidioides spp.</i>	1
	<i>Trichoderma orientale</i>	1
Eye	<i>Pichia anomala</i>	1
	<i>Fusarium oxysporum</i>	1
	<i>Rhizopus oryzae</i>	1
	<i>Scedosporium dehoogii</i>	1
Bone and joint	<i>Phaeoacremonium parasiticum</i>	1
	<i>Pseudallescheria ellipsoidea</i>	1
Sinus	<i>Fusarium proliferatum</i>	1
Gastro-intestinal tract	<i>Mucor indicus</i>	1
Lung		1
Cardiovascular	<i>Histoplasma capsulatum</i>	1
Bone and joint		1
Skin	Possible mycetoma	1

Table S5. Cases of co-occurring invasive fungal diseases in patients with autoimmune diseases (France, 2012-2018)

Combination	n
<i>Pneumocystis jirovecii</i> pneumonia and invasive aspergillosis	7
Fungemia and invasive aspergillosis	2
Invasive aspergillosis and mucormycosis	1
<i>Pneumocystis jirovecii</i> pneumonia and cryptococcosis	1
Fungemia, <i>Pneumocystis jirovecii</i> pneumonia, and invasive aspergillosis	1
<i>Pneumocystis jirovecii</i> pneumonia, invasive aspergillosis, and mucormycosis	1

Table S6. Infectious sites and species among the cases of invasive aspergillosis in patients with autoimmune diseases (France, 2012-2018)

	Lung	Sinus	Bone and joint	Brain	Eye	Blood	Total
<i>Aspergillus fumigatus</i>	38	2	2	0	1	1	44
<i>Aspergillus flavus</i>	2	0	0	0	0	0	2
<i>Aspergillus tubingensis</i>	2	0	0	0	0	0	2
<i>Aspergillus neoniveus</i>	1	0	0	0	0	0	1
<i>Aspergillus quadrilineatus</i>	1	0	0	0	0	0	1
<i>Aspergillus spp.</i>	1	0	0	0	0	0	1
<i>Emmericella nidulans</i>	1	0	0	0	0	0	1
Undocumented infection	29	2	0	1	0	0	32
Total	75	4	2	1	1	1	84

Table S7. Patients with autoimmune disease and without any other major risk factor for invasive fungal disease (IFD) among malignancy, solid organ transplantation, or recent surgery presenting an episode of IFD (France, 2012-2018)

	<i>Pneumocystis</i> pneumonia (189)	Fungemia (70)	Invasive aspergillosis (39)	Other IFD (37)	Multiple IFD (7)	Total (342)
Age (years) (median [IQR])	69 [59-76]	64 [45-75]	60 [52-71]	62 [53-69]	69 [61-72]	65 [55-75]
Female gender	99 (52.4)	35 (50.0)	12 (30.8)	24 (64.9)	5 (71)	175 (51.2)
Diabetes mellitus	35 (18.5)	8 (11.4)	8 (20.5)	5 (13.5)	1 (14)	57 (16.7)
Central catheter	9 (4.8)	51 (72.9)	7 (18.0)	2 (5.4)	2 (29)	71 (20.8)
Neutropenia	0 (0)	2 (2.9)	2 (5.1)	1 (2.7)	0 (0)	5 (1.5)
Chronic renal failure	20 (10.6)	12 (17.1)	5 (12.8)	0 (0)	2 (29)	39 (11.4)
Chronic respiratory failure	11 (5.8)	9 (12.9)	5 (12.8)	2 (5.4)	2 (29)	29 (8.5)
Cirrhosis	8 (4.2)	5 (7.1)	7 (18.0)	0 (0)	1 (14)	21 (6.1)
Intensive care unit	57 (30.2)	33 (47.1)	14 (35.9)	6 (16.2)	5 (71)	115 (33.6)
Corticosteroids	148 (78.3)	37 (52.9)	26 (66.7)	24 (64.9)	5 (71)	240 (70.2)
> 0.3mg/kg/day for > 1 month	106 (56.1)	27 (38.6)	20 (51.3)	15 (40.5)	3 (43)	171 (50.0)

Median daily dose (IQR) ^a	25 (11-45)	30 (11-55)	40 (15-60)	12.5 (8.5-37.5)	15 (7.5-25)	24 (10-47)
Immunosuppressant ^b	114 (60.3)	26 (37.1)	22 (56.4)	20 (54.1)	3 (43)	185 (54.1)
Methotrexate	77 (40.7)	6 (8.6)	5 (12.8)	7 (18.9)	1 (14)	96 (28.1)
Azathioprine	14 (7.4)	3 (4.3)	4 (10.3)	4 (10.8)	1 (14)	26 (7.6)
Cyclophosphamide	10 (5.3)	2 (2.9)	6 (15.4)	2 (5.4)	0 (0)	20 (5.8)
Mycophenolate	1 (0.5)	1 (1.4)	1 (2.6)	3 (8.1)	0 (0)	6 (1.8)
Other	10 (5.3)	9 (12.9)	7 (17.9)	2 (5.4)	1 (14)	29 (8.5)
TNF-α inhibitor ^c	13 (6.9)	4 (5.7)	8 (20.5)	4 (10.8)	1 (14)	30 (8.8)
Infliximab	4 (2.1)	2 (2.9)	3 (7.7)	2 (5.4)	1 (14)	12 (3.5)
Adalimumab	3 (1.6)	1 (1.4)	3 (7.7)	1 (2.7)	0 (0)	9 (2.6)
Other	2 (1.1)	0 (0)	0 (0)	1 (2.7)	0 (0)	3 (0.9)
Other biologic	29 (15.3)	7 (10)	10 (25.6)	3 (8.1)	1 (14)	50 (14.6)
Rituximab	23 (12.2)	3 (4.3)	5 (12.8)	1 (2.7)	0 (0)	32 (9.4)
Mortality at 30 days ^d	35/174 (20.1)	30/68 (44.1)	12/38 (31.6)	4/35 (11.4)	4/7 (57)	85/322 (26.4)
Mortality at 90 days ^e	44/154 (28.6)	34/63 (54.0)	13/37 (35.1)	5/34 (14.7)	4/7 (57)	100/295 (33.9)

Legend: results are presented as n (%); a: prednisone-equivalent dose among those on GCs, missing data for the detailed dose: 54/240 (22.5%); b: 12 patients had a combination of at least two immunosuppressants; c: missing detail on TNFi in 6 patients; d: missing data for 20 patients, 5.9%; e: missing data for 47 patients, 13.7%.

Table S8. Autoimmune diseases in patients presenting an episode of invasive fungal disease (IFD) and without any other major risk factor for IFD among malignancy, solid organ transplantation, or recent surgery (France, 2012-2018)

	<i>Pneumocystis</i> pneumonia (189)	Fungemia (70)	Invasive aspergillosis (39)	Other IFD (37)	Multiple IFD (7)	Total (342)
Rheumatoid arthritis	51 (27)	10 (14.3)	10 (25.6)	5 (13.5)	1 (14)	77 (22.5)
Inflammatory bowel disease (IBD)	12 (6.3)	16 (22.9)	1 (2.6)	2 (5.4)	0 (0)	31 (9.1)
Crohn's disease	8 (4.2)	13 (18.6)	1 (2.6)	2 (5.4)	0 (0)	24 (7)
Ulcerative colitis	4 (2.1)	3 (4.3)	0 (0)	0 (0)	0 (0)	7 (2)
Sarcoidosis	17 (9)	6 (8.6)	5 (12.8)	4 (10.8)	1 (14)	33 (9.6)
ANCA-associated vasculitis	22 (11.6)	1 (1.4)	6 (15.4)	2 (5.4)	1 (14)	32 (9.4)
Granulomatosis with polyangiitis	8 (4.2)	1 (1.4)	3 (7.7)	0 (0)	0 (0)	12 (3.5)
Microscopic polyangiitis	11 (5.8)	0 (0)	3 (7.7)	0 (0)	0 (0)	14 (4.1)
Eosinophilic granulomatosis with polyangiitis	1 (0.5)	0 (0)	0 (0)	2 (5.4)	0 (0)	3 (0.9)
Unclassified ANCA-associated vasculitis	2 (1.1)	0 (0)	0 (0)	0 (0)	1 (14)	3 (0.9)
Systemic lupus erythematosus	5 (2.6)	3 (4.3)	1 (2.6)	4 (10.8)	0 (0)	13 (3.8)
Dermatomyositis	17 (9)	5 (7.1)	1 (2.6)	4 (10.8)	0 (0)	27 (7.9)
Systemic sclerosis	10 (5.3)	7 (10)	1 (2.6)	2 (5.4)	0 (0)	20 (5.8)
Giant-cell arteritis	8 (4.2)	0 (0)	1 (2.6)	1 (2.7)	0 (0)	10 (2.9)
Spondylarthritis	2 (1.1)	1 (1.4)	2 (5.1)	3 (8.1)	0 (0)	8 (2.3)
Sjögren's syndrome	4 (2.1)	1 (1.4)	0 (0)	2 (5.4)	0 (0)	7 (2)
Autoimmune hepatitis	0 (0)	1 (1.4)	1 (2.6)	1 (2.7)	1 (14)	4 (1.2)
Polymyalgia rheumatica	3 (1.6)	1 (1.4)	0 (0)	1 (2.7)	0 (0)	5 (1.5)
Autoimmune hemolytic anemia	3 (1.6)	1 (1.4)	0 (0)	1 (2.7)	0 (0)	5 (1.5)
Myasthenia gravis	2 (1.1)	1 (1.4)	1 (2.6)	1 (2.7)	0 (0)	5 (1.5)
Multiple sclerosis	0 (0)	3 (4.3)	1 (2.6)	0 (0)	0 (0)	4 (1.2)
Psoriasis	4 (2.1)	0 (0)	1 (2.6)	0 (0)	0 (0)	5 (1.5)
Psoriatic arthritis	4 (2.1)	0 (0)	0 (0)	0 (0)	0 (0)	4 (1.2)
Immune thrombocytopenic purpura	4 (2.1)	1 (1.4)	1 (2.6)	0 (0)	0 (0)	6 (1.8)
Other	21 (11.1)	12 (17.1)	6 (15.4)	4 (10.8)	3 (43)	46 (13.5)

Legend: only one AID per patient reported: 54 patients had at least two concomitant AIDs (most frequent combination: rheumatoid arthritis and Sjögren's syndrome in 7 patients), 7 had three concomitant AIDs.

Table S9. Details on the underlying autoimmune diseases in patients classified as “others” (table 2) with an episode of invasive fungal disease (France, 2012-2018)

	<i>Pneumocystis pneumonia</i>	Fungemia	Invasive aspergillosis	Other IFD	Multiple IFD	Total
Unspecific auto-immune cirrhosis	1	3	1	0	1	6
Bullous pemphigoid	1	3	0	0	1	5
Evans syndrome	2	2	0	0	1	5
Unclassified chronic inflammatory rheumatism	2	1	2	0	0	5
IgA vasculitis	1	1	0	2	0	4
Pemphigus vulgaris	3	0	0	1	0	4
Polyarteritis nodosa	0	2	2	0	0	4
Celiac disease	0	2	1	0	0	3
IgA nephropathy	2	0	1	0	0	3
Still disease	1	1	1	0	0	3
Antiphospholipid syndrome	1	0	1	0	0	2
Behçet's disease	0	1	0	1	0	2
Cryoglobulinemic vasculitis	1	1	0	0	0	2
IgG4-related disease	0	1	0	0	1	2
Langerhans cell histiocytosis	0	1	0	1	0	2
Unclassified connective tissue disease	2	0	0	0	0	2
Usual interstitial pneumonia	2	0	0	0	0	2
Atypical hemolytic uremic syndrome	0	0	0	1	0	1
Basedow disease	1	0	0	0	0	1
Castelman disease	1	0	0	0	0	1
Cerebral vasculitis	1	0	0	0	0	1
Clippers syndrome	0	1	0	0	0	1
Cogan	0	0	1	0	0	1
Cryptogenic interstitial pneumonia	0	0	1	0	0	1
Degos disease	0	1	0	0	0	1
Good syndrome	0	1	0	0	0	1
Goodpasture syndrome	0	1	0	0	0	1
Hypocomplementemic urticarial vasculitis syndrome	1	0	0	0	0	1
Idiopathic bone marrow failure	0	0	1	0	0	1
Idiopathic pulmonary fibrosis	1	0	0	0	0	1
Marburg multiple sclerosis	0	0	1	0	0	1
Mixed connective tissue disease	0	1	0	0	0	1
Non-specific interstitial pneumonia	1	0	0	0	0	1
Overlap connective tissue disease	1	0	0	0	0	1
Primary biliary cholangitis	1	0	0	0	0	1
Pulmonary alveolar proteinosis	1	0	0	0	0	1
Rasmussen's encephalitis	0	1	0	0	0	1
Relapsing polychondritis	0	1	0	0	0	1
Retroperitoneal fibrosis	0	1	0	0	0	1
Sweet's disease	0	0	1	0	0	1
Unclassified interstitial pneumonia	1	0	0	0	0	1
Unclassified vasculitis	0	0	1	0	0	1
Total	29	27	15	6	4	81

Table S10. Combinations of co-existing autoimmune diseases in patients with an episode of invasive fungal disease (France, 2012-2018)

Autoimmune disease 1	Autoimmune disease 2	Autoimmune disease 3	n
Rheumatoid arthritis	Sjögren's syndrome		8
Giant cell arteritis	Rheumatoid arthritis		3
Immune thrombocytopenic purpura	Autoimmune hemolytic anemia		3
Sarcoidosis	Psoriasis		3
Systemic lupus erythematosus	Anti-phospholipid syndrome		3
Systemic lupus erythematosus	Rheumatoid arthritis		2
Systemic sclerosis	Sjögren's syndrome		2
Anti-phospholipid syndrome	Unclassified interstitial pneumonia		1
Auto-immune hepatitis	Primary biliary cholangitis		1
Celiac disease	Psoriasis		1
Crohn's disease	Basedow disease		1
Crohn's disease	Primary sclerosing cholangitis		1
Crohn's disease	Lichen planus		1
Crohn's disease	Systemic lupus erythematosus		1
Crohn's disease	Psoriasis		1
Crohn's disease	Spondylarthritis		1
Dermatomyositis	Sjögren's syndrome		1
Eosinophilic granulomatosis with polyangiitis	Ulcerative colitis		1
Giant cell arteritis	Sjögren's syndrome		1
Granulomatosis with polyangiitis	Rheumatoid arthritis		1
Granulomatosis with polyangiitis	Rheumatoid arthritis		1
Idiopathic pulmonary fibrosis	Immune thrombocytopenic purpura		1
Microscopic polyangiitis	Relapsing polychondritis		1
Microscopic polyangiitis	Rheumatoid arthritis		1
Multiple sclerosis	Rheumatoid arthritis		1
Polyarteritis nodosa	Common variable immunodeficiency		1
Polyarteritis nodosa	Anti-phospholipid syndrome		1
Psoriasis	Spondylarthritis		1
Rheumatoid arthritis	IgG4-related disease		1
Rheumatoid arthritis	Crohn's disease		1
Rheumatoid arthritis	Minimal change disease		1
Rheumatoid arthritis	Autoimmune neutropenia		1
Sarcoidosis	Systemic lupus erythematosus		1
Sarcoidosis	Pyoderma gangrenosum		1
Sarcoidosis	Psoriatic rheumatism		1
Sarcoidosis	Hemophagocytic lymphohistiocytosis		1
Sarcoidosis	Sjögren's syndrome		1
Sjögren's syndrome	Anti-phospholipid syndrome		1
Sjögren's syndrome	Myasthenia-like syndrome		1
Spondylarthritis	Hashimoto disease		1
Spondylarthritis	Unclassified medium vessel vasculitis		1
Still disease	Unclassified interstitial pneumonia		1
Still disease	Systemic sclerosis		1
Systemic lupus erythematosus	Autoimmune hemolytic anemia		1
Systemic lupus erythematosus	Dermatomyositis		1
Systemic lupus erythematosus	Systemic sclerosis		1
Systemic sclerosis	Giant cell arteritis		1
Systemic sclerosis	Dermatomyositis		1
Systemic sclerosis	Hashimoto disease		1
Systemic sclerosis	Spondylarthritis		1
Ulcerative colitis	Rheumatoid arthritis		1
Ulcerative colitis	Anti-phospholipid syndrome		1
Ulcerative colitis	Spondylarthritis		1
Urticarial vasculitis	Dermatomyositis		1
Systemic sclerosis	Microscopic polyangiitis	Antiphospholipid syndrome	1
Immune thrombocytopenic purpura	Autoimmune hemolytic anemia	Common variable immunodeficiency	1

Autoimmune disease 1	Autoimmune disease 2	Autoimmune disease 3	n
Dermatomyositis	Autoimmune hemolytic anemia	Immune thrombocytopenic purpura	1
Castelman disease	IgA vasculitis	Lichen planus	1
Rheumatoid arthritis	Sjögren's syndrome	Primary biliary cholangitis	1
Systemic lupus erythematosus	Cryoglobulinemic vasculitis	Primary biliary cholangitis	1
Ulcerative colitis	Auto-immune hepatitis	Primary sclerosing cholangitis	1
Rheumatoid arthritis	Hashimoto disease	Sjögren's syndrome	1
Systemic lupus erythematosus	Rheumatoid arthritis	Sjögren's syndrome	1
Mixed connective tissue disease	Sjögren's syndrome	Systemic lupus erythematosus	1

Table S11. Description of the study population across different autoimmune diseases (AIDs) (France, 2012-2018)

	Rheumatoid arthritis (113)	Inflammatory bowel diseases (54)	Sarcoidosis (46)	ANCA-associated vasculitis (46)	Systemic lupus erythematosus (36)	Dermatomyositis (33)	Systemic sclerosis (28)	Giant-cell arteritis (16)	Spondyl-arthritis (16)	Sjögren's syndrome (14)	Autoimmune hepatitis (11)	Polymyalgia rheumatica (10)	Other AID (126)	Total (549)
Pneumocystis pneumonia	55 (48.7)	13 (24)	19 (41)	25 (54)	6 (17)	21 (64)	12 (43)	11 (69)	2 (13)	7 (50)	0 (0)	5 (50)	51 (40.5)	227 (41.4)
Fungemia	28 (24.8)	36 (67)	10 (22)	7 (15)	12 (33)	7 (21)	12 (43)	0 (0)	4 (25)	4 (29)	6 (55)	3 (30)	38 (30.2)	167 (30.4)
Invasive aspergillosis	15 (13.3)	2 (4)	10 (22)	10 (22)	9 (25)	1 (3)	1 (4)	1 (6)	7 (44)	1 (7)	2 (18)	1 (10)	24 (19.1)	84 (15.3)
Other IFD	13 (11.5)	3 (6)	6 (13)	2 (4)	7 (19)	4 (12)	3 (11)	4 (25)	3 (19)	2 (14)	1 (9)	1 (10)	9 (7.1)	58 (10.6)
Multiple IFD	2 (1.8)	0 (0)	1 (2)	2 (4)	2 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)	4 (3.2)	13 (2.4)
Age, years (median, IQR)	72 (61-77)	54.5 (35-66)	55.5 (42-66)	68.5 (58-75)	54.5 (45-63)	64 (47-74)	63 (54.5-73)	69 (75.5-80)	60.5 (53.5-66.5)	67 (54-76)	56 (39-65)	76.5 (74-80)	65 (57-73)	65 (55-74)
Female sex	60 (53.1)	23 (43)	16 (35)	26 (57)	24 (67)	19 (58)	18 (64)	10 (63)	4 (25)	11 (79)	5 (45)	6 (60)	53 (42.1)	275 (50.1)
Solid cancer	14 (12.4)	8 (15)	4 (9)	3 (7)	1 (3)	4 (12)	3 (11)	3 (19)	3 (19)	3 (21)	3 (27)	2 (20)	12 (9.5)	63 (11.5)
Hematological malignancy	11 (9.7)	2 (4)	8 (17)	4 (9)	10 (28)	0 (0)	0 (0)	4 (25)	3 (19)	4 (29)	3 (27)	3 (30)	22 (17.5)	74 (13.5)
Solid organ transplantation	1 (0.9)	3 (6)	2 (4)	4 (9)	8 (22)	0 (0)	4 (14)	0 (0)	3 (19)	0 (0)	3 (27)	0 (0)	4 (3.2)	32 (5.8)
Diabetes mellitus	12 (10.6)	4 (7)	11 (24)	5 (11)	9 (25)	4 (12)	3 (11)	4 (25)	1 (6)	2 (14)	3 (27)	5 (50)	28 (22.2)	91 (16.6)
Central catheter	24 (21.2)	29 (54)	8 (17)	6 (13)	14 (39)	8 (24)	13 (46)	1 (6)	2 (13)	2 (14)	8 (73)	1 (10)	36 (28.6)	152 (27.7)
Neutropenia	4 (3.5)	1 (2)	1 (2)	2 (4)	5 (14)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	3 (27)	0 (0)	12 (9.5)	29 (5.3)
Chronic renal failure	10 (8.9)	5 (9)	3 (7)	16 (35)	11 (31)	1 (3)	4 (14)	2 (13)	2 (13)	1 (7)	1 (9)	2 (20)	19 (15.1)	77 (14)
Chronic respiratory failure	12 (10.6)	1 (2)	6 (13)	1 (2)	3 (8)	2 (6)	2 (7)	0 (0)	1 (6)	2 (14)	1 (9)	0 (0)	15 (11.9)	46 (8.4)
Cirrhosis	2 (1.8)	4 (7)	3 (7)	0 (0)	1 (3)	1 (3)	2 (7)	1 (6)	1 (6)	0 (0)	1 (9)	0 (0)	9 (7.1)	25 (4.6)
Recent surgery	15 (13.3)	15 (28)	1 (2)	4 (9)	8 (22)	3 (9)	2 (7)	1 (6)	2 (13)	3 (21)	2 (18)	2 (20)	15 (11.9)	73 (13.3)
Glucocorticoids	74 (65.5)	22 (41)	30 (65)	37 (80)	26 (72)	31 (94)	15 (54)	16 (100)	8 (50)	7 (50)	7 (64)	9 (90)	83 (65.9)	365 (66.5)
High-dose glucocorticoids ^a	38 (33.6)	20 (37)	23 (50)	29 (63)	16 (44)	25 (76)	9 (32)	12 (75)	4 (25)	6 (43)	5 (45)	3 (30)	64 (50.8)	254 (46.3)
Immunosuppressive agent^b	79 (69.9)	26 (48)	12 (26)	25 (54)	27 (75)	23 (70)	17 (61)	7 (44)	5 (31)	6 (43)	9 (82)	3 (30)	46 (36.5)	285 (51.9)
Methotrexate	56 (49.6)	2 (11)	9 (75)	6 (26)	3 (16)	8 (38)	8 (47)	5 (83)	1 (25)	1 (17)	2 (22)	2 (67)	11 (33.3)	114 (0.2)
Azathioprine	0 (0)	14 (74)	0 (0)	6 (26)	2 (11)	3 (14)	0 (0)	0 (0)	0 (0)	1 (17)	3 (33)	0 (0)	8 (24.2)	37 (15.1)
Cyclophosphamide	1 (1.4)	0 (0)	0 (0)	8 (35)	2 (11)	9 (27)	2 (12)	0 (0)	0 (0)	2 (33)	0 (0)	0 (0)	3 (9.1)	27 (0)

	Rheumatoid arthritis (113)	Inflammatory bowel diseases (54)	Sarcoidosis (46)	ANCA-associated vasculitis (46)	Systemic lupus erythematosus (36)	Dermatomyositis (33)	Systemic sclerosis (28)	Giant-cell arteritis (16)	Spondylarthritis (16)	Sjögren's syndrome (14)	Autoimmune hepatitis (11)	Polymyalgia rheumatica (10)	Other AID (126)	Total (549)
Mycophenolate	1 (0.9)	1 (2)	1 (2)	2 (4)	3 (8)	2 (6)	5 (18)	0 (0)	2 (13)	0 (0)	2 (18)	0 (0)	3 (2.4)	22 (4)
Other	21 (18.6)	9 (17)	2 (4)	3 (7)	17 (47)	3 (9)	2 (7)	2 (13)	2 (13)	2 (14)	2 (18)	1 (10)	22 (17.5)	88 (16)
TNF-alpha blocker	10 (8.9)	14 (26)	6 (13)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	6 (38)	0 (0)	0 (0)	0 (0)	5 (4)	42 (7.7)
Infliximab	1 (0.9)	6 (11)	5 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	0 (0)	15 (2.7)
Adalimumab	4 (3.5)	4 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	3 (2.4)	12 (2.2)
Other	3 (2.7)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	1 (0.8)	6 (1.1)
Other biologic	16 (14.2)	4 (7)	4 (9)	13 (28)	3 (8)	6 (18)	2 (7)	1 (6)	0 (0)	1 (7)	1 (9)	0 (0)	24 (19.1)	75 (13.7)
Rituximab	6 (5.3)	0 (0)	1 (2)	12 (26)	2 (6)	4 (12)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	20 (15.9)	46 (8.4)
Chemotherapy	3 (2.7)	2 (4)	5 (11)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	11 (8.7)	25 (4.6)
Intensive care unit	36 (31.9)	16 (30)	7 (15)	12 (26)	14 (39)	14 (42)	12 (43)	4 (25)	6 (38)	3 (21)	6 (55)	2 (20)	54 (42.9)	186 (33.9)
Mortality at 30 days^c	26/97 (26.8)	9/47 (19)	8/45 (18)	10/43 (23)	9/33 (27)	10/31 (32)	9/28 (32)	3/14 (21)	7/16 (44)	1/12 (8)	8/11 (73)	2/9 (22)	41/122 (33.6)	143/508 (28.1)
Mortality at 90 days^d	32/90 (35.6)	10/40 (25)	13/43 (30)	13/39 (33)	14/32 (44)	12/28 (43)	11/25 (44)	3/14 (21)	7/14 (50)	1/10 (10)	9/11 (82)	3/9 (33)	46/115 (40.0)	174/470 (37.0)

Legend: results are presented as n (%); only one AID per patient reported; IQR: interquartile range; a: over 0.3 mg/kg/day prednisone-equivalent dose for at least month; b: 35 patients had a combination of at least two immunosuppressants including 3 with a combination of the four agents detailed in the table (these 3 patients appear twice in the table); c: missing data for 41 patients, 7.5%; d: missing data for 79 patients, 14.4%.

Table S12. Comparison of observed and age- and sex-standardized estimates of the main patient characteristics across various autoimmune diseases in patients with invasive fungal diseases

	Rheumatoid arthritis (113)		Inflammatory bowel diseases (54)		Sarcoidosis (46)		ANCA-associated vasculitis (46)		Systemic lupus erythematosus (36)		Dermatomyositis (33)		Systemic sclerosis (28)		Giant-cell arteritis (16)		Spondylarthritis (16)		Sjögren's syndrome (14)		Auto-immune hepatitis (11)		Poly-myalgia rheumatica (10)		Other AID (126)	
	Obs.	Std.	Obs.	Std.	Obs.	Std.	Obs.	Std.	Obs.	Std.	Obs.	Std.	Obs.	Std.	Obs.	Std.	Obs.	Std.	Obs.	Std.	Obs.	Std.	Obs.	Std.	Obs.	Std.
Solid cancer	12.4	3.8	15	9	9	6	7	3	3	2	12	5	11	5	19	4	19	4	21	6	27	8	20	4	9.5	5
Hematological malignancy	9.7	7.5	4	2	17	7	9	4	28	17	0	0	0	0	25	3	19	5	29	7	27	7	30	4	17.5	14.2
Solid organ transplantation	0.9	0.5	6	3	4	5	9	3	22	19	0	0	14	7	0	0	19	4	0	0	27	7	0	0	3.2	3
Diabetes mellitus	10.6	3.8	7	9	24	10	11	4	25	13	12	5	11	3	25	4	6	1	14	4	27	6	50	7	22.2	10.3
Central catheter	21.2	8.9	54	46	17	12	13	10	39	22	24	15	46	20	6	1	13	4	14	5	73	18	10	1	28.6	31.1
Neutropenia	3.5	1.4	2	2	2	1	4	2	14	8	0	0	4	1	0	0	0	0	0	0	27	5	0	0	9.5	9.4
Chronic renal failure	8.9	3.1	9	8	7	2	35	14	31	21	3	1	14	5	13	2	13	2	7	3	9	3	20	3	15.1	9.4
Chronic respiratory failure	10.6	6	2	1	13	11	2	0	8	3	6	4	7	3	0	0	6	2	14	5	9	3	0	0	11.9	7.7
Cirrhosis	1.8	0.5	7	9	7	2	0	0	3	3	3	3	7	2	6	1	6	1	0	0	9	3	0	0	7.1	3.3
Glucocorticoids	65.5	32.8	41	42	65	36	80	43	72	47	94	56	54	23	100	21	50	10	50	14	64	13	90	13	65.9	48.2
High-dose glucocorticoids ^a	33.6	17.5	37	38	50	29	63	35	44	29	76	44	32	11	75	17	25	5	43	12	45	8	30	4	50.8	40.4
Immunosuppressive agent	69.9	36.4	48	46	26	14	54	26	75	48	70	42	61	22	44	11	31	8	43	12	82	18	30	6	36.5	29.6
TNF-alpha blocker	8.9	7.1	26	26	13	6	0	0	0	0	0	0	0	0	6	1	38	9	0	0	0	0	0	0	4	1.3
Other biologic	14.2	10.2	7	7	9	7	28	17	8	8	18	12	7	3	6	1	0	0	7	2	9	2	0	0	19.1	19.3
Chemotherapy	2.7	1	4	3	11	9	0	0	8	5	0	0	0	0	0	0	6	3	0	0	0	0	0	0	8.7	11.8
Recent surgery	31.9	6.4	30	23	15	1	26	5	39	14	42	5	43	6	25	1	38	2	21	7	55	6	20	3	42.9	10.9
Intensive care unit	13.3	10.3	28	19	2	7	9	14	22	27	9	29	7	12	6	6	13	8	21	7	18	13	20	3	11.9	29.2
Mortality at 30 days ^b	26.8	8.9	19	10	18	7	23	7	27	17	32	19	32	12	21	4	44	9	8	2	73	16	22	3	33.6	21.6
Mortality at 90 days ^c	35.6	14.2	25	14	30	17	33	15	44	30	43	24	44	14	21	4	50	11	10	2	82	19	33	6	40	23.5

Legend: Obs: observed; Std: standardized estimates based on the age and sex structure of the general French population in 2015 (World bank data); a: over 0.3 mg/kg/day prednisone-equivalent dose for at least month; b: missing data for 41 patients, 7.5%; c: missing data for 79 patients, 14.4%.

Table S13. Comparison of observed and age- and sex-standardized estimates of main patient characteristics across the three main invasive fungal diseases in patients with autoimmune diseases

	<i>Pneumocystis pneumonia</i> (227)		Fungemia (167)		Invasive aspergillosis (84)	
	Observed	Standardized	Observed	Standardized	Observed	Standardized
Solid cancer	7.1	2.7	19.8	12.1	7.1	3.6
Hematological malignancy	5.7	3.6	12.6	8.1	35.7	29.1
Solid organ transplantation	3.5	4.7	5.4	6.3	14.5	13.5
Diabetes mellitus	18.5	7.8	16.2	8.9	16.7	10.0
Central catheter	5.3	3.0	66.5	64.1	21.4	19.1
Neutropenia	0	0	6.0	5.4	16.7	15.3
Chronic renal failure	11.9	5.4	19.2	11.0	14.3	8.9
Chronic respiratory failure	5.7	5.1	12.6	9.6	8.3	3.0
Cirrhosis	4.0	2.8	3.6	2.8	10.7	4.1
Glucocorticoids	78.4	55.9	53.3	51.1	58.3	44.9
High-dose glucocorticoids ^a	55.1	38.1	37.7	42.4	42.9	32.1
Immunosuppressive agent	59.5	41.2	40.1	43.8	59.5	44.2
TNF-alpha blocker	6.2	6.3	6.6	19.2	13.1	8.2
Other biologic	14.5	11.6	12.0	12.5	19.1	13.6
Chemotherapy	0.4	0.1	5.4	7.1	14.3	19.6
Recent surgery	1.3	0.7	32.9	28.7	7.1	5.2
Intensive care unit	29.5	14.5	43.1	36.0	36.9	29.6
Mortality at 30 days ^b	20.3	9.0	43.7	27.3	28.4	15.7
Mortality at 90 days ^c	29.5	16.2	52.1	34.4	39.2	25.1

Legend: standardized estimates based on the age and sex structure of the general French population in 2015 (World bank data); a: over 0.3 mg/kg/day prednisone-equivalent dose for at least month; b: missing data for 41 patients, 7.5%; c: missing data for 79 patients, 14.4%.

Table S14. Association of autoimmune disease-specific treatments, demographic characteristics, underlying conditions, type of invasive fungal disease (IFD) and type of autoimmune disease (AID) with 30-day mortality in univariable and multivariable logistic regression models (France, 2012-2018)

	Overall population (n=508)		Patients without any other major risk factor for IFD (n=322) ^a	
	Univariable model	Multivariable model	Univariable model	Multivariable model
Treatment at IFD diagnosis				
High-dose glucocorticoids ^b	1.6 (1.1 ; 2.3)	1.9 (1.2 ; 3.1)	1.8 (1.1 ; 3.0)	2.9 (1.5 ; 5.8)
Immunosuppressant	1.0 (0.7 ; 1.5)	1.6 (0.9 ; 2.6)	1.0 (0.6 ; 1.7)	1.8 (0.9 ; 3.4)
TNF- α blocker	0.6 (0.3 ; 1.4)	1.0 (0.4 ; 2.6)	0.9 (0.4 ; 2.3)	2.0 (0.7 ; 6.0)
Other biologic	0.9 (0.5 ; 1.6)	0.9 (0.5 ; 1.8)	0.5 (0.2 ; 1.1)	0.5 (0.2 ; 1.4)
Age (per year)	1.0 (1.0 ; 1.0)	1.0 (1.0 ; 1.1)	1.0 (1.0 ; 1.1)	1.1 (1.0 ; 1.1)
Male sex	1.7 (1.1 ; 2.5)	1.6 (1.0 ; 2.6)	1.7 (1.0 ; 2.8)	1.4 (0.8 ; 2.5)
Solid cancer	1.6 (0.9 ; 2.9)	1.2 (0.6 ; 2.3)	-	-
Hematological malignancy	0.9 (0.5 ; 1.6)	1.0 (0.5 ; 1.9)	-	-
Solid organ transplantation	1.5 (0.7 ; 3.2)	1.8 (0.7 ; 4.9)	-	-
Cirrhosis	6.0 (2.5 ; 14.3)	8.0 (2.9 ; 21.7)	6.5 (2.5 ; 16.7)	8.3 (2.6 ; 27.2)
Chronic kidney failure	1.8 (1.1 ; 3.0)	1.2 (0.6 ; 2.2)	1.9 (0.9 ; 4.0)	1.0 (0.4 ; 2.6)
Chronic respiratory failure	2.5 (1.3 ; 4.8)	2.2 (1.0 ; 4.6)	2.4 (1.1 ; 5.4)	2.3 (0.9 ; 6.1)
Co-occurring bacterial infection	1.8 (1.0 ; 3.2)	0.8 (0.4 ; 1.6)	2.8 (1.4 ; 5.8)	1.4 (0.6 ; 3.8)
Co-occurring viral infection	2.2 (0.9 ; 5.2)	2.1 (0.8 ; 5.8)	1.9 (0.7 ; 5.6)	1.3 (0.4 ; 4.9)
Invasive fungal disease (IFD)				
Pneumocystis pneumonia	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Fungemia	3.1 (1.9 ; 4.9)	5.4 (3.0 ; 9.8)	3.1 (1.7 ; 5.7)	6.1 (2.6 ; 14.6)
Invasive aspergillosis	1.6 (0.9 ; 2.8)	1.6 (0.8 ; 3.3)	1.8 (0.8 ; 4.0)	1.8 (0.7 ; 4.7)
Other IFD	0.5 (0.2 ; 1.2)	0.7 (0.3 ; 1.7)	0.5 (0.2 ; 1.5)	0.7 (0.2 ; 2.4)
Multiple IFD	3.4 (1.1 ; 10.5)	3.4 (0.9 ; 12.8)	5.3 (1.1 ; 24.8)	4.3 (0.7 ; 27.9)
Autoimmune disease (AID)				
Rheumatoid arthritis	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Other chronic inflammatory rheumatism	1.2 (0.5 ; 2.7)	1.6 (0.6 ; 4.2)	0.5 (0.1 ; 1.9)	1.3 (0.3 ; 5.7)
Other connective tissue disease	1.1 (0.6 ; 1.9)	1.2 (0.6 ; 2.5)	1.0 (0.4 ; 2.1)	1.3 (0.5 ; 3.4)
Vasculitis	0.9 (0.4 ; 1.7)	1.0 (0.4 ; 2.3)	0.7 (0.3 ; 1.7)	0.8 (0.3 ; 2.5)
Sarcoidosis	0.6 (0.2 ; 1.4)	0.7 (0.2 ; 1.9)	0.5 (0.2 ; 1.4)	0.7 (0.2 ; 2.7)
Inflammatory bowel disease	0.6 (0.3 ; 1.5)	0.5 (0.2 ; 1.4)	0.8 (0.3 ; 2.2)	0.8 (0.2 ; 2.8)
Other AID	1.9 (1.0 ; 3.4)	1.7 (0.8 ; 3.4)	1.8 (0.9 ; 3.8)	1.6 (0.6 ; 4.2)

Legend: a: Patients without any malignancy (solid cancer or hematological malignancy), recent surgery, or solid organ transplantation; b: High-dose glucocorticoids: over 0.3 mg/kg/day for over 1 month

Table S15. Time from autoimmune diagnosis to *Pneumocystis* pneumonia by type of autoimmune disease (France, 2012-2018)

Autoimmune disease	n	Years, median (IQR)
Rheumatoid arthritis	43	9 (3-18)
ANCA-associated vasculitides	20	1 (0-3.5)
Dermatomyositis	21	0 (0-1)
Sarcoidosis	15	1 (0-19)
Inflammatory bowel diseases	10	5 (1-13)
Systemic sclerosis	10	2.5 (0-10)
Giant cell arteritis	7	1 (0-3)
Other autoimmune disease	58	2 (1-13)