SUPPLEMENTARY MATERIAL

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METHODS

Infection screening and monitoring processes

Tuberculosis

Patients with evidence of active tuberculosis (TB) were excluded from Phase 3 trials. Patients with latent TB infection (LTBI), as documented by a positive purified protein derivative (PPD) or positive interferon-gamma release assay (IGRA), with no clinical symptoms or chest x-ray consistent with active TB, could be randomized after 4 weeks of appropriate LTBI therapy with agreement to complete the remainder of the treatment during the study. Patients with a prior history of active TB or LTBI with documented evidence of appropriate, completed treatment were permitted to enroll in the study without requiring further TB treatment.

Herpes zoster

Patients with symptomatic herpes zoster (HZ) infection within 12 weeks prior to the study were excluded. In the originating double-blind studies, patients diagnosed with HZ were to be permanently discontinued from study drug. In the long-term extension (LTE), patients diagnosed with HZ had study drug temporarily withheld and resumed when skin lesions were crusted and resolving. Phase 3 studies recommended HZ vaccination (in countries where the vaccine was available) at study entry for all patients who had not previously received the HZ vaccine; this live attenuated virus vaccination must have occurred >30 days prior to randomization.

Hepatitis B and C

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Patients were excluded from Phase 3 trials if they had active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection. Specifically, patients with the following hepatitis B serology results were excluded: 1) positive for hepatitis B surface antigen, 2) positive for anti-hepatitis B core antibody (HBcAb) but negative for hepatitis B surface antibody (HBsAb) (except where patients were permitted to enroll if HBV DNA negative), or 3) positive for anti-HBsAb and positive for HBV DNA, where required. Patients with positive anti-hepatitis C antibody with confirmed presence of HCV (assayed by immunoblot and/or polymerase chain reaction [PCR]) were excluded.

Ongoing surveillance of HBV DNA results was performed in Japan for patients with HBcAb+ and/or HBsAb+ at screening. This routine monitoring was later implemented for patients across all geographies with HBcAb+ at screening in accordance with HBV management guidelines (1).

Infection case identification and description

Serious infection was defined as any serious adverse event meeting International Conference on Harmonisation (ICH) E2A seriousness criteria (2) coded under the Infections and Infestations System Organ Class (SOC) of the Medical Dictionary for Regulatory Activities (MedDRA) v.20.0. Additionally, for all infection events, details were collected in the clinical database including the type of infection (bacterial, fungal, viral), the primary anatomical location of the infection, the infecting organism, and whether the infection was acquired in a healthcare setting. For tabulation of infections leading to death, all death events, including those reported as noninfectious adverse event terms, were reviewed by the sponsor to determine whether an underlying infectious process

contributed to death. Treatment-emergent (TE) TB infections were identified by sponsor-defined preferred terms from the MedDRA Tuberculosis Infections High Level Terms (HLT) and were summarized separately (Table S2). Cases of HZ were identified by sponsor-defined search criteria from the Herpes Viral Infections HLT in the MedDRA Infections and infestations SOC (Table S2). Opportunistic infections (OIs) were identified using sponsor-defined preferred terms from the MedDRA Infections and infestations SOC (Table S2). While TB is characterized as an OI, TE TB events in the baricitinib program were analyzed separately from other OIs.

Infection case reviews

For the TB, HZ, and OIs identified, all available data were reviewed, including medical history, concomitant medications, and laboratory test results. Investigators were queried for additional details to further characterize the case, such as confirmatory diagnostic test methods and results, relevant patient history, and recent travel or exposure. For HZ specifically, investigators were queried to provide details including the location and number of dermatomes affected, whether the dermatomes involved were contiguous and on the same side of the body, and whether there was associated motor neuropathy. These data were reviewed by the sponsor to further categorize the events. An external committee of 3 clinicians with infectious disease expertise independently reviewed the TB, multidermatomal HZ, and OI events in the baricitinib rheumatoid arthritis program using previously published OI consensus case definitions (3).

RESULTS

Infections

Tuberculosis

As baricitinib is associated with increased incidence of liver enzyme elevation compared to placebo (4), a post-hoc analysis was conducted to evaluate the hepatic safety in patients who received concomitant isoniazid (Phase 3 trials RA-BEAM, RA-BUILD, and RA-BEACON). Patients who reached a specified alanine aminotransferase (ALT) abnormality category (≥1, 3, 5, or 10 times the upper-limit-of-normal [ULN]) at any time post-baseline up to Week 24 were evaluated. The proportion of patients with ALT ≥1 time the ULN was numerically higher in patients who received isoniazid, compared to those who did not, and was consistent across treatment groups; few patients had elevated ALT ≥3 times the ULN (Table S7).

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Tables

Table S1. Patient populations

Study	Treatments	Dataset	Prior RA treatments	Rescue (Wk)[a]	Period Length (Wk)
Phase 1b					
I4V-MC-JADB(5) Open-label	Bari 15-mg Bari 10-mg Bari 5-mg BID	All-bari-RA	Background MTX	-	28 days
Phase 2					
NCT01185353(6)	Placebo Bari 8-mg Bari 4-mg Bari 2-mg Bari 1-mg	Placebo-controlled 2mg-4mg extended All-bari-RA	MTX-IR bDMARD naive	-	12 DB 12 BE 52 OE 52 OE
NCT00902486	Placebo Bari 10-mg Bari 7-mg Bari 4-mg	Placebo-controlled All-bari-RA	csDMARD-IR prior bDMARD allowed	-	12 DB 12 BE
NCT01469013(7) (Japan)	Placebo Bari 8-mg Bari 4-mg Bari 2-mg Bari 1-mg	Placebo-controlled 2mg-4mg extended All-bari-RA	MTX-IR prior bDMARD allowed[b]	-	12 DB 52 BE
Phase 3					
RA-BEAM(8); NCT01710358	Placebo Bari 4-mg Adalimumab	Placebo-controlled All-bari-RA	MTX-IR bDMARD naive	16	24 DB 28 DB[c] 52 DB[d]

RA-BEACON(9); NCT01721044	Placebo Bari 4-mg Bari 2 mg	Placebo-controlled 2mg-4mg extended All-bari-RA	TNFi-IR	16	24 DB
RA-BUILD(10); NCT01721057	Placebo Bari 4-mg Bari 2-mg	Placebo-controlled 2mg-4mg extended All-bari-RA	csDMARD-IR bDMARD naive	16	24 DB
RA-BEGIN(11); NCT01711359	MTX mono Bari 4-mg mono Bari 4-mg+MTX	All-bari-RA	DMARD naive	24	52 DB
LTE[e] RA-BEYOND; NCT01885078	Bari 4-mg Bari 2-mg	2mg-4mg extended All-bari-RA	Varied	PRN	Up to 6 years[f]

[a]First available rescue.

[b]Prior bDMARD allowed; however, patients could not have stopped treatment due to insufficient response.

[c]Double-blind with no placebo.

[d]Trial RA-BEAM had 24 weeks of placebo control and 52 weeks of active control.

[e]Studies contributing to LTE RA-BEYOND included Phase 2 trial NCT01185353 and Phase 3 trials RA-BEAM, RA-BEACON, RA-BUILD, and RA-BEGIN.

[f]Ongoing trial with data as of April 1, 2017.

Bari, baricitinib; BID, twice-daily; DB, double-bind; bDMARD, biologic DMARD; BE, blinded extension with no placebo; csDMARD-IR, conventional synthetic DMARD inadequate responder; DMARD, disease-modifying antirheumatic drug;

LTE, long-term extension; mono, monotherapy; MTX, methotrexate; MTX-IR, methotrexate inadequate responder; OE, open-label extension; PRN, pro re nata (as needed); RA, rheumatoid arthritis; TNFi-IR, tumor necrosis factor-inhibitor inadequate responder; Wk, week.

Table S2. Sponsor-defined MedDRA v.20.0 preferred terms for tuberculosis, herpes zoster, and other potential opportunistic infections

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
Mycobacterial/ Actino	Tuberculosis (I)	Adrenal gland tuberculosis	10001358
		Bone tuberculosis	10056377
		Bovine tuberculosis	10006049
		Choroid tubercles	10008779
		Congenital tuberculosis	10010657
		Conjunctivitis tuberculous	10010754
		Cutaneous tuberculosis	10011684
		Disseminated tuberculosis	10014027
		Ear tuberculosis	10015004
		Epididymitis tuberculous	10064445
		Erythema induratum	10015213
		Extrapulmonary tuberculosis	10061150
		Female genital tract tuberculosis	10072796
		Immune reconstitution inflammatory syndrome associated tuberculosis	10072797
		Interferon gamma release assay positive	10072866
		Intestinal tuberculosis	10075268
		Joint tuberculosis	10056367
		Latent tuberculosis	10065048
		Lupus vulgaris	10025143
		Lymph node tuberculosis	10025183
		Male genital tract tuberculosis	10061234
		Meningitis tuberculous	10027259
		Mycobacterium tuberculosis complex test positive	10070325
		Oesophageal tuberculosis	10030200
		Oral tuberculosis	10076879

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
		Pericarditis tuberculous	10055069
		Peritoneal tuberculosis	10053583
		Prostatitis tuberculous	10064743
		Pulmonary tuberculoma	10066927
		Pulmonary tuberculosis	10037440
		Renal tuberculosis	10038534
		Tuberculin test positive	10044728
		Salpingitis tuberculous	10039463
		Silicotuberculosis	10068876
		Spleen tuberculosis	10041640
		Thyroid tuberculosis	10043774
		Tuberculoma of central nervous system	10052883
		Tuberculosis	10044755
		Tuberculosis bladder	10044758
		Tuberculosis gastrointestinal	10061390
		Tuberculosis liver	10058120
		Tuberculosis of central nervous system	10061391
		Tuberculosis of eye	10044819
		Tuberculosis of genitourinary system	10044828
		Tuberculosis of intrathoracic lymph nodes	10044846
		Tuberculosis of peripheral lymph nodes	10044965
		Tuberculosis ureter	10045026
		Tuberculous abscess central nervous system	10052884
		Tuberculous endometritis	10071559
		Tuberculous laryngitis	10045072
		Tuberculous pleurisy	10045104
		Tuberculous tenosynovitis	10059161
		Tuberculin test false negative	10074840
Bacteria	Bartonellosis (disseminated disease only) (V)	Bacillary angiomatosis	10003971
		Bartonella test	10075209
		Bartonella test positive	10070157

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
		Bartonellosis	10004145
		Cat scratch disease	10007729
		Peliosis hepatis	10034229
		Splenic peliosis	10068851
		Trench fever	10044582
	Campylobacteriosis (invasive disease only) (V)	Campylobacter colitis	10076769
		Campylobacter gastroenteritis	10007048
		Campylobacter infection	10051226
		Campylobacter sepsis	10070681
		Campylobacter test positive	10070025
	Legionellosis (II)	Legionella infection	10061266
		Legionella test	10070410
		Legionella test positive	10070092
		Pneumonia legionella	10035718
		Pontiac fever	10054161
	Listeria monocytogenes (invasive disease only) (II)	Listeria encephalitis	10054116
		Listeria sepsis	10063085
		Listeria test	10075707
		Listeria test positive	10070094
		Listeriosis	10024641
		Meningitis listeria	10027248
	Salmonellosis (invasive disease only) (II)	Aortitis salmonella	10074937
		Arthritis salmonella	10003271
		Meningitis salmonella	10027254
		Osteomyelitis salmonella	10031262
		Paratyphoid fever	10033971
		Pneumonia salmonella	10035733
		Salmonella bacteraemia	10058924
		Salmonella sepsis	10058878
		Salmonella test positive	10070127
		Salmonellosis	10039447

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
		Typhoid fever	10045275
	Shigellosis (invasive disease only) (V)	Shigella infection	10054178
		Shigella test positive	10070129
		Shigella sepsis	10074481
	Vibriosis (invasive disease due to *V. vulnificus*) (V)	Gastroenteritis vibrio	10017917
		Vibrio test positive	10070161
Fungal	Aspergillosis (invasive disease only) (II)	Aspergillus infection	10074171
		Aspergillosis oral	10003489
		Aspergillus test	10070450
		Aspergillus test positive	10070488
		Bronchopulmonary aspergillosis	10006473
		Cerebral aspergillosis	10051597
		Meningitis aspergillus	10073245
		Oro-pharyngeal aspergillosis	10053029
		Sinusitis aspergillus	10051016
	Blastomycosis (IV)	Blastomycosis	10005098
		Epididymitis blastomyces	10015001
		Osteomyelitis blastomyces	10031255
		Pneumonia blastomyces	10035671
	Candidiasis (invasive disease, or oral not limited to the tongue) (II)	Bladder candidiasis	10058523
		Candida endophthalmitis	10059449
		Candida infection	10074170
		Candida osteomyelitis	10064699
		Candida pneumonia	10053158
		Candida retinitis	10068612
		Candida sepsis	10053166
		Candida test	10070453
		Candida test positive	10070451
		Candidiasis of trachea	10064459
		Cerebral candidiasis	10078126
		Endocarditis candida	10014669

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
		Gastrointestinal candidiasis	10017938
		Hepatic candidiasis	10049653
		Hepatosplenic candidiasis	10051590
		Meningitis candida	10027205
		Mucocutaneous candidiasis	10028080
		Oesophageal candidiasis	10030154
		Oral candidiasis	10030963
		Oropharyngeal candidiasis	10050346
		Peritoneal candidiasis	10056562
		Respiratory moniliasis	10038705
		Splenic candidiasis	10051725
		Systemic candida	10042938
	Coccidioidomycosis (II)	Coccidioides encephalitis	10054214
		Coccidioidomycosis	10009825
		Cutaneous coccidioidomycosis	10068747
		Meningitis coccidioides	10027207
	Cryptococcosis (II)	Cryptococcal cutaneous infection	10054216
		Cryptococcal fungaemia	10067112
		Cryptococcosis	10011490
		Cryptococcus test	10070456
		Cryptococcus test positive	10070455
		Disseminated cryptococcosis	10013439
		Gastroenteritis cryptococcal	10011485
		Meningitis cryptococcal	10027209
		Neurocryptococcosis	10068368
		Pneumonia cryptococcal	10067565
	Histoplasmosis (II)	Acute pulmonary histoplasmosis	10001027
		Chronic pulmonary histoplasmosis	10009115
		Endocarditis histoplasma	10014676
		Histoplasmosis	10020141
		Histoplasmosis cutaneous	10049142

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
		Histoplasmosis disseminated	10020144
		Meningitis histoplasma	10027243
		Pericarditis histoplasma	10034489
		Presumed ocular histoplasmosis syndrome	10063664
		Retinitis histoplasma	10038912
	Microsporidiosis (IV)	Microsporidia infection	10053982
	Other invasive fungi: Mucormycosis (=zygomycosis) [Rhizopus, Mucor, and Lichtheimia], *Scedosporum/ Pseudallescheria boydii*, *Fusarium* (II)	Allescheriosis	10001754
		Fusarium infection	10051919
		Mucormycosis	10028098
		Scedosporium infection	10059045
		Pseudallescheria infection	10061919
		Pseudallescheria sepsis	10058973
	Paracoccidioides infections (V)	Paracoccidioides infection	10061906
	Penicillium marneffei (V)	Penicillium infection	10078580
	Pneumocystis jirovecii (II)	Blood beta-D-glucan	10068725
		Blood beta-D-glucan abnormal	10051795
		Blood beta-D-glucan increased	10051793
		Gomori methenamine silver stain	10075549
		Carbon monoxide diffusing capacity decreased	10065906
		Carbon monoxide diffusing capacity	10071738
		Pneumocystis jirovecii infection	10073756
		Pneumocystis jirovecii pneumonia	10073755
		Pneumocystis test positive	10070454
	Sporothrix schenckii (V)	Cutaneous sporotrichosis	10011676
		Sporotrichosis	10041736
Viral	Cytomegalovirus disease (V)	Cytomegalovirus chorioretinitis	10048843
		Cytomegalovirus colitis	10048983
		Cytomegalovirus duodenitis	10049014
		Cytomegalovirus enteritis	10049074
		Cytomegalovirus enterocolitis	10049015
		Cytomegalovirus gastritis	10049016

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
		Cytomegalovirus gastroenteritis	10051349
		Cytomegalovirus gastrointestinal infection	10052817
		Cytomegalovirus gastrointestinal ulcer	10075619
		Cytomegalovirus hepatitis	10011830
		Cytomegalovirus infection	10011831
		Cytomegalovirus mononucleosis	10011834
		Cytomegalovirus mucocutaneous ulcer	10065036
		Cytomegalovirus myelomeningoradiculitis	10065621
		Cytomegalovirus myocarditis	10056261
		Cytomegalovirus nephritis	10079095
		Cytomegalovirus oesophagitis	10049018
		Cytomegalovirus pancreatitis	10049566
		Cytomegalovirus pericarditis	10056721
		Cytomegalovirus syndrome	10056262
		Cytomegalovirus test	10061806
		Cytomegalovirus test positive	10051620
		Cytomegalovirus urinary tract infection	10051350
		Cytomegalovirus viraemia	10058854
		Disseminated cytomegaloviral infection	10049075
		Encephalitis cytomegalovirus	10014586
		Pneumonia cytomegaloviral	10035676
	HBV reactivation (IV)	Asymptomatic viral hepatitis	10063838
		Chronic hepatitis B	10008910
		HBV-DNA polymerase increased	10058937
		Hepatitis B	10019731
		Hepatitis B antigen	10063414
		Hepatitis B antigen positive	10063411
		Hepatitis B core antigen	10051160
		Hepatitis B core antigen positive	10052328
		Hepatitis B DNA assay	10060027
		Hepatitis B DNA assay positive	10060047

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
		Hepatitis B DNA increased	10068379
		Hepatitis B e antigen	10050914
		Hepatitis B e antigen positive	10052329
		Hepatitis B reactivation	10058827
		Hepatitis B surface antigen	10050529
		Hepatitis B surface antigen positive	10019742
		Hepatitis B virus test	10068415
		Hepatitis B virus test positive	10070217
		Hepatitis infectious	10019780
		Hepatitis post transfusion	10019791
		Hepatitis viral	10019799
		Withdrawal hepatitis	10071220
	HCV progression (V)	Chronic hepatitis C	10008912
		Hepatitis C	10019744
		Hepatitis C RNA	10019748
		Hepatitis C RNA fluctuation	10068727
		Hepatitis C RNA increased	10068377
		Hepatitis C RNA positive	10019750
		Hepatitis C virus test	10068416
		Hepatitis C virus test positive	10070218
	Herpes simplex (invasive disease only) (IV)	Colitis herpes	10051782
		Eczema herpeticum	10014197
		Gastritis herpes	10051784
		Genital herpes	10018150
		Genital herpes simplex	10073931
		Herpes dermatitis	10062639
		Herpes oesophagitis	10052330
		Herpes ophthalmic	10062004
		Herpes pharyngitis	10066888
		Herpes sepsis	10058876
		Herpes simplex	10019948

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
		Herpes simplex colitis	10074239
		Herpes simplex encephalitis	10019953
		Herpes simplex gastritis	10074240
		Herpes simplex hepatitis	10067389
		Herpes simplex meningitis	10019956
		Herpes simplex meningoencephalitis	10074247
		Herpes simplex meningomyelitis	10074250
		Herpes simplex necrotising retinopathy	10074252
		Herpes simplex oesophagitis	10074242
		Herpes simplex otitis externa	10019959
		Herpes simplex pharyngitis	10074244
		Herpes simplex pneumonia	10065046
		Herpes simplex sepsis	10074246
		Herpes simplex visceral	10019963
		Herpes virus infection	10019973
		Meningitis herpes	10027242
		Meningoencephalitis herpetic	10027285
		Meningomyelitis herpes	10074249
		Nasal herpes	10074936
		Ophthalmic herpes simplex	10073938
		Oral herpes	10067152
		Pneumonia herpes viral	10035703
	Herpes zoster (any form) (II)	Disseminated varicella zoster vaccine virus infection	10076667
		Gastritis herpes	10051784
		Genital herpes zoster	10072210
		Herpes zoster	10019974
		Herpes zoster cutaneous disseminated	10074297
		Herpes zoster disseminated	10065038
		Herpes zoster infection neurological	10061208
		Herpes zoster meningitis	10074259

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
		Herpes zoster meningoencephalitis	10074248
		Herpes zoster meningomyelitis	10074251
		Herpes zoster necrotising retinopathy	10074253
		Herpes zoster oticus	10063491
		Herpes zoster pharyngitis	10074245
		Ophthalmic herpes zoster	10030865
		Varicella zoster gastritis	10074241
		Varicella zoster oesophagitis	10074243
		Varicella zoster pneumonia	10074254
		Varicella zoster virus infection	10075611
	Human polyomavirus infection including BK virus disease and PVAN (V), and progressive multifocal leukoencephalopathy (IV)	BK virus infection	10055181
		Human polyomavirus infection	10057366
		JC virus granule cell neuronopathy	10074361
		JC virus infection	10023163
		JC virus test	10068794
		Polyomavirus-associated nephropathy	10065381
		Polyomavirus test	10075038
		Polyomavirus test positive	10070342
		Progressive multifocal leukoencephalopathy	10036807
	Post-transplant lymphoproliferative disorder (EBV) (V)	Epstein-Barr viraemia	10065110
		Epstein-Barr virus associated lymphoma	10071441
		Epstein-Barr virus associated lymphoproliferative disorder	10068349
		Epstein-Barr virus infection	10015108
		Lymphoproliferative disorder	10061232
		Lymphoproliferative disorder in remission	10061233
		Oral hairy leukoplakia	10030979
		Post transplant lymphoproliferative disorder	10051358
Parasites	Trypanosoma cruzi infection (Chagas' Disease) (disseminated disease only) (V)	American trypanosomiasis	10001935
		Trypanosomiasis	10044707
		Meningitis trypanosomal	10027258

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
	Cryptosporidium species (chronic disease only) (IV)	Biliary tract infection cryptosporidial Cryptosporidiosis infection Gastroenteritis cryptosporidial	10067319 10011502 10017899
	Leishmaniasis (Visceral only) (IV)	Leishmaniasis Visceral leishmaniasis	10024198 10047505
	Stronglyoides (hyperinfection syndrome and disseminated forms only) (IV)	Strongyloidiasis	10042254
	Toxoplasmosis (IV)	Cerebral toxoplasmosis Eye infection toxoplasmal Hepatitis toxoplasmal Meningitis toxoplasmal Myocarditis toxoplasmal Pneumonia toxoplasmal Toxoplasma serology Toxoplasmosis	10057854 10015939 10019798 10048848 10028617 10067566 10050941 10044272
Non-specific terms	Non-specific terms	Abscess fungal Alternaria infection Arthritis fungal Biliary tract infection fungal Central nervous system fungal infection Cerebral fungal infection Encephalitis fungal Erythema induratum Eye infection fungal Fungaemia Fungal abscess central nervous system Fungal endocarditis Fungal labyrinthitis Fungal oesophagitis Fungal peritonitis	10000269 10054207 10060966 10065203 10072805 10049657 10065170 10015213 10015933 10017523 10017524 10017529 10065174 10049656 10061138

Category	Potential Opportunistic Infection	Preferred Term (MedDRA Version 20.0)	Preferred Term Code
		Fungal pharyngitis	10076516
		Fungal retinitis	10068613
		Fungal sepsis	10058872
		Hepatic infection fungal	10065217
		Meningitis fungal	10027236
		Mycotic endophthalmitis	10063202
		Myocarditis mycotic	10059026
		Oral fungal infection	10061324
		Oropharyngitis fungal	10061891
		Osteomyelitis fungal	10065239
		Otitis media fungal	10065175
		Pancreatitis fungal	10065190
		Pericarditis fungal	10065220
		Phaehyphomycosis	10034799
		Pneumonia fungal	10061354
		Pulmonary mycosis	10037422
		Pulmonary trichosporonosis	10068184
		Sinusitis fungal	10058678
		Splenic infection fungal	10065194
		Systemic mycosis	10052366

HBV, hepatitis B virus; HCV, hepatitis C virus; JC virus, John Cunnigham virus; PVAN, polyomavirus-associated nephropathy.

Table S3. Baseline demographics and disease characteristics

	Placebo-controlled (to Week 24)		**2mg-4mg-extended**		**All-bari-RA**
Baseline Demographics	Placebo N=1070	Bari 4-mg N=997	Bari 2-mg N=479	Bari 4-mg N=479	All-bari-RA N=3492[a]
Age, years, mean (SD)	52.9 (11.9)	53.7 (12.0)	53.2 (12.0)	53.6 (11.7)	52.9 (12.2)
Female, n (%)	862 (80.6)	794 (79.6)	386 (80.6)	391 (81.6)	2760 (79.0)
Duration of RA[b], years, mean (SD)	8.9 (8.4)	8.9 (8.6)	9.0 (8.1)	9.1 (8.6)	7.7 (8.2)
Region, n (%)					
United States/Canada	240 (22.4)	225 (22.6)	162 (33.8)	162 (33.8)	840 (24.1)
Central and South America/Mexico	203 (19.0)	197 (19.8)	54 (11.3)	54 (11.3)	701 (20.1)
Asia (excluding Japan)	84 (7.9)	83 (8.3)	38 (7.9)	35 (7.3)	226 (6.5)
Japan	156 (14.6)	132 (13.2)	36 (7.5)	39 (8.1)	514 (14.7)
European Union	263 (24.6)	246 (24.7)	125 (26.1)	124 (25.9)	783 (22.4)
Rest of World	124 (11.6)	114 (11.4)	64 (13.4)	65 (13.6)	428 (12.3)
Glucocorticoid use[c], n (%)					
None	460 (43.0)	459 (46.0)	233 (48.6)	229 (47.8)	1738 (49.8)

0.1-4.9 mg/day	122(11.4)	95 (9.5)	40 (8.4)	39 (8.1)	326 (9.3)
5-7.4 mg/day	274 (25.6)	254 (25.5)	121 (25.3)	112 (23.4)	831 (23.8)
7.5+ mg/day	214 (20.0)	189 (19.0)	85 (17.7)	99 (20.7)	597 (17.1)
Baseline MTX use, n (%)	967 (90.4)	903 (90.6)	386 (80.6)	394 (82.3)	2661 (76.2)
Baseline MTX dose, mg/week, median (25^{th}, 75^{th} percentile)	15.0 (10.0, 20.0)	15.0 (12.0, 20.0)	15.0 (11.3, 20.0)	15.0 (12.5, 20.0)	15.0 (10.0, 20.0)
BMI, kg/m^2, mean (SD)	27.8 (7.1)	28.0 (6.8)	29.0 (7.4)	29.2 (7.6)	27.7 (6.7)
Baseline disease characteristics	Placebo N=1070	Bari 4-mg N=997	Bari 2-mg N=479	Bari 4-mg N=479	All-bari-RA N=3439[d]
ACPA positive, n (%)	758 (80.7)	731 (79.9)	313 (73.3)	304 (71.0)	2474 (81.6)
RF positive, n (%)	856 (82.9)	799 (82.8)	358 (74.7)	360 (75.3)	2770 (83.6)
Swollen join count, of 66, mean (SD)	15.0 (9.2)	14.8 (8.0)	15.7 (10.4)	14.5 (7.7)	12.0 (9.6)
Tender joint count, of 68, mean (SD)	23.8 (14.3)	24.0 (13.8)	25.6 (15.3)	24.7 (14.6)	19.6 (15.2)
hsCRP, mg/L, mean (SD)	18.3 (21.5)	18.9 (21.3)	17.8 (21.6)	15.8 (19.4)	17.3 (22.4)
ESR, mm/hour, mean (SD)	46.2 (24.9)	46.0 (25.1)	43.8 (22.3)	42.9 (24.3)	42.4 (25.4)
CDAI, mean (SD)	37.2 (12.7)	37.7 (12.4)	38.4 (13.3)	37.3 (12.6)	30.8 (16.7)
DAS28-ESR, mean (SD)	6.3 (1.0)	6.4 (1.0)	6.4 (1.0)	6.3 (1.0)	5.7 (1.5)
DAS28-hsCRP, mean (SD)	5.6 (1.0)	5.7 (0.9)	5.7 (1.0)	5.6 (1.0)	5.1 (1.5)

[a]All-bari-RA (patients who received any baricitinib dose) includes patients who switched from placebo, adalimumab, or methotrexate to baricitinib, in addition to patients randomized to any baricitinib dose. Thus, it is a larger group than the 2-mg and 4-mg groups added together.

[b]Time from RA diagnosis.

[c]Expressed as prednisone-equivalent dose.

[d]The number for the all-bari-RA group is smaller for disease activity measures than for demographics because efficacy baseline disease activity measures are only available for Phase 2/3 studies.

ACPA, anti-citrullinated peptide antibody; Bari, baricitinib; BMI, body mass index; CDAI, Clinical Disease Activity Index; DAS28-ESR, 28-joint Disease Activity Score based on the ESR; DAS28-hsCRP, DAS28 based on the hsCRP level; ESR, erythrocyte sedimentation rate; hsCRP, high sensitivity C-reactive protein; MTX, methotrexate; n, number of patients in the specified category; N, number of patients in the analysis set; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation.

Table S4. Serious infection incidence rate by selected subgroups for the placebo-controlled analysis set

	Placebo-controlled (to Week 24)[a]		
	Placebo N=1070 IR (n/Ns)	Bari 2-mg[b] N=479 IR (n/Ns)	Bari 4-mg N=997 IR (n/Ns)
Total patients with ≥1 serious infections	4.2 (17/1070)	4.2 (8/479)	3.8 (16/997)
Line of therapy			
bDMARD-IR	7.4 (5/176)	5.6 (4/174)	7.9 (6/177)
csDMARD-IR	3.6 (12/894)	3.3 (4/305)	2.9 (10/820)
Age			
<65	3.3 (11/897)	3.1 (5/397)	3.0 (10/798)
≥65	9.3 (6/173)	9.0 (3/82)	7.2 (6/199)
Region			
Asia (excluding Japan)	3.0 (1/84)	5.8 (1/38)	2.8 (1/83)
Central and South America/Mexico	3.6 (3/203)	4.8 (1/54)	3.5 (3/197)
European Union	5.0 (5/263)	3.8 (2/125)	2.9 (3/246)
Japan	1.8 (1/156)	0	1.9 (1/132)
United States/Canada	4.6 (4/240)	3.0 (2/162)	3.3 (3/225)
Rest of World	6.7 (3/124)	8.1 (2/64)	10.8 (5/114)
BMI (kg/m^2)			
<18 (underweight)	0	0	10.3 (1/24)

18-24 (normal)	2.8 (4/388)	1.7 (1/156)	2.0 (3/353)
25-29 (overweight)	0.9 (1/310)	7.7 (4/125)	3.0 (4/318)
≥30 (obese)	9.4 (12/333)	4.0 (3/184)	6.4 (8/301)
Glucocorticoid use			
Yes	5.6 (13/610)	4.0 (4/246)	5.3 (12/538)
No	2.3 (4/460)	4.3 (4/233)	2.1 (4/459)

[a]Data from treatment period up to Week 24, with data up to rescue.

[b]Baricitinib 2-mg data in the placebo-controlled analysis set are derived from 4 studies in which both baricitinib 2-mg and 4-mg were options during randomization.

Bari, baricitinib; bDMARD-IR, biologic disease-modifying antirheumatic drug inadequate responder; BMI, body mass index; csDMARD-IR, conventional synthetic DMARD inadequate responder; IR, incident rate; N, number of patients in the analysis set; n, number of patients in the specified category; Ns, number of patients by subset in each category.

Table S5. Tuberculosis rates and events by endemic region: general population and baricitinib RA program

Country	Published TB IR in General Population[a] per 100 People/Year[b]	Reports of TB in Patients Receiving Bari IR (n/N)
Argentina	0.024	0.09 (1/424)
Taiwan	0.039[c]	1.26 (3/92)
Russian Federation	0.066	0.29 (1/130)
South Korea	0.077	0.48 (1/84)
India	0.211	1.00 (2/131)
South Africa	0.781	1.99 (3/65)

[a]General population refers to the non-RA patient population; incidence rate in the RA population is estimated at 4- to 10-fold higher than the general population (12).

[b]Source: World Health Organization 2018 (13). Data were converted from 100,000 to 100 people/year.

[c]Source: Taiwan Centers for Disease Control 2019 (14).

Bari, baricitinib; IR, incidence rate; n, number of patients with TB; N, number of patients treated; RA, rheumatoid arthritis; TB, tuberculosis.

Table S6. Vignettes for patients with tuberculosis

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Asia (excluding Japan) Age: 50- <60 BMI: 18.5- <25 [hydroxychloroquine, MTX 15-mg PO weekly, methylprednisolone 2-mg PO QD] Originating study: Adalimumab	Screening IGRA negative. Miliary TB including lungs and spleen, Day 169, adalimumab. Occurred 9 days after last dose of adalimumab. Treated and recovered.
Region: Asia (excluding Japan) Age: 50- <60 BMI: 18.5- <25 [hydroxychloroquine, methylprednisolone 4-mg PO QD, MTX 10-mg PO weekly] Originating study: Bari 4-mg	Screening IGRA indeterminate; no repeat or latent TB Rx (deviation). Miliary TB including lungs, Day 137, Bari 4-mg. Occurred on Bari 4-mg. Treated and recovered.
Region: Rest of World Age: 40- <50 BMI: 25 - <30 [MTX 20-mg PO weekly] Originating study: Placebo, rescued to Bari 4-mg	Screening PPD skin test negative. TB included supraclavicular lymph node, Day 218, Bari 4-mg. Occurred on Bari 4-mg. Treated, not recovered by time of discontinuation from study.
Region: Rest of World Age: 30- <40 BMI: 25- <30 [MTX 15-mg PO weekly] Originating study: Bari 4-mg LTE: Bari 4-mg	Screening IGRA negative. Lesions including T-L vertebrae, Day 396, Bari 4-mg. Occurred 8 days after last dose of Bari 4-mg. No organism confirmed; PCR and culture not performed. Treated, recovering; study discontinued due to bone tuberculosis.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Rest of World Age: 50- <60 BMI: <18.5 [MTX 20-mg PO weekly] Originating study: Bari 4-mg LTE: Bari 4-mg	Screening PPD skin test negative. Lesions including T-L vertebrae and psoas abscess, Day 474, Bari 4-mg. Occurred on Bari 4-mg. No organism confirmed; PCR and culture not performed. Treated, recovered, Bari resumed.
Region: Rest of World Age: 30- <40 BMI: 25- <30 [MTX 20-mg PO weekly, methylprednisolone 8-mg PO QD] Originating study: Bari 4-mg LTE: Bari 4-mg	Screening IGRA pos x1, neg x1; no latent TB Rx (deviation). Lesions including lungs, Day 516, Bari 4-mg. Occurred 1 day after last dose of Bari 4-mg. No organism confirmed. Treated, not recovered at the time of discontinuation from study due to TB.
Region: Central and South America/Mexico Age: 30- <40 BMI: 25- <30 [MTX 10-mg PO weekly] Originating study: Bari 4-mg LTE: Bari 4-mg	Screening IGRA negative. TB including mediastinum, Day 566, Bari 4-mg. Occurred 10 days after last dose of Bari 4-mg. Prednisone stopped approximately 2 months prior to TB. Co-infection with paracoccidiodes. Treated and considered recovered.
Region: Asia (excluding Japan) Age: 50- <60 BMI: 18.5- <25 [sulfasalazine, hydroxychloroquine] Originating study: Bari 4-mg LTE: Bari 4-mg	Screening IGRA positive; latent TB treated with isoniazid for approximately 6 months during study participation; treatment completed prior to onset of TB infection event. TB including lung, Day 617, Bari 4-mg. Occurred on Bari 4-mg. Also had Dengue Fever (serious adverse event). Treated; recovered from Dengue Fever, latent TB ongoing.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Rest of World Age: 60- <70 BMI: 18.5- <25 [MTX 25-mg PO weekly, prednisone 5-mg PO QOD] Originating study: Adalimumab LTE: Bari 4-mg	Screening PPD skin test negative. TB including lungs and abdomen, Day 161, Bari 4-mg. Occurred 7 days after last dose of Bari 4-mg. Sustained elevation acute phase markers, leukocytes, immunoglobulins, and significant weight loss began during adalimumab treatment in originating study. Treated, fatal outcome.
Region: Asia (excluding Japan) Age: 60- <70 BMI: 18.5- <25 [MTX 15-mg PO weekly, sulfasalazine, prednisolone 5-mg PO QD] Originating study: Bari 4-mg LTE: Bari 4-mg	IGRA was indeterminate at screening and upon retest. Latent TB treated with isoniazid for approximately 1 year during study participation; treatment completed prior to onset of TB infection event. Granulomatous lesion lymph node neck, Day 851, Bari 4-mg. Occurred on Bari 4-mg. No organism confirmed tissue and sputum stains. No PCR provided. Treated, recovered, Bari resumed.
Region: Asia (excluding Japan) Age: 60- <70 BMI: 25- <30 [MTX 15-mg PO weekly, prednisone 5-mg PO QD, hydroxychloroquine] Originating study: Adalimumab, rescued to Bari 4-mg LTE: Bari 4-mg	Screening IGRA negative. TB including lung, Day 545, Bari 4-mg. Occurred on Bari 4-mg. Treatment for TB administered. The patient died due to acute myocardial infarction 6 months after TB event onset.
Region: Rest of World Age: 30- <40 BMI: <18.5 [hydroxychloroquine, MTX 17.5-mg PO weekly] Originating study: Placebo LTE: Bari 4-mg	Screening IGRA negative. TB including abdomen, Day 952, Bari 4-mg. Occurred on Bari 4-mg. Concurrent event of typhoid fever. Treated, recovering.

[a]Central and South America/Mexico included Argentina, Brazil, and Mexico; Asia (excluding Japan) included China, South Korea, and Taiwan; European Union included Austria, Belgium, Croatia, Czech Republic, Denmark, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and United Kingdom; Rest of World included Australia, India, Israel, Russia, South Africa, Switzerland, Turkey, and Ukraine.

Bari, baricitinib; BMI, body mass index; DMARD, disease-modifying antirheumatic drug; GC, glucocorticoid; IGRA, interferon gamma release assay (QuantiFERON); LTE, long-term extension; MTX, methotrexate; PCR, polymerase chain reaction; PPD, purified protein derivative; PO, by mouth; QD, daily; QOD, every other day; Rx, treatment; TB, tuberculosis; T-L, thoracolumbar.

Table S7. Maximum ALT through Week 24 in patients receiving concomitant isoniazid versus no isoniazid[a]

	Placebo N=892		**Bari 2-mg** N=403		**Bari 4-mg** N=891	
	INH (Ns=57)	No INH (Ns=835)	INH (Ns=27)	No INH (Ns=376)	INH (Ns=58)	No INH (Ns=833)
ALT maximum, n (%)						
≥1xULN	21 (36.8)	183 (21.9)	9 (33.3)	82 (21.8)	24 (41.4)	260 (31.2)
≥3xULN	2 (3.5)	13 (1.6)	2 (7.4)	6 (1.6)	0	13 (1.6)
≥5xULN	2 (3.5)	3 (0.4)	1 (3.7)	1 (0.3)	0	5 (0.6)
≥10xULN	0	0	1 (3.7)	0	0	2 (0.2)

[a]Data reported in patients with available laboratory results and who received isoniazid (Phase 3 trials RA-BEAM, RA-BUILD, RA-BEACON).

ALT, alanine aminotransferase; Bari, baricitinib; INH, isoniazid; N, number of patients in the treatment group; n, number of patients in the specified category; Ns, number of patients by subset in each category; ULN, upper limit of normal.

Table S8. Herpes zoster incidence rate by region in the All-bari-RA analysis set

	All-bari-RA N=3492 IR (n/NAR)
Number of patients with herpes zoster	3.3 (258/3492)
Region[a]	
United States/Canada	4.2 (68/840)
Central and South America/Mexico	1.7 (30/701)
Asia (excluding Japan)	6.3 (32/226)
Japan	6.9 (68/514)
European Union	2.2 (43/783)
Rest of World	1.8 (17/428)

[a]Central and South America/Mexico included Argentina, Brazil, and Mexico; Asia (excluding Japan) included China, South Korea, and Taiwan; European Union included Austria, Belgium, Croatia, Czech Republic, Denmark, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and United Kingdom; Rest of World included Australia, India, Israel, Russia, South Africa, Switzerland, Turkey, and Ukraine.

Bari, baricitinib; IR, incidence rate; N, number of patients in the analysis set; n, number of patients in the specified category; NAR, number of patients at risk.

Table S9. Herpes zoster incidence rate by glucocorticoid dose in the All-bari-RA analysis set

	All-bari-RA N=3492 IR (n/NAR)
Glucocorticoid dose at first Bari dose[a]	
None	3.4 (111/1738)
0.1–4.9 mg/day	5.0 (32/326)
≥5 mg/day	2.9 (83/1428)

[a]Expressed as prednisone-equivalent dose.

Bari, baricitinib; IR, incidence rate; N, number of patients in the analysis set; n, number of patients in the specified category; NAR, number of patients at risk; RA, rheumatoid arthritis.

Table S10. Vignettes for patients with viral infections of interest

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Multidermatomal Herpes Zoster[b]	
Region: European Union Age: ≥70 BMI: 18.5- <25 [prednisone 5-mg PO QD] Originating study: Placebo	Onset of HZ: 2 days after the first dose of placebo. Dermatomes T7 through T12. Serious: no; Severity: moderate. Treated and resolved.
Region: Asia (excluding Japan) Age: 40- <50 BMI: 25- <30 [prednisolone 5-mg PO QD] Originating study: Bari 4-mg	Onset of HZ: 69 days after the first dose of Bari, while on Bari 4-mg. The patient presented with an itchy, red rash over right chest and right back with pain. Dermatomes T7 through T10 were involved. The patient also experienced complication of post-herpetic neuralgia, which resolved, along with the HZ, 1 month after the onset of the HZ. Serious: no; Severity: moderate. Treated and resolved.
Region: Japan Age: 50- <60 BMI: 25- <30 [MTX 2-mg PO thrice weekly, methylprednisolone 4-mg PO QD] Originating study: Bari 1-mg, switched to Bari 8-mg	Onset of HZ: 160 days after the first dose of Bari (76 days after switch to Bari 8-mg); onset while on Bari 8-mg. The patient had a rash without blisters accompanied by tingling pain on the left side of the body (head to lower leg: back of left head, left back, left breech, thigh, and lower leg). Concurrently developed chondrosarcoma in left femur. Serious: yes; Severity: severe. Treated and ongoing at the time of study discontinuation.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Japan Age: 50- <60 BMI: 25- <30 [MTX 10-mg PO weekly] Originating study: Bari 4-mg	Onset of HZ: 171 days after the first dose of Bari, while on Bari 4-mg. The patient had red blisters in large area from right arm (C5 and C6 dermatomes) to the head occipital and parietal regions (C2 and C3 dermatomes). Serious: no; Severity: mild. Treated and ongoing at the time of study discontinuation. At the time of the post study safety follow-up visit, the patient had skin pigmentation but no neuralgia was noted.
Region: Japan Age: 50- <60 BMI: 18.5- <25 [MTX 16-mg PO weekly, prednisolone 6-mg PO QD] Originating study: Placebo, rescued to Bari 4-mg LTE: Bari 4-mg	Onset of HZ: 228 days after the first dose of Bari, while on Bari 4-mg. The patient had blisters appear on the left temporal region and the right side of the abdomen to the back side. Involvement of dermatomes C2 and T9 were noted. Serious: yes; Severity: mild. Treated and resolved.
Region: Asia (excluding Japan) Age: ≥70 BMI: 18.5- <25 [MTX 15-mg PO weekly] Originating study: Placebo LTE: Bari 4-mg but received 2-mg (due to renal impairment)	Onset of HZ: 233 days after the first dose of Bari while on Bari 2-mg (due to renal impairment). Multidermatomal involvement reported: L2/L4/S1, primary location was noted on the skin of the right thigh. Serious: no; Severity: moderate. Treated and resolved.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Central and South America/Mexico Age: 60- <70 BMI: 18.5- <25 [MTX 7.5-mg PO twice weekly] Originating study: Bari 2-mg LTE: Bari 2-mg, rescued to Bari 4-mg (but continued to receive 2-mg due to renal impairment)	First case: Onset of HZ: 252 days after the first dose of Bari, while on Bari 2-mg. One dermatome (L4) in the left femoral region was affected. Second case: Onset of HZ: 1032 days after the first dose of Bari, while on Bari 4-mg. The second case was determined to be multidermatomal as dermatomes T1 through T6 were affected (right thoracic region). An AE of "herpetic neuralgia" was recorded with the same onset date as the second case and ended 6 days after the HZ. Serious: no (both cases); Severity: moderate (both cases). Treated and resolved (both cases).
Region: Asia (excluding Japan) Age: 50- <60 BMI: 25- <30 [none] Originating study: Placebo LTE: Bari 4-mg	Onset of HZ: 517 days after the first dose of Bari, while on Bari 4-mg. Multidermatomal involvement reported: The primary location was noted on left side of back with dermatomes T8-12 affected. Serious: no; Severity: mild. Treated and resolved.
Region: Japan Age: ≥70 BMI: 18.5- <25 [MTX 4-mg PO weekly, prednisolone 1-mg PO QD] Originating study: Placebo, switched to Bari 4-mg LTE: Bari 4-mg	Onset of HZ: 313 days after the first dose of Bari, while on Bari 4-mg. Multidermatomal involvement reported: Dermatomes of the first division of the trigeminal nerve bilaterally and the left side only for the second and third division of the trigeminal nerve, C7, T2, and L2. Serious: no; Severity: mild. Treated and resolved.
Region: Asia (excluding Japan) Age: 40- <50 BMI: 18.5- <25 [MTX 12.5-mg PO weekly, triamcinolone 2-mg PO QD, hydroxychloroquine] Originating study: Placebo, rescued to Bari 4-mg LTE: Bari 4-mg	Onset of HZ: 433 days after the first dose of Bari, while on Bari 4-mg. Reported to involve 3 noncontiguous dermatomes on the right thigh and back. Serious: no; Severity: moderate. No treatment reported and event resolved.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Japan Age: 60- <70 BMI: 25- <30 [MTX 13-mg PO weekly] Originating study: Bari 4-mg LTE: Bari 4-mg	Onset of HZ: 675 days after the first dose of Bari, while on Bari 4-mg. Patient first presented with blisters in left anterior chest, left upper back, and left upper arm (C1 to C4). Additional medical report stated that HZ was seen in the area of trigeminal nerve third division on the left side of face to the neck (V5-3 to C1). Serious: yes; Severity: moderate. Treated and resolved.
Region: United States/Canada Age: 60- <70 BMI: ≥30 [MTX 17.5-mg PO weekly] Originating study: Bari 4-mg LTE: Bari 4-mg, step-down to Bari 2-mg, rescued to Bari 4-mg	Onset of HZ: 829 days after the first dose of Bari, while on Bari 2-mg. Multidermatomal involvement reported: Dermatomes T8-T12 on the left side with small amount of blister development. Serious: no; Severity: mild. Treated and resolved.
Region: United States/Canada Age: 50- <60 BMI: 25- <30 [MTX 15-mg PO weekly] Originating study: Bari 4-mg + MTX LTE: Bari 4-mg	Onset of HZ: 965 days after the first dose of Bari, while on Bari 4-mg. Dermatomes T12 on lower left back and L3 on left inner thigh. Serious: no; Severity: moderate. Treated and resolved.
Region: Japan Age: 50- <60 BMI: 18.5- <25 [MTX 6-mg PO weekly] Originating study: MTX LTE: Bari 4-mg	Onset of HZ: 538 days after the first dose of Bari, while on Bari 4-mg. Investigator reported as disseminated zoster. Multidermatomal involvement reported: Erythema appeared at nose and left side of face (V1 and V2) and rash showed up on trunk. Serious: no; Severity: moderate. Treated and resolved.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Japan Age: 60- <70 BMI: 25- <30 [MTX 8-mg PO weekly, prednisolone 3-mg PO QD] Originating study: Bari 4-mg LTE: Bari 4-mg	Onset of HZ: 651 days after the first dose of Bari, while on Bari 4-mg. Multidermatomal involvement reported: 5 dermatomes affected; right breast, armpit, back. Serious: no; Severity: mild. Treated and resolved.
Region: Japan Age: 50- <60 BMI: 25- <30 [MTX 12-mg PO weekly, prednisolone 2-mg PO QD] Originating study: Bari 4-mg LTE: Bari 4-mg	Onset of HZ: 770 days after the first dose of Bari, while on Bari 4-mg. Multidermatomal involvement reported: 6 dermatomes on the left buttock. Serious: no; Severity: mild. Treated and resolved.
Region: Japan Age: 60- <70 BMI: 25- <30 [MTX 10-mg PO weekly] Originating study: Adalimumab LTE: Bari 4-mg, step-down to Bari 2-mg	Onset of HZ: 782 days after the first dose of Bari, while on Bari 2-mg. Multidermatomal involvement reported: C3, C5, and C7. Serious: no; Severity: mild. Treated and resolved.
Region: Japan Age: 60- <70 BMI: 18.5- <25 [MTX 8-mg PO weekly] Originating study: Bari 4-mg LTE: Bari 4-mg, step-down to Bari 2-mg	Onset of HZ: 785 days after the first dose of Bari, while on Bari 2-mg. Multidermatomal involvement reported: Right lower extremity, right buttock extending down to lateral aspect of right toes, also left side of lip and right forehead and right neck. Dermatomes listed as L4, L5, S1, S2, S3, and C2. Serious: yes; Severity: moderate. Treated and recovering.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Japan Age: <30 BMI: 18.5- <25 [MTX 6-mg PO weekly] Originating study: Placebo, switched to Bari 4-mg LTE: Bari 4-mg	Onset of HZ: 826 days after the first dose of Bari, while on Bari 4-mg. Multidermatomal involvement reported: buttocks (S2), right thigh (L2, S2), and right ankle (L4). Serious: no; Severity: mild. Treated and resolved.
Region: Japan Age: 50- <60 BMI: 18.5- <25 [MTX 8-mg PO weekly, prednisolone 4-mg PO QD] Originating study: Placebo, rescued to Bari 4-mg LTE: Bari 4-mg	Onset of HZ: 858 days after the first dose of Bari, while on Bari 4-mg. Multidermatomal involvement reported: Left arm only - C5, C6, C8, and T1. Serious: no; Severity: moderate. Not treated but resolved.
Region: Japan Age: 40- <50 BMI: 18.5- <25 [MTX 4-mg PO weekly, prednisolone 1-mg PO QD] Originating study: Bari 4-mg LTE: Bari 4-mg	Onset of HZ: 862 days after the first dose of Bari, while on Bari 4-mg. Multidermatomal involvement reported: Right T4, T5, T6, and T7 from right back to right side. Serious: yes; Severity: moderate. Treated and resolved.
Region: Central and South America/Mexico Age: 50- <60 BMI: 25- <30 [MTX 7.5-mg PO twice weekly] Originating study: Bari 4-mg LTE: Bari 4-mg	Onset of HZ: 874 days after the first dose of Bari, while on Bari 4-mg. Multidermatomal involvement reported: Same side of body from T5 to T10. Serious: no; Severity: mild. Treated and resolved.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Central and South America/Mexico Age: 50- <60 BMI: 25- <30 [prednisone 5-mg PO QD] Originating study: Bari 4-mg LTE: Bari 4-mg, step-down to Bari 2-mg, rescued to Bari 4-mg	Onset of HZ: 1033 days after the first dose of Bari, while on Bari 4-mg. Multidermatomal involvement reported: Left C3, C4, left posterior C5 and C6. Serious: no; Severity: moderate. Treated and resolved.
Cytomegalovirus	
Region: Central and South America/Mexico Age: 40- <50 BMI: 18.5- <25 [MTX 20-mg PO weekly, prednisone 5-mg PO QD] Originating study: Bari 4-mg LTE: Bari 4-mg	Day 711 post first dose of Bari; CMV infection; severe, serious due to hospitalization. Occurred on Bari 4-mg. Fever, recent antibiotics for UTI, elevated transaminases, Blood PCR + for CMV 850 copies/mL. Elevated transaminases prompted CMV investigation; anatomic site reported as blood. Serum CMV IgG +, IgM - Recovered (25 days) following treatment with valganciclovir.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: United States/Canada Age: 60- <70 BMI: ≥30 [MTX 20-mg PO weekly] Originating study: Adalimumab LTE: Bari 4-mg	Day 736 post first dose of Bari; CMV infection (identified after the patient had been hospitalized, intubated, and transferred to ICU due to severe septic shock) moderate, nonserious. Concurrent events of oral and esophageal candidiasis (both identified after initial hospitalization due to pneumonia). Occurred 11 days after last dose of Bari 4-mg. Preexisting splenectomy. BAL and blood PCR positive for CMV. Pneumonia infecting agent unknown; blood cultures positive for gram positive diplococci. CMV infection treated with ganciclovir. Pneumonia treated with multiple antibiotics. Outcome: Patient discontinued study drug and study due to death from pneumonia.
Region: European Union Age: 40- <50 BMI: ≥30 [Leflunomide] Originating study: Placebo, rescued to Bari 4-mg LTE: Bari 4-mg	Day 895 post first dose of Bari; CMV infection; moderate, nonserious. Occurred on Bari 4-mg. Primary site of infection unknown. No details on clinical features or method of diagnosis available. Treated with lamaline and paracetamol. Outcome: Recovered; infection lasted less than 1 month.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Japan Age: 50- <60 BMI: ≥30 [MTX 16-mg PO weekly] Originating study: Placebo, rescued to Bari 4-mg LTE: Bari 4-mg	Day 1023 post first dose of Bari; pneumonia; severe, nonserious. At the time of the CMV pneumonia diagnosis, the patient was hospitalized in ICU for infective cholangitis and septic shock and was subsequently diagnosed with pancreatic carcinoma with multiple liver metastases. Occurred 21 days after last dose of Bari 4-mg. Tobacco use (10 cigarettes/day). Primary site of infection = lung. Blood CMV antigen positive. Treated with ganciclovir and paracetamol. Outcome: Resolved (26-day duration); patient discontinued study drug and study due to infective cholangitis.
Region: Asia (excluding Japan) Age: 60- <70 BMI: 25- <30 [MTX 15-mg PO weekly, prednisolone 5-mg PO QD] Originating study: Placebo LTE: Bari 4-mg	Day 1035 post first dose of Bari; pneumonia; severe, serious due to hospitalization. Occurred on Bari 4-mg. Primary site of infection = lung. Primary infecting agent was CMV and secondary infection agent was *Pneumocystis carinii*. BAL PCR + for CMV and PCP; blood PCR + for CMV. Treatment for pneumonia included peramivir, Bactrim, levofloxacin, piperacillin, valganciclovir, cefepime, fluconazole, teicoplanin, ganciclovir, clindamycin, primaquine, meropenem, and immunoglobulin human normal. Outcome: Patient discontinued study drug and study due to pneumonia. Following the prolonged hospitalization, the patient died due to CMV PCP pneumonia (50 days after the last dose of Bari and 22 days after study discontinuation).
Epstein-Barr virus	

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Japan Age: 60- <70 BMI: 18.5- <25 [MTX 16-mg PO weekly, prednisolone 0.5-mg PO QD] Originating study: Bari 4-mg	Day 141 post first dose of Bari. Mild, nonserious Epstein-Barr virus infection. Alcohol use reported, but no history of liver disease or cholecystitis. Patient received prophylactic isoniazid and pyridoxal. Low elevation of ALT was noted. Evaluation included EBNA-1 positive, VCA-IgG positive, VCA-IgM positive and hep A IgM positive. No event of lymphoproliferative disorder or other concurrent symptoms were reported. Folic acid dose was increased from 1-mg to 1.5-mg in response to the event, but no treatment was administered. Baricitinib was continued and the event resolved.
Hepatitis E virus	
Region: Rest of World Age: 30- <40 BMI: 25- <30 [prednisolone 5-mg PO QD] Originating study: MTX LTE: Bari 4-mg	Day 78 post first dose of Bari and 3 days after the last dose patient was diagnosed with acute hepatitis E. Medical history included viral hepatitis. Patient reported pregnancy 11 weeks after starting Bari, elected to terminate the pregnancy and discontinued the study. Liver enzymes were well above normal. IgM hep A ab negative, total hep A ab positive, hep B surface antigen negative, hep B surface ab positive, hep E IgM and hep E IgG positive, and hep E PCR positive. Patient was clinically asymptomatic and recovered.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Central and South America/Mexico Age: 30- <40 BMI: 18.5- <25 [none] Originating study: MTX LTE: Bari 4-mg	198 days after first dose of Bari, patient was diagnosed with a hepatitis E infection. Medical history included alcohol use and cholecystectomy. Liver enzymes were well above normal. Hep E IgM, Hep E IgG and Hep E PCR positive; Hep A IgM, Hep B core antibody, Hep B surface antigen, and Hep B surface antibody negative; Hep A antibody positive. Abdominal ultrasound showed liver steatosis but no other findings. The patient was asymptomatic during the course of the event. Patient discontinued study drug and study due to the event.
Hepatitis B virus	
Region: Rest of World Age: <30 BMI: 25- <30 [methylprednisolone 8-mg PO QD] Originating study: Bari 8-mg	281 days after first dose of Bari, patient was diagnosed with acute hepatitis B. Reported as a serious adverse event. Medical history included smoking (1 pack/day for 12 years), biliary dyskinesia; meloxicam and MTX use (stopped approximately 1 month prior to the event). Patient visited dentist 1 month prior to symptom onset. Hep B core antibody negative at baseline. At time of event, liver enzymes were significantly elevated. Hep B core antibody positive. Patient discontinued study drug and study due to the event and recovered.
Region: United States/Canada Age: 50- <60 BMI: ≥30 [none] Originating study: Bari 4-mg + MTX	282 days after first dose of Bari and 2 days after last dose, patient was diagnosed with acute hepatitis B. Reported as a serious adverse event. Medical history included meloxicam use; patient's spouse tested positive for hepatitis B. Hep B core antibody negative at baseline. At time of event, liver enzymes were significantly elevated. Hep B core antibody reactive, hep B surface antigen positive. Patient discontinued study drug and study due to the event.

[a]Central and South America/Mexico included Argentina, Brazil, and Mexico; Asia (excluding Japan) included China, South Korea, and Taiwan; European Union included Austria, Belgium, Croatia, Czech Republic, Denmark, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and United Kingdom; Rest of World included Australia, India, Israel, Russia, South Africa, Switzerland, Turkey, and Ukraine.

[b]Infection distributed beyond primary and adjacent dermatomes.

Ab, antibody; AE, adverse event; ALT, alanine aminotransferase; BAL, bronchoalveolar lavage; Bari, baricitinib; BMI, body mass index; CMV, cytomegalovirus; DMARD, disease-modifying antirheumatic drug; EBNA, Epstein-Barr nuclear antigen; GC, glucocorticoid; Hep, hepatitis; HZ, herpes zoster; ICU, intensive care unit; Ig, immunoglobulin; LTE, long-term extension; MTX, methotrexate; PCP, *Pneumocystis* pneumonia; PCR, polymerase chain reaction; PO, orally; QD, daily; UTI, urinary tract infection; VCA, viral capsid antigen.

Table S11. Vignettes for patients with fungal infections of interest

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Aspergillus infection	
Region: Japan Age: 50- <60 BMI: 18.5- <25 [MTX 16-mg PO weekly, prednisolone 1-mg PO QD] Originating study: Bari 4-mg LTE: Bari 4-mg	Day 139 post first dose of Bari. Occurred on Bari 4-mg. Originally reported as mucocutaneous candidiasis. Subsequently, the event term was changed to aspergillosis. Mild, non-serious; skin around both eyes affected. Biopsy quantitative PCR and aspergillus antibody was negative, although diagnosis was deep fungal infection (aspergillus suspected). Treated with antibiotics and antifungals, including amphotericin B, voriconazole, and clotrimazole. Infection ongoing. Adverse events of HTLV carrier and preexisting condition of tinea versicolor of the trunk were also noted.
Candidiasis (nonsuperficial)	
Region: Central and South America/Mexico Age: 50- <60 BMI: 25- <30 [MTX 15-mg PO weekly, prednisone 10-mg PO QD] Originating study: Bari 4-mg	Day 11 post first dose of Bari; esophageal candidiasis EGD; moderate, non-serious. Occurred 10 days after last dose of Bari 4-mg. Permanently discontinued study drug 1 day after randomization (and first and only dose of Bari 4-mg) with dyspepsia and liver abnormality. Culture negative. Treated with fluconazole.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Central and South America/Mexico Age: 50- <60 BMI: ≥30 [MTX 15-mg PO weekly, prednisone 5-mg PO QD] Originating study: Placebo, rescued to Bari 4-mg	Onset of muscle abscess (gluteal region) while still on placebo, and event resolved prior to first dose of Bari; moderate, serious due to hospitalization. Etiology not provided. Preexisting condition of diabetes and candiuria. Site reported infecting agents of the abscess as *Candida albicans*, *Candida tropicalis*, *Staphylococcus*, and *Klebsiella pneumoniae*. Treated with amoxicillin and clavulanic acid. Also treated during the trial for preexisting condition of candiduria with fluconazole. Day 62 after rescued to first dose of Bari, subject was hospitalized for a left hand soft tissue infection. Culture showed methicillin-resistant *Staphylococcus*, *K pneumoniae*, and *C tropicalis*.
Region: Japan Age: ≥70 BMI: 25- <30 [none] Originating study: Bari 4-mg + MTX	Day 70 post first dose of Bari 4-mg + MTX; esophageal candidiasis; mild, nonserious. Occurred on Bari 4-mg + MTX. Seen concurrent with erosive gastritis and *Helicobacter pylori* infection. No interruption to study drug. No antifungal Rx reported.
Region: Rest of World Age: 60- <70 BMI: 25- <30 [MTX 15-mg PO weekly, prednisolone 5-mg PO QD] Originating study: Bari 4-mg	Day 120 post first dose of Bari; esophageal candidiasis; mild, non-serious. Occurred on Bari 4-mg. Preexisting chronic gastritis, hiatal hernia, and gastro-esophageal reflux disease. EGD showed erosive gastritis. Reported as “clinical symptom of candida esophagitis due to white raid on gullet.” Biopsy was done and candida was not confirmed. Discontinued study due to gastric ulcer. No antifungal Rx reported.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Japan Age: ≥70 BMI: 18.5- <25 [MTX 10-mg PO weekly, prednisolone 10-mg PO QD] Originating study: Bari 2-mg, switched to 8-mg, switched to 4-mg	Day 146 post first dose of Bari; esophageal candidiasis; mild, non-serious. Occurred on Bari 8-mg. History of diabetes mellitus. Recent antibiotics for cataract surgery. No interruption to study drug. Treated with itraconazole and amphotericin B.
Region: Japan Age: ≥70 BMI: 25- <30 [MTX 8-mg PO weekly] Originating study: Placebo, switched to Bari 4-mg	Day 154 post first dose of Bari; esophageal candidiasis; mild, non-serious. Occurred on Bari 4-mg. Reported concurrently with gastritis and *H pylori* infection. No interruption to study drug. Received miconazole oral gel.
Region: European Union Age: 60- <70 BMI: 18.5- <25 [MTX 15-mg PO weekly] Originating study: Bari 4-mg LTE: Bari 4-mg	Day 492 post first dose of Bari; lung infection; moderate, non-serious. Occurred on Bari 4-mg. Preexisting condition of bronchiectasis. Treated with fluconazole, levofloxacin, and pristinamycin. Recovered.
Region: Rest of World Age: 40- <50 BMI: ≥30 [leflunomide] Originating study: Placebo, rescued to Bari 4-mg LTE: Bari 4-mg	Day 72 post first dose of Bari; sinusitis, mild, non-serious. Occurred on Bari 4-mg. Preexisting conditions of asthma, allergic rhinitis, otitis media, and viral upper respiratory tract infection. Primary site of infection in paranasal sinus. Infection of mixed aerobic and anaerobic bacteria with the primary infecting agent of *Candida glabrata*. Treated with spektramox (augmentin duo forte) and prednisone. Recovered (duration of infection 28 days); patient discontinued study drug and study due to lack of efficacy.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Central and South America/Mexico Age: 50- <60 BMI: 25- <30 [MTX 20-mg IM weekly, leflunomide, prednisone 5-mg PO QD] Originating study: Bari 4-mg LTE: Bari 4-mg	Day 540 post first dose of Bari; oesophageal candidiasis; moderate, non-serious. Occurred 5 days after last dose of Bari 4-mg. Smoker, preexisting condition of dyspepsia. Treated with nystatin and miconazole gel. Infection ongoing at time of study drug discontinuation.
Region: United States/Canada Age: 60- <70 BMI: ≥30 [MTX 20-mg PO weekly, hydroxychloroquine] Originating study: Adalimumab LTE: Bari 4-mg	Day 729 post first dose of Bari; oral candidiasis and esophageal candidiasis (both identified after patient was hospitalized for pneumonia); moderate (both), non-serious (both). Patient had concurrent CMV infection (identified after admittance to ICU due to bacterial sepsis). Occurred 4 days after last dose of Bari 4-mg. Preexisting conditions of splenectomy, hypothyroidism, hypersensitivity, and obesity. Treated with nystatin. Outcome: Both infections resolved (24-day duration); patient discontinued study drug and study due to death from pneumonia.
Cryptococcal infection	
Region: Japan Age: 60- <70 BMI: 25- <30 [MTX 6-mg PO weekly, sulfasalazine] Originating study: Bari 2-mg LTE: Bari 2-mg	Day 460 post first dose of Bari; cryptococcal pneumonia; severe, serious due to hospitalization. Occurred 21 days after last dose of Bari 2-mg. The patient reported touching bird droppings when she cleaned car windows or clotheslines without gloves. Occupation: nurse. Pathological diagnosis from right lung tumor was cryptococcal pulmonary. Blood was positive for *Cryptococcus neoformans* antigen. Treated with fosfluconazole, fluconazole, and amoxicillin. Patient was reported as recovering from the infection.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Histoplasmosis	
Region: United States/Canada Age: <30 BMI: ≥30 [MTX 20-mg PO weekly, sulfasalazine] Originating study: Bari 2-mg LTE: Bari 2-mg	Day 264 post first dose of Bari; histoplasmosis; severe, serious due to hospitalization. Occurred 8 days after last dose of Bari 2-mg. Resident of a region in the United States where histoplasmosis is common. Biopsy of paratracheal lymph node was performed, although histoplasma cultures were not sent. Infectious disease impression was mediastinal histoplasmosis (presumed). All titers were negative (CFT<1:8) except for 1 that was + at a titer of 1:2048 in the CFT against yeast antigen. Treated with itraconazole, salbutamol, morphine, laryton, and procet. Patient was reported as recovering from the infection.
Paracoccidiodes	
Region: Central and South America/Mexico Age: 30- <40 BMI: 25- <30 [MTX 10-mg PO weekly] Originating study: Bari 4-mg LTE: Bari 4-mg	Day 566 post first dose of Bari; paracoccidioides infection; moderate, serious due to hospitalization. Co-infection with tuberculosis. Occurred 10 days after last dose of Bari 4-mg. Prednisone stopped approximately 2 months prior to infection. Pathology report from biopsy of lung confirmed lesions were compatible with paracoccidioidomycosis. (The same sample later also yielded a mycobacterium, identified as TB by PCR.) Treated with itraconazole; reported as asymptomatic, but not recovered.
Pneumocystis	
Region: Japan Age: 60- <70 BMI: <18.5 [MTX 8-mg PO weekly] Originating study: Placebo, switched to Bari 4-mg	Day 69 post first dose of Bari; severe, serious due to hospitalization. Occurred day after last dose of Bari 4-mg. Baseline lymphocytes ↓ (800 x 10^9 cells/L), screening eGFR < 60 mL/min. Asymptomatic, modest ↑ β-d-glucan. Ground glass chest CT. No microbiology. Recovered following treatment for PCP.

Region[a] / Age (years) / BMI (kg/m^2) [Concomitant DMARD/glucocorticoid; MTX and GC dose at time of event] **Study Drug**	**Brief Description**
Region: Japan Age: 60- <70 BMI: 18.5- <25 [none] Originating study: Bari 4-mg + MTX	Day 99 post first dose of Bari + MTX; severe, serious due to hospitalization. Occurred while on Bari 4-mg + MTX. Fever, dyspnea, modest ↑ β-d-glucan local laboratory. Ground glass chest CT. No microbiology. Recovered following treatment for PCP.
Region: Japan Age: 50- <60 BMI: <18.5 [MTX 6-mg PO weekly, methylprednisolone 1-mg PO BID] Originating study: Bari 2-mg, switched to Bari 8-mg	Day 148 post first dose of Bari, Day 60 post first dose Bari 8-mg; severe, serious due to hospitalization. Occurred 7 days after last dose of Bari 8-mg. Baseline lymphocytes ↓ (640 x 10^9 cells/L). Sputum production, modest ↑ β-d-glucan. Ground glass chest CT. Sputum PCR positive for PCP at site, negative at hospital. Recovered following treatment for PCP.
Region: Asia (excluding Japan) Age: 60- <70 BMI: 25- <30 [MTX 15-mg PO weekly, prednisolone 5-mg PO QD] Originating study: Placebo LTE: Bari 4-mg	Day 1035 post first Bari dose; pneumonia; severe, serious due to hospitalization and life-threatening. Occurred on Bari 4-mg. Primary site of infection = lung. Primary infecting agent was CMV and secondary infection agent was *Pneumocystis carinii*. BAL PCR + for CMV and PCP; blood PCR + for CMV. Treatment for pneumonia included peramivir, Bactrim, levofloxacin, piperacillin, valganciclovir, cefepime, fluconazole, teicoplanin, ganciclovir, clindamycin, primaquine, meropenem, and immunoglobulin human normal. Outcome: Patient discontinued study drug and study due to pneumonia. Following prolonged hospitalization, the patient died due to CMV PCP pneumonia (50 days after the last dose of Bari and 22 days after study. discontinuation).

[a]Central and South America/Mexico included Argentina, Brazil, and Mexico; Asia (excluding Japan) included China, South Korea, and Taiwan; European Union included Austria, Belgium, Croatia, Czech Republic, Denmark, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and United Kingdom; Rest of World included Australia, India, Israel, Russia, South Africa, Switzerland, Turkey, and Ukraine.

BAL, bronchoalveloar lavage; Bari, baricitinib; BID, twice daily; BMI, body mass index; CFT, Complement fixation test; CMV, cytomegalovirus; CT, computed tomography; DMARD, disease-modifying antirheumatic drug; EGD, esophagogastroduodenoscopy; EGFR, estimated glomerular filtration rate; GC, glucocorticoid; HTLV, human T-lymphotropic virus; ICU, intensive care unit; IM, intramuscular; LTE, long-term extension; MTX, methotrexate; PCP, *Pneumocystis* pneumonia; PCR, polymerase chain reaction; PO, orally; QD, daily; Rx, treatment; TB, tuberculosis.

Table S12. Hepatitis B virus DNA detected after randomization in baricitinib RA clinical studies

Patients with HBV DNA testing, n	290
Patients with detectable HBV DNA, n (%)	36[a] (12.4%)
DNA not quantifiable (<29 IU/mL), n	27
DNA quantifiable (≥29 IU/mL), n	9[b]
HBcAb+ at screening, n	8
Received antiviral treatment, n	3
ALT/AST ≥3 x ULN, n	0

[a]One patient with detectable HBV DNA in the all-bari-RA analysis set first became detectable while receiving adalimumab in study RA-BEAM before switching to baricitinib 4-mg in the extension study.

[b]Nine patients had levels of 31, 36, 60, 76, 92, 256, 257, 869, and 1547 IU/mL.

ALT, alanine transaminase; AST, aspartate transaminase; Bari, baricitinib; HBcAb, anti-hepatitis B core antibody; HBV, hepatitis B virus; n, number of patients in the specified category; RA, rheumatoid arthritis; ULN, upper limit of normal.

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