

Online supplementary material

Systematic literature review informing the 2022 EULAR recommendations on the screening and prophylaxis of chronic and opportunistic infections

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1. Literature search and screening strategy

A. Domains of interest

1. Infection
2. Rheumatic Diseases
3. Immunosuppression
4. Screening
5. Prophylaxis

B. Databases searched

1. PubMed
2. Embase
3. Cochrane

C. Studies included

Domains (1st AND 2nd AND 3rd) AND (4th OR 5th)

D. Dates of search

From inception till 5th December 2021

PubMed

<http://www.ncbi.nlm.nih.gov/pubmed?otool=leiden>

(("Infections"[mesh] OR "Bacteria"[mesh] OR "Viruses"[mesh] OR "Parasites"[mesh] OR "Fungi"[mesh] OR "infection"[tw] OR "infections"[tw] OR "Tuberculosis"[tw] OR "hepatitis B"[tw] OR "hepatitis C"[tw] OR "Human immunodeficiency virus"[tw] OR "herpes zoster"[tw] OR "varicella zoster"[tw] OR "HZV"[tw] OR "VZV"[tw] OR "pneumocystis carinii"[tw] OR "pneumocystis jiroveci"[tw] OR "PCP"[tw] OR "human papilloma virus"[tw] OR "HPV"[tw] OR "opportunistic infections"[tw] OR "chronic infections"[tw] OR "Leishmaniasis"[tw] OR "strongyloidiasis"[tw] OR "strongyloides"[tw] OR "histoplasmosis"[tw] OR "histoplasma"[tw] OR "toxoplasmosis"[tw] OR "toxoplasma"[tw] OR "trypanosoma cruzi"[tw] OR "trypanosomiasis"[tw] OR "CMV"[tw] OR "Cytomegalovirus"[tw] OR "Epstein Barr virus"[tw] OR "EBV"[tw] OR "non-tuberculous mycobacteria"[tw] OR "west nile virus"[tw] OR "cryptosporidiosis"[tw] OR "nocardiosis"[tw] OR "nocardia"[tw] OR "actynomycosis"[tw] OR

"actinomyces"[tw] OR "Bartonellosis"[tw] OR "bartonella"[tw] OR "campylobacter"[tw] OR "legionellosis"[tw] OR "leptospirosis"[tw] OR "leptospira"[tw] OR "listeriosis"[tw] OR "listeria"[tw] OR "salmonellosis"[tw] OR "salmonella"[tw] OR "shigellosis"[tw] OR "shigella"[tw] OR "syphilis"[tw] OR "aspergillosis"[tw] OR "Coccidioidomycosis"[tw] OR "candidiasis"[tw] OR "candida"[tw] OR "molds"[tw] OR "leprosy"[tw] OR "Isosporiasis"[tw] OR "isospora"[tw] OR "bacteria"[tw] OR "viruses"[tw] OR "fungi"[tw] OR "parasites"[tw] OR "mycoses"[tw] OR "bacterium"[tw] OR "virus"[tw] OR "fungus"[tw] OR "parasite"[tw] OR "mycosis"[tw] OR "hepatitis E"[tw] OR "chicken pox"[tw] OR "shingles"[tw] OR "Chagas"[tw] OR "legionella"[tw] OR "treponema"[tw] OR "aspergillus"[tw] OR "mycobacterium"[tw] OR "mycobacteria"[tw] OR "JC virus"[tw] OR "ancylostoma"[Mesh] OR "ancylostoma"[tw] OR "ancylostomas"[tw] OR "ancylostomiasis"[Mesh] OR "ancylostomiasis"[tw] OR "ancylostomases"[tw] OR "ascariasis"[Mesh] OR "ascariasis"[tw] OR "ascaris"[Mesh] OR "ascaris"[tw] OR "ascari"[tw] OR "chlamydia"[Mesh] OR "chlamydia"[tw] OR "chlamydiae"[tw] OR "chlamydias"[tw] OR "coccidioidal"[tw] OR "coccidioides"[Mesh] OR "coccidioides"[tw] OR "cryptococcosis"[Mesh] OR "cryptococcosis"[tw] OR "cryptococcoses"[tw] OR "cryptococcus"[Mesh] OR "cryptococcus"[tw] OR "cryptosporidium"[Mesh] OR "cryptosporidium"[tw] OR "cyclospora"[Mesh] OR "cyclospora"[tw] OR "cyclosporiasis"[Mesh] OR "cyclosporiasis"[tw] OR "echinococcosis"[Mesh] OR "echinococcosis"[tw] OR "echinococcoses"[tw] OR "echinococcus"[Mesh] OR "echinococcus"[tw] OR "endamoeba"[tw] OR "entamoeba"[Mesh] OR "entamoeba"[tw] OR "entameba"[tw] OR "entamoebas"[tw] OR "entamoebae"[tw] OR "enterobiasis"[Mesh] OR "enterobiasis"[tw] OR "enterobius"[Mesh] OR "enterobius"[tw] OR "enterobius vermicularis"[tw] OR "fasciola"[Mesh] OR "fasciola"[tw] OR "fascioliasis"[Mesh] OR "fascioliasis"[tw] OR "filariasis"[Mesh] OR "filariasis"[tw] OR "filiarieses"[tw] OR "Giardia lamblia"[Mesh] OR "Giardia lamblia"[tw] OR "neisseria gonorrhoeae"[Mesh] OR "neisseria gonorrhoeae"[tw] OR "gonococcus"[tw] OR "haemophilus influenzae"[tw] OR "haemophilus influenzae"[Mesh] OR "haemophilus influenzae"[tw] OR "hemophilus influenzae"[tw] OR "herpes simplex"[Mesh] OR "herpes simplex"[tw] OR "herpesvirus 8, human"[Mesh] OR "human herpesvirus 8"[tw] OR "hhv8"[tw] OR "hiv"[Mesh] OR "hiv"[tw] OR "ancylostomatoidea"[Mesh] OR "ancylostomatoidea"[tw] OR "hookworm"[tw] OR "hookworms"[tw] OR "HSV"[tw] OR "human t lymphotropic virus 1"[Mesh] OR "human t lymphotropic virus 1"[tw] OR "htlv 1"[tw] OR "deltaretrovirus"[Mesh] OR "deltaretrovirus"[tw] OR "human t lymphotropic virus"[tw] OR "influenza, human"[Mesh] OR "human influenza"[tw] OR "influenza"[tw] OR "influenzae"[tw] OR "influenzas"[tw] OR "giardiasis"[Mesh] OR "giardiasis"[tw] OR "lambliasis"[tw] OR "leishmania"[Mesh] OR "leishmania"[tw] OR "leishmanias"[tw] OR "leishmaniae"[tw] OR "loa"[Mesh] OR "loa"[tw] OR "loa loa"[tw] OR "mucormycosis"[Mesh] OR "mucormycosis"[tw] OR "mucormycoses"[tw] OR "neisseria"[Mesh] OR "neisseria"[tw] OR "neisseriae"[tw] OR "neisserias"[tw] OR "nontuberculous mycobacteria"[Mesh] OR "nontuberculous mycobacteria"[tw] OR "non tuberculous mycobacteria"[tw] OR "onchocerca"[Mesh] OR "onchocerca"[tw] OR "onchocerciasis"[Mesh] OR "onchocerciasis"[tw] OR "onchocerциases"[tw] OR "paracoccidioides"[Mesh] OR "paracoccidioides"[tw] OR "paragonimiasis"[Mesh] OR "paragonimiasis"[tw] OR "paragonimiases"[tw] OR "paragonimus"[Mesh] OR "paragonimus"[tw] OR "parvovirus b19, human"[Mesh] OR "human parvovirus b19"[tw] OR "parvovirus b19"[tw] OR "streptococcus pneumoniae"[Mesh] OR "streptococcus pneumoniae"[tw] OR "pneumococcus"[tw] OR

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OR "rilonacept"[Supplementary Concept] OR "rituximab"[mesh] OR
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Embase (OVID version)

<http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=main&MODE=ovid&D=oemezd>

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Cochrane Library

<https://www.cochranelibrary.com/advanced-search/search-manager>

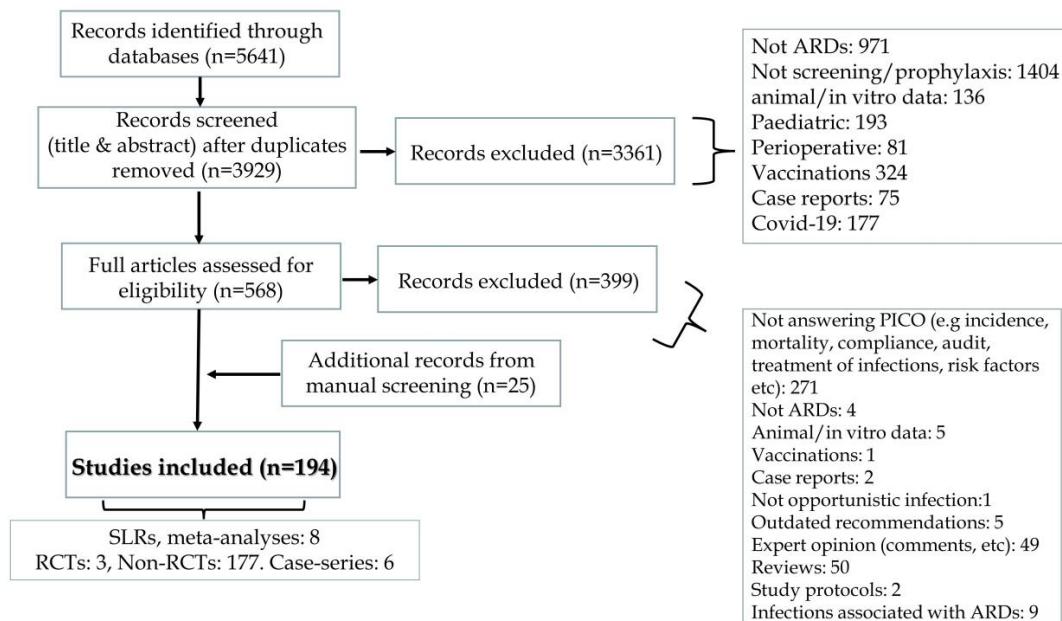
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OR "dermatomyositis" OR "immunoglobulin g4 related disease" OR "relapsing polychondritis" OR "familial mediterranean fever" OR "juvenile arthritis" OR "ANCA vasculitis" OR "antiphospholipid syndrome" OR "anti phospholipid syndrome" OR "arthritic" OR "arthritis" OR "Autoimmune rheumatic disease" OR "Autoimmune rheumatic diseases" OR "autoinflammatory disease" OR "autoinflammatory diseases" OR "behcet syndrome" OR "Behcet's disease" OR "cryoglobulinemic vasculitis" OR "dermatomyositis" OR "familial Mediterranean fever" OR "giant cell arteritis" OR "IgG4 related disease" OR "immunoglobulin g4 related disease" OR "inflammatory myopathy" OR "lupus" OR "musculoskeletal disease" OR "musculoskeletal diseases" OR "polyarteritis nodosa" OR "psoriatic arthritis" OR "relapsing polychondritis" OR "relapsing polychondritis" OR "rheumatic disease" OR "rheumatic diseases" OR "Rheumatic musculoskeletal disease" OR "Rheumatic musculoskeletal diseases" OR "rheumatica polymyalgia" OR "rheumatoid" OR "rheumatoid arthritis" OR "Rheumatology" OR "seronegative spondyloarthropathies" OR "seronegative spondyloarthropathy" OR "sjogren syndrome" OR "Sjogren's syndrome" OR "sjogrens syndrome" OR "spondylarthropathies" OR "spondylarthropathy" OR "still's disease" OR "stills disease" OR "Systemic lupus erythematosus" OR "systemic lupus" OR "SLE" OR "systemic scleroderma" OR "systemic sclerosis" OR "Takayasu arteritis" OR "vasculitis" OR "ankylosing spondylitis" OR "cutaneous limited sclerosis" OR "cutaneous sclerosis" OR "inflammatory myopathy" OR "limited scleroderma" OR "limited sclerosis" OR "Myositis" OR "Myositis" OR "Dermatomyositis" OR "Pyomyositis" OR "Scleroderma" OR "Scleroderma, Systemic" OR "Scleroderma" OR "Systemic Sclerosis") :ti AND ("steroid" OR "corticosteroid" OR "glucocorticoid" OR "prednisolone" OR "prednisone" OR "methylprednisolone" OR "cortisone" OR "methotrexate" OR "leflunomide" OR "sulfasalazine" OR "cyclophosphamide" OR "tofacitinib" OR "baricitinib" OR "janus kinase inhibitor" OR "infliximab" OR "etanercept" OR "adalimumab" OR "golimumab" OR "certolizumab pegol" OR "abatacept" OR "tocilizumab" OR "sarilumab" OR "ustekinumab" OR "secukinumab" OR "ixekizumab" OR "canakinumab" OR "interleukin 1 receptor antagonist protein" OR "rilonacept" OR "rituximab" OR "belimumab" OR "guselkumab" OR "Antirheumatic Agent" OR "abatacept" OR "adalimumab" OR "adrenal cortex hormone" OR "adrenal cortex hormones" OR "anakinra" OR "baricitinib" OR "belimumab" OR "biologic DMARD" OR "biologic DMARDs" OR "biological DMARD" OR "biological DMARDs" OR "canakinumab" OR "certolizumab" OR "corticosteroid" OR "corticosteroids" OR "cortisone" OR "cyclophosphamide" OR "disease modifying anti rheumatic" OR "disease modifying anti rheumatic drugs" OR "DMARD" OR "DMARDs" OR "etanercept" OR "glucocorticoid" OR "glucocorticoids" OR "glucocorticosteroid" OR "glucocorticosteroids" OR "golimumab" OR "guselkumab" OR "infliximab" OR "interleukin 1 receptor antagonist" OR "interleukin 1 receptor antagonists" OR "ixekizumab" OR "JAK inhibitor" OR "JAK inhibitors" OR "janus kinase inhibitor" OR "janus kinase inhibitors" OR "leflunomide" OR "methotrexate" OR "methylprednisolone" OR "mycophenolate" OR "prednisolone" OR "prednisone" OR "rilonacept" OR "rituximab" OR "sarilumab" OR "secukinumab" OR "steroid" OR "steroids" OR "sulfasalazine" OR "tocilizumab" OR "tofacitinib" OR "ustekinumab" OR "immunosuppres*" OR "immuno suppresses*" OR "immune suppresses*" OR "Immunosuppressive Agent" OR "Immunosuppression" OR "tofacitinib" OR "tofacitinib" OR "baricitinib" OR "baricitinib" OR "upadacitinib" OR "upadacitinib" OR "upadacitinib" OR "upadacitinib" OR "Rinvoq") :ti,ab,kw AND ("mass screening" OR "screening" OR "tuberculin test" OR "interferon gamma release assay" OR "thorax radiography" OR "enzyme linked

immunospot assay" OR "hepatitis b surface antigen" OR "anti HBc" OR "anti HBV" OR "anti HCV" OR "anti HIV" OR "antiHBc" OR "antiHBV" OR "antiHCV" OR "antiHIV" OR "chest X ray" OR "elispot" OR "HBsAg" OR "HBV DNA" OR "IGRA" OR "Mantoux" OR "quantiferon" OR "screening" OR "tuberculin skin test" OR "tuberculin skin tests" OR "HBc" OR "HBV" OR "HCV" OR "HIV" OR "T Spot" OR "varicella serology" OR "anti VZV" OR "VZV" OR "varicella zoster virus" OR "chicken pox" OR "shingles" OR "anti VZV" OR "chickenpox" OR "chickenpox" OR "chicken pox" OR "HBc" OR "HBV" OR "HCV" OR "hiv" OR "hiv" OR "herpes zoster" OR "herpes zoster" OR "shingles" OR "shingle" OR "herpesvirus 3, human" OR "human herpesvirus 3" OR "varicella zoster virus" OR "T Spot" OR "TSpot" OR "Mycobacterium tuberculosis test kit" OR "varicella" OR "prevention and control" OR "Primary Prevention" OR "Secondary Prevention" OR "Tertiary Prevention" OR "Prophylaxis" OR "rifampin" OR "rifapentine" OR "itraconazole" OR "fluconazole" OR "azithromycin" OR "clarithromycin" OR "herpes zoster immunoglobulin" OR "entecavir" OR "tenofovir" OR "lamivudine" OR "acyclovir" OR "pentamidine" OR "valganciclovir" OR "acyclovir" OR "Azithromycin" OR "chemophrophylaxis" OR "chemophrophyl*" OR "Clarithromycin" OR "entecavir" OR "fluconazole" OR "isoniazide" OR "Itraconazole" OR "lamivudine" OR "pentamidine" OR "prevent*" OR "prophylaxis" OR "prophyla*" OR "rifampicin" OR "rifampin" OR "rifapentine" OR "sulfomethoxazole" OR "tenofovir" OR "trimethoprine" OR "valganciclovir" OR "Varicella zoster immune globulin*" OR "septrim" OR "co trimoxazole" OR "valacyclovir" OR "valacyclovir" OR "valaciclovir" OR "cotrimoxazole" OR "Trimethoprim, Sulfamethoxazole Drug Combination" OR "Centrin" OR "Cotrimoxazole" OR "Eslectin" OR "Insozalin" OR "TMP SMX" OR "Trimethoprim Sulfamethoxazole" OR "Sulfamethoxazole Trimethoprim" OR "Trimezole" OR "Co Trimoxazole" OR "TMP SMX" OR "Centran" OR "Trimedin" OR "Septrin" OR "Trimethoprimulsfa" OR "Bactifor" OR "Sumetrolim" OR "Abactrim" OR "Bactrim" OR "Biseptol" OR "Biseptol 480" OR "Biseptol480" OR "Drylin" OR "Eusaprim" OR "Kepinol" OR "Kepinol Forte" OR "Lescot" OR "Metomide" OR "Oriprim" OR "Septra" OR "Sulprim" OR "Trimosulfa" OR "Valacyclovir" OR "Valacyclovir" OR "Valaciclovir"):ti,ab,kw)

2. Supplementary Figure-1: Flow chart of the systematic literature review



3. Supplementary tables for Tuberculosis: The following tables present data about the conversion rate of tuberculin skin test and Interferon gamma release assay, after treatment with biologic disease modifying drugs, and also the various schemes used for latent TB reactivation, depending on the tuberculosis geographical burden

Supplementary Table 1: Conversion of TST or IGRA in AIIRD patients treated with bDMARDs

Author-date/Country	Patients (N)	Disease	Treatment	Conversion rate	Time	RoB
TST						
Hatzara 2014/Greece	70	AIIRD	TNFi	13%	12 months	8
Hejazi 2020/Iran	50	AIIRD	TNFi	2%	16 weeks	6
Thomas 2020/Greece	50	AIIRD	bDMARDs	22%	1.4 years and 6.9 years*	6
Cerda 2018/Argentina	85	IA	bDMARDs	9.4%	2-22 months	6
Cuomo 2017/Italy	249	RA	bDMARDs	13.6% [#]	24 months (median)	6
Park 2009/South Korea	86	AIIRD	TNFi	32.6%	12 months	6
Perez 2016/Spain	140	AIIRD	TNFi	4.3%	4.9 years (mean)	5
Chen 2008/Taiwan	43	RA	Adalimumab	37%	12 months	5
Bonfiglioli 2014/Brazil	202	RA	TNFi	9.8%	NS	5
Xie 2011/China	58	AIIRD	Infliximab	13.7%	12 months	4
IGRA						
Hatzara 2014/Greece	70	AIIRD	TNFi	10% [^] and 5% ^{\$}	12 months	8
He 2013/China	101	AIIRD	TNFi	11.2%	6 months	8
Kim 2019/South Korea	119	IA	TNFi	11.8%	25.9 months	7
Goel 2020/USA	115	RA	TNFi	9.6%	12 months	6
Thomas 2020/Greece	50	AIIRD	bDMARDs	4.8%	1.4 years and 6.9 years*	6
Cuomo 2017/Italy	249	RA	bDMARDs	13.6% [#]	24 months (median)	6
Son 2014/South Korea	127	AS	TNFi	7.9%	22.6 months (median)	6
Park 2009/South Korea	86	AIIRD	TNFi	14.1%	21.5 months (median)	6
Scrivo 2012/Italy	102	AIIRD	TNFi	13.6%	12 months	5

AIIRD: autoimmune inflammatory rheumatic diseases, AS: ankylosing spondylitis, bDMARDs: biologic DMARDs, IA: inflammatory arthritis, IGRA: interferon gamma release assay, N: number, RA: rheumatoid arthritis, RoB: risk of bias assessed by Newcastle-Ottawa scale (score 0-9), TNFi: TNF inhibitors, TST: tuberculin skin test

* two re-screenings, # converted TST and/or IGRA, ^ T-Spot, § quantiferon

Supplementary Table 2: Tuberculosis prophylaxis schemes in low-burden countries*

Author date/Country	Patients (N)	Disease	Treatment	Prophylaxis	TB reactivation rates	RoB
Carmona 2005/Spain	324	AIIRD	TNFi	INH9	34 (0.6%)**	9
Winthrop 2015/USA	286	RA	Tofacitinib	INH9	0 (0%)	8
Reino 2007/Spain	950	IA	TNFi	INH9	1 (0.11%)	8
Watanabe 2016/Japan	22	RA	Adalimumab	INH6-9	0 (0%)	7
Aggarwal 2009/USA	78	AIIRD	Etanercept	INH9	0 (0%)	7
Kurt 2013/Turkey	58	AIIRD	TNFi	INH9	0 (0%)	6
Hsia 2013/mixed	317	IA	Golimumab	INH6	0 (0%)	6
Bray 2006 France	93	IA	TNFi	RH3	0 (0%)	6
Sichletidis 2006/Greece	36	AIIRD	TNFi	INH6 or RH3	7 (19.4%)	5
Valls 2015/Spain	69	IA	TNFi	RH3	0 (0%)	4

AIIRD: autoimmune inflammatory rheumatic diseases, IA: Inflammatory arthritis, INH6-9: isoniazid for 6 to 9 months, RA: Rheumatoid arthritis, RH3: rifampicin, isoniazid for 3 months, RoB: risk of bias assessed by Newcastle-Ottawa scale (score 0-9), TB: tuberculosis, TNFi: TNF-inhibitors

* based on World Health Organization classification (please see main SLR manuscript) ** Comparing pre and post publication of national recommendations for management of latent TB, active TB rates decreased by 78% (incidence risk ratio 0.22, 95% CI [0.03–0.88] P=0.008)

Supplementary Table 3: Tuberculosis prophylaxis schemes in medium/high-burden countries*

Author-date/Country	Patients (N)	Disease	Treatment	Prophylaxis	TB reactivation rates N (%)	RoB
Malaviya 2018/India	267	IA	bDMARDs	INH6 or RH4	5 (1.9%)	7
Shobha 2018/India	21	AIIRDs	bDMARDs	RIF6 (n=14), INH6-9 (n=7)	0 (0.0%)	7
Shin 2021/South Korea	9474	RA	bDMARDs	INH9/RIF4/RH3	18/2249 (0.8%)**	6
Chen 2018/Taiwan	21 (3HP) and 23 INH9	RA	b- or ts- DMARDs	3HP vs INH9	0 (0.0%)	6
Gaitonde 2002/India	97	SLE	GC	INH12	2/95 (2.1%)	6
Bonfiglioli 2014/Brazil	66	RA	TNFi	INH6	0 (0.0%)	5
Song 2021/South Korea	187	RA	b- or ts- DMARDs	INH9	0 (0.0%)	5
Shen 2018/China	12	BD	TNFi	INH 6-9 or RIF3-4 or RH3-4	1 (8.3%)^	4

AIIRD: autoimmune inflammatory rheumatic diseases, bDMARDs: biologic DMARDs, GC: glucocorticoids, N: number, RA: rheumatoid arthritis, RoB: risk of bias assessed by Newcastle-Ottawa scale (score 0-9), IA: Inflammatory arthritis, INH6-9: isoniazid for 6 to 9 months, N: number, RIF 3-4: rifampicin for 3-4 months, SLE: systemic lupus erythematosus, TB: tuberculosis, TNFi: TNF-inhibitors, tsDMARDs: targeted synthetic DMARDs, 3HP: rifapentine, isoniazid for 3 months

* based on World Health Organization classification (please see manuscript) ** In this study, 100/7225 were not on prophylaxis: 1.38% (reactivation rate); HR: 0.52 (0.32, 0.86), in favor of those being on prophylaxis, ^ this patient refused to receive prophylaxis

4. Supplementary table for hepatitis B: the following table present the existing data for HBV-reactivation in HBsAg-positive patients with AIIRD treated with various immunosuppressives/immunomodulators, in relation to administration of anti-viral prophylaxis.

Supplementary Table 4: Antiviral prophylaxis and HBV reactivation in HBsAg-positive patients.

Author-date/Country	Patients (N)	Disease	Treatment	Prophylaxis N (%)	Reactivation N (%)	RoB
Su 2018/NA ⁺	2162*	AIIRD	anti-rheumatic drugs [#]	Yes: 111 (30.5) No: 253 (69.5)	RR: 0.51 (95% CI 0.26 - 0.98) RD: - 0.16 (95% CI -0.26 to - 0.06)	Medium quality
Lin 2016/NA ⁺	87 **	IA	csDMARDs	Yes: 29 (33.3) No: 58 (66.7)	Pooled Rate, % (95CI): 27.1 (12.4-44.8) Pooled rate, % (95CI): 22.4 (8.1-40.8)	High quality
Mo 2015/China	36	RA	anti-rheumatic drugs [#]	Yes: 18 (50.0) No: 18 (50.0)	7 (38.9) ^v 6 (33.3)	8
Matsuzaki 2017/Japan	20 ^{a,c}	RA	anti-rheumatic drugs [#]	0 (0)	4 (20.0)	7
Tan 2012/China	27	RA	csDMARDs	0 (0)	2/23 (8.7)	7
Chen 2017/Taiwan	123	RA	anti-rheumatic drugs [#]	0 (0)	30 (24.4)	6
Kalyoncu 2015/Turkey	76 ^a	IA	anti-rheumatic drugs [#]	Yes: 41 (54.0) No: 33 (43.4)	5 (12.2) 8 (24.2)	6
Chen 2021/Taiwan	55	SLE	Immunosuppressants	0 (0)	30 (54.5)	6
Jeong 2021/Taiwan	141	RA	anti-rheumatic drugs [#]	0 (0)	24 (17.0)	5
Kalyoncu 2009/Turkey	11	AIIRD	anti-rheumatic drugs [#]	11 (100)	0 (0)	5
Lin 2017/Taiwan	38	SLE	Immunosuppressants	Yes: 4 (10.5) No: 34 (89.5)	0 (0) 8 (23)	5
Yang 2007/Taiwan	98	DM/Pemphigus	GC	0 (0)	4/98 (4.1)	4
Xu 2015/China	17	RA	Leflunomide	ND	5 (31.3)	3
bDMARDs						
Lin 2016/NA ⁺	121	IA	TNF α	Yes: 57 (47.1) No: 64 (52.9)	Pooled Rate, % (95CI): 4.4 (0.4-11.7) Pooled Rate, % (95CI): 15.6 (2.3-35.7)	High quality
Giardina 2013/Italy	4	IA	TNF α	4 (100)	0 (0)	6
Ye 2014/China	31 ^{a,f}	IA	TNF α	Yes: 9 (29.0) No: 22 (71.0)	0 (0) 6 (27.3)	4
Zingarelli 2009/Italy	23 ^a	AIIRD	TNF α	Yes: 7 (30.4)	1 (14.3)	19 NA

				No: 16 (69.6)	12 (75.0)	
Ryu 2012/Korea	49	RA/AS	TNF _i	Yes: 20 (40.8)	1 (5)	5
				No: 29 (59.2)	2 (6.9)	
Lan 2011/Taiwan	18	RA	TNF _i	Yes: 10 (55.6)	0 (0)	8
				No: 8 (44.4)	5 (62.5)	
Vassilopoulos 2010/Greece	14	IMID	TNF _i	14 (100)	1 (7.1)	7
Lin 2019/Taiwan	11	RA	Tocilizumab	11 (100)	0 (0)	6
Chen 2017/China	7	RA	Tocilizumab	Yes: 2 (28.6)	0 (0)	6
				No: 5 (71.4)	3 (60.0)	
Kuo 2020/Taiwan	7	RA	Tocilizumab	Yes: 4 (57.1)	0 (0)	6
				No: 3 (42.9)	3 (100)	
Padovan 2016/Italy	47 ^{a, b}	RA	Abatacept	Yes: 9 (19.2)	0 (0)	6
				No: 38 (80.9)	0 (0)	
Chen 2018/Taiwan	6	RA	Tofacitinib	Yes: 2 (33.3)	0 (0)	6
				No: 4 (66.7)	2 (50.0)	
Wang 2021/Taiwan	8	RA	Tofacitinib	Yes: 2 (25.0)	0 (0)	6
				No: 6 (75.0)	2 (33.3)	

AIIRD: autoimmune inflammatory rheumatic diseases, AS: ankylosing spondylitis, bDMARDs: biologic DMARDs, CI: confidence intervals, csDMARDs: conventional synthetic DMARDs, GC: glucocorticoids, HBV: hepatitis B virus, IA: inflammatory arthritis, N: number, RA: rheumatoid arthritis, RD: rate

difference, RoB: risk of bias assessed by Newcastle-Ottawa scale (score 0-9) for all studies except from meta-analyses marked with this symbol ([†]) in which AMSTAR2 tool (quality score: critically low, low, moderate, high) was used, RR: rate ratio, SLE: systemic lupus erythematosus, TNFi: TNF-inhibitors

[†] meta-analysis, * 53 studies were included, # various types of anti-rheumatic drugs used ** 25 studies were included, ^ inactive carriers. § Four other patients were chronic carriers and received treatment with tenofovir and adefovir (2 each). They did not display any HBV reactivation. ¶ Four other patients were chronic carriers. Only those who did not receive prophylaxis (n=2) developed HBV reactivation, ^c None from the active carriers (n=22) developed reactivation (11 patients received prophylaxis)

^v5/7 had discontinued prophylaxis 1-7 months later

5. Supplementary table for *Pneumocystis jirovecii*: the following tables present the various dosage schemes of trimethoprim-sulfamethoxazole (TMP/SMX) that have been used as a prophylaxis for *pneumocystis jirovecii* as well as outcomes when regimes other than TMP/SMX are given for prophylaxis against this infectious agent.

Supplementary Table 5: Various dosage schemes of trimethoprim-sulfamethoxazole, as prophylaxis for PCP

Author-date/Country	Patients (N)	Disease	Treatment	Prophylaxis with TMP/SMX	Results	RoB
Utsunomiya 2017/Japan [†]	183	AIIRD	GC*	SS (n=58), HS (n=59), ES (n=55)	PCP 0% for all groups at week 24 AE: HS and ES lower DC due to AEs, Vs SS	High
Utsunomiya 2020/Japan [†]	172	AIIRD	GC*	SS (n=58), HS (n=59), ES (n=55)	PCP 0% for all groups at week 52 AE: lower in HS (19.1%, p<0.007) and ES (20.3%, p<0.007) than in SS (41.8%).	Some concerns
Harada 2021/Japan	220	AIIRD	antirheumatic drugs [#]	SS or 960/thrice weekly (n=145) Vs dose-reduction (n=75) [^] .	PCP 0% for all groups SS more AEs (p=0.017)	8
Takenaka 2013/Japan	44	AIIRD	antirheumatic drugs [#]	Routine group (n=28) Vs. Escalation group (n=13)	Escalation group: higher retention (100% Vs 71.4 %, p=0.032)	6
Suyama 2016/Japan	59	SLE	Immunosuppressants	SS (n=31) Vs graded administration (n=28)	Graded administration had less AE (p=0.009)	5

AIIRD: autoimmune inflammatory rheumatic diseases, AE: adverse events, ES: escalated strength, HS: half strength, N: number, PCP: *Pneumocystis Pneumonia*, RoB: risk of bias assessed by Newcastle-Ottawa scale (score 0-9) for all studies except RCTs in which Cochrane risk of bias tool (score for risk of bias: low, high, some concerns) was used, SLE: systemic lupus erythematosus, SS: single strength: 480mg/daily, TMP/SMX: trimethoprim-sulfamethoxazole, Vs: versus

[†] randomized controlled trial (RCT), * prednisolone>0.6mg/kg, # various types of anti-rheumatic drugs used, [^]dose reduction: 480 every-other day or thrice weekly

Supplementary Table 6: Alternative regimes (other than trimethoprim-sulfamethoxazole) as prophylaxis for PCP

Author-date/Country	Patients (N)	Disease	Treatment	Intervention	Outcome [§]	RoB
Kitazawa 2019/Japan	96	AIIRD	GC*	<ul style="list-style-type: none"> • TMP/SMX 480mg/day (n=55)[^] • Pentamidine 300mg/month (n=28)[^] • Atovaquone 1500mg/day (n=7)[^] 	PCP: 0% Treatment continuation (1 year) <ul style="list-style-type: none"> • TMP/SMX: 55.3%, • pentamidine: 66.8%, • atovaquone: 100% 	6
Schmajuk 2019/USA	316	Vasculitis, Myositis, SLE	anti-rheumatic drugs [#]	39% received prophylaxis <ul style="list-style-type: none"> • TMP/SMX (73%) • Dapsone (16%) • Atovaquone (10%) • Pentamidine (1%) 	PCP: 0%	8
Jinno 2021/Japan	388	AIIRD	GC**	<ul style="list-style-type: none"> • TMP/SMX 480mg/day (n=281) • Atovaquone 1500mg/day (n=107) 	Similar efficacy for PCP prevention (HR 0.97, 95% CI 0.19–5.09)	7
Sonomoto 2021/Japan	3787	RA	anti-rheumatic drugs [#]	<ul style="list-style-type: none"> • TMP/SMX (80–560 mg/week) (n=1520) • Pentamidine 300mg/visit (n=102) • Atovaquone 1500mg/day (n=3) 	TMP/SMX more effective Vs pentamidine (p<0.0001)	5

AIIRD: autoimmune inflammatory rheumatic diseases, CI: confidence intervals, GC: glucocorticoids, HR: hazard ratio, N: number, PCP: Pneumocystis Pneumonia, RoB: risk of bias assessed by Newcastle-Ottawa scale (score 0-9), SLE: systemic lupus erythematosus, TMP/SMX: trimethoprim-sulfamethoxazole
[§] efficiency in preventing PCP, *dose not defined, **prednisolone ≥20mg for ≥4 weeks, [^] final selection of agents in this study, # various types of anti-rheumatic drugs used