Safety and efficacy of bimekizumab in patients with psoriatic arthritis: 2-year results from two phase 3 studies

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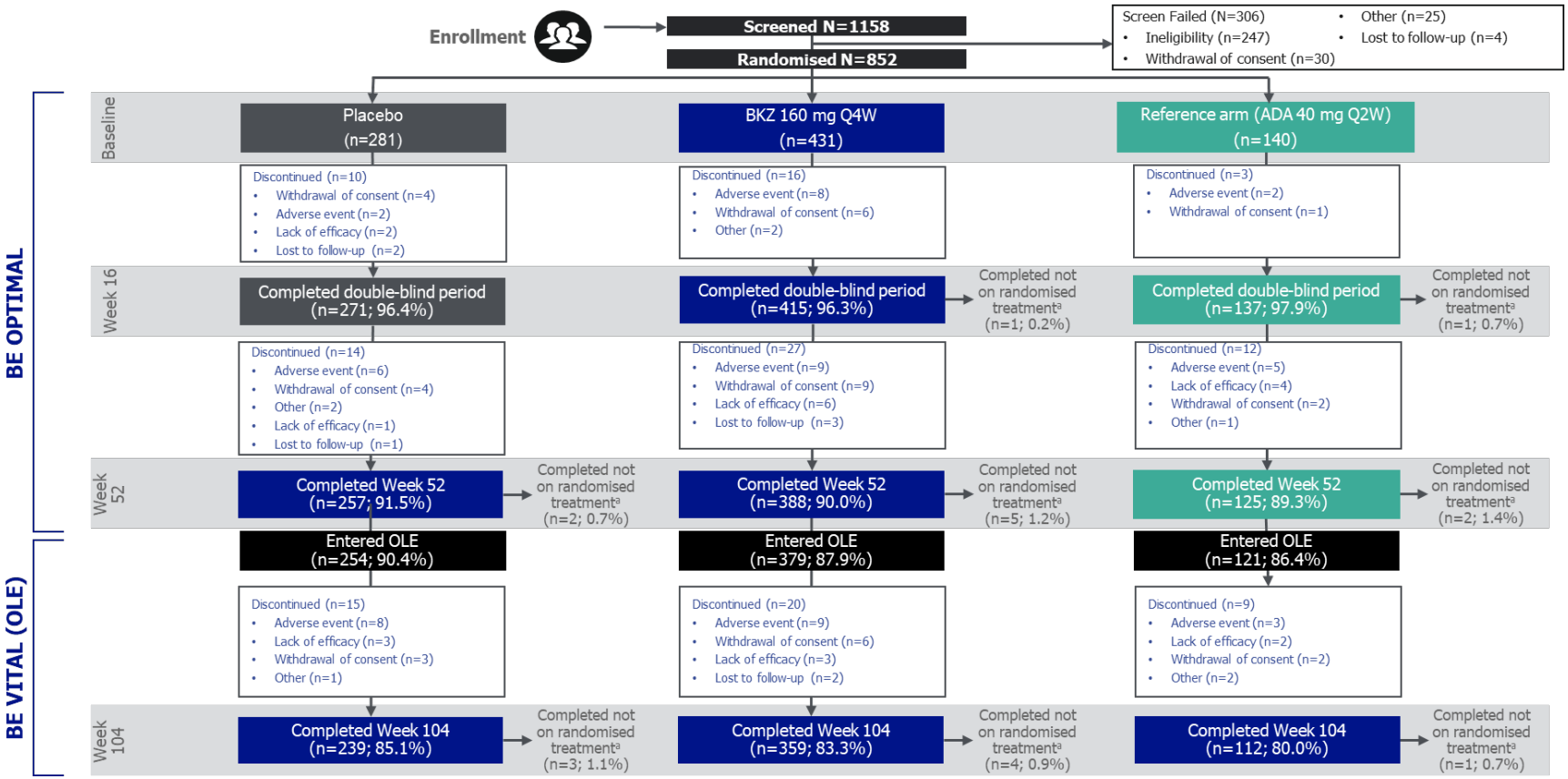
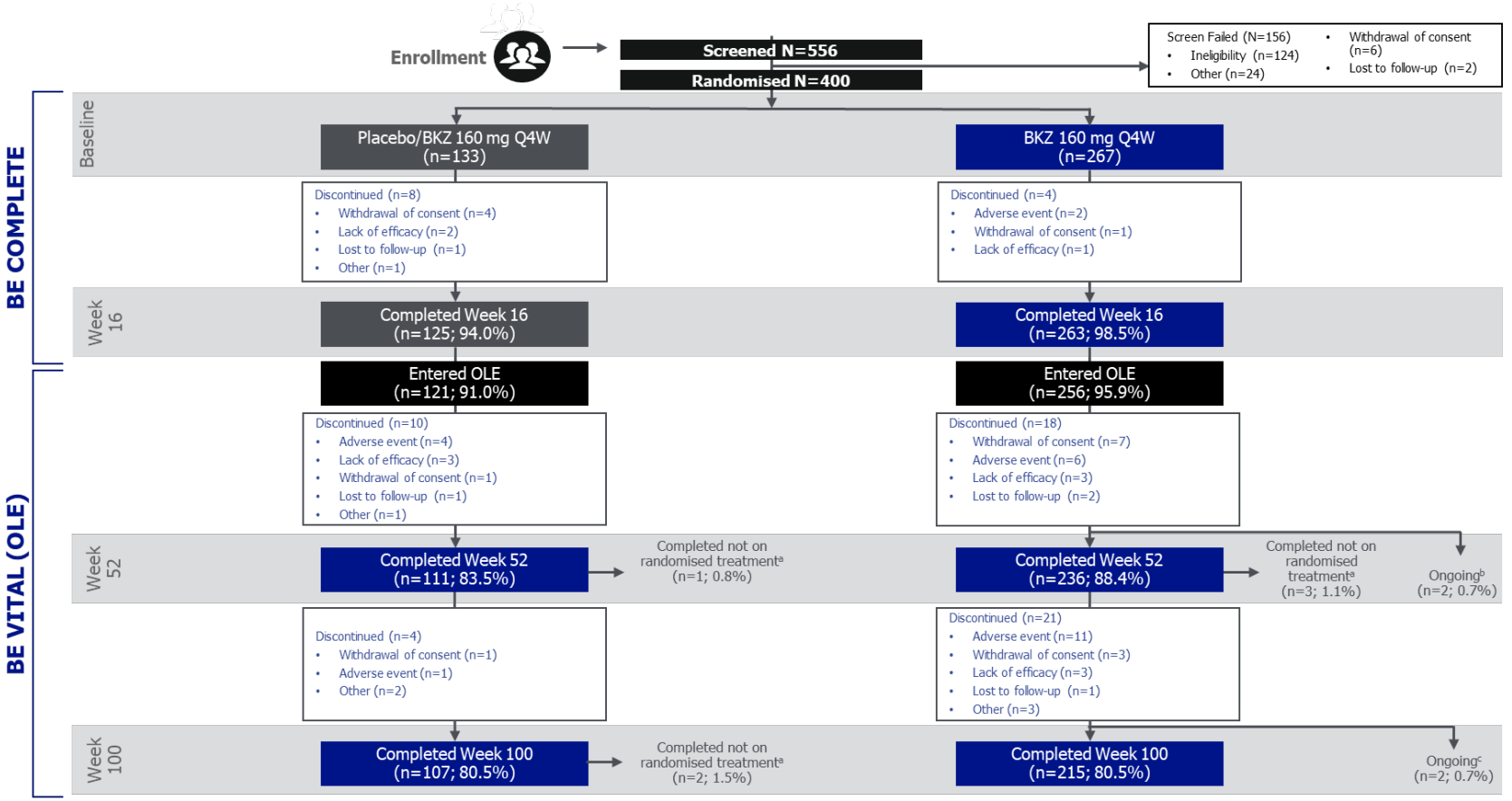
SUPPLEMENTARY APPENDIX

Supplementary Figure S1. Patient disposition in BE OPTIMAL and BE COMPLETE

I. BE OPTIMAL



II. BE COMPLETE



Patients completing safety follow-up period: BE OPTIMAL PBO (n=19, 45.2%), BKZ (n=38, 52.8%), ADA (n=17, 60.7%); BE COMPLETE PBO (n=12, 42.9%); BKZ (n=28, 53.8%). Safety reported to Week 104 in BE COMPLETE. [a] Patients who withdrew from the study medication but returned for the final visit (Week 52 or Week 104) were

considered as having completed the treatment period not on randomised treatment; [b] 2 patients classified as ongoing as they did not have a visit for Week 52 but no formal discontinuation reason was reported; [c] Ongoing includes patients who did not have a Week 100 visit and no visits after in the BE VITAL OLE but have not discontinued within the timeframe. ADA: adalimumab; BKZ: bimekizumab; OLE: open-label extension; PBO: placebo.

Supplementary Table S1. Baseline demographics and disease characteristics

	BE OPTIMAL (bDMARD-naïve)			BE COMPLETE (TNFi-IR)	
	PBO → BKZ 160 mg Q4W n=281	BKZ 160 mg Q4W n=431	ADA → BKZ 160 mg Q4W[a] n=140	PBO → BKZ 160 mg Q4W n=133	BKZ 160 mg Q4W n=267
Age, years, mean (SD)	48.7 (11.7)	48.5 (12.6)	49.0 (12.8)	51.3 (12.9)	50.1 (12.4)
Sex, male, n (%)	127 (45.2)	201 (46.6)	71 (50.7)	60 (45.1)	130 (48.7)
BMI, kg/m^2, mean (SD)	29.6 (6.1)	29.2 (6.8)	28.4 (5.9)	29.0 (5.4)	30.1 (6.5)
Time since PsA diagnosis,[b] years, mean (SD)	5.6 (6.5)	6.0 (7.3)	6.1 (6.8)	9.2 (8.1)	9.6 (9.9)
Any csDMARD at baseline	194 (69.0)	301 (69.8)	99 (70.7)	63 (47.4)	139 (52.1)
Concomitant methotrexate, n (%)	163 (58.0)	252 (58.5)	82 (58.6)	51 (38.3)	119 (44.6)
Prior TNFi exposure, n (%)					
Inadequate response to 1 TNFi	–	–	–	103 (77.4)	203 (76.0)
Inadequate response to 2 TNFi	–	–	–	15 (11.3)	30 (11.2)
Intolerance to TNFi	–	–	–	15 (11.3)	34 (12.7)
TJC (of 68 joints), mean (SD)	17.1 (12.5)	16.8 (11.8)	17.5 (13.1)	19.3 (14.2)	18.4 (13.5)
SJC (of 66 joints), mean (SD)	9.5 (7.3)	9.0 (6.2)	9.6 (7.1)	10.3 (8.2)	9.7 (7.5)
hs-CRP ≥6 mg/L, n (%)	121 (43.1)	158 (36.7)	44 (31.4)	59 (44.4)	118 (44.2)
Affected BSA ≥3%, n (%)	140 (49.8)	217 (50.3)	68 (48.6)	88 (66.2)	176 (65.9)
PASI score,[c] mean (SD)	7.9 (5.6)	8.2 (6.8)	8.5 (7.6)	8.5 (6.6)	10.1 (9.1)
Enthesitis (LEI >0),[d] n (%)	70 (24.9)	143 (33.2)	36 (25.7)	36 (27.1)	106 (39.7)
LEI score,[e] mean (SD)	2.9 (1.5)	2.5 (1.5)	2.3 (1.6)	2.9 (1.6)	2.6 (1.5)
Dactylitis (LDI >0),[f] n (%)	33 (11.7)	56 (13.0)	11 (7.9)	14 (10.5)	34 (12.7)
LDI score,[g] mean (SD)	47.3 (41.1)	46.7 (54.3)	49.7 (31.9)	66.4 (127.6)	72.7 (114.4)

	BE OPTIMAL (bDMARD-naïve)			BE COMPLETE (TNFi-IR)	
	PBO → BKZ 160 mg Q4W n=281	BKZ 160 mg Q4W n=431	ADA → BKZ 160 mg Q4W[a] n=140	PBO → BKZ 160 mg Q4W n=133	BKZ 160 mg Q4W n=267
Nail psoriasis (mNAPSI >0),[h] n (%)	156 (55.5)	244 (56.6)	75 (53.6)	83 (62.4)	159 (59.6)
mNAPSI score,[i] mean (SD)	4.0 (2.1)	4.1 (2.5)	3.7 (2.3)	4.5 (2.8)	4.3 (2.8)
HAQ-DI score,[j] mean (SD)	0.89 (0.61)	0.82 (0.59)	0.86 (0.54)	1.04 (0.69)	0.97 (0.59)
BASDAI total score,[k] mean (SD)	6.2 (1.3)	6.1 (1.3)	6.1 (1.3)	6.5 (1.3)	6.2 (1.3)

Randomised set. [a] Reference arm: study not powered for statistical comparisons of ADA to BKZ or PBO; [b] BE OPTIMAL: Data missing for two PBO patients, eight BKZ patients and one ADA patient; BE COMPLETE: Data missing for one PBO patient and one BKZ patient; [c] In patients with ≥3% BSA with psoriasis at baseline; [d] BE OPTIMAL: data missing for six BKZ patients and one ADA patient, BE COMPLETE: data missing for one PBO patient; [e] In patients with enthesitis at baseline; [f] BE OPTIMAL: data missing for seven BKZ patients and one ADA patient, BE COMPLETE: data missing for one PBO patient; [g] In patients with dactylitis at baseline; [h] Data missing for seven BKZ patients in BE OPTIMAL and one PBO patient in BE COMPLETE; [i] In patients with nail psoriasis at baseline; [j] Data missing for one BKZ patient in BE OPTIMAL; [k] In patients with a BASDAI total score >4 at baseline (BE OPTIMAL: 213 PBO, 311 BKZ, 107 ADA; BE COMPLETE: 96 PBO, 204 BKZ). ADA: adalimumab; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; BSA: body surface area; BMI: body mass index; csDMARD: conventional synthetic disease-modifying antirheumatic drug; HAQ-DI: Heath Assessment Questionnaire-Disability Index; hs-CRP: high sensitivity C-reactive protein; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; mNAPSI: modified nail psoriasis severity index; PASI: Psoriasis Area and Severity Index; PBO: placebo; PsA: psoriatic arthritis; Q2W: every 2 weeks; Q4W: every 4 weeks; SD: standard deviation; SJC: swollen joint count; TJC: tender joint count; TNFi: tumour necrosis factor inhibitors; TNFi-IR: prior inadequate response or intolerance to TNFi.

Supplementary Table S2. Fungal events of interest from Week 0–52 and Week 52–104

EAIR (95% CI) /100 PY	BE OPTIMAL (bDMARD-naïve)				BE COMPLETE (TNFi-IR)	
	Week 0–52		Week 52–104	Week 52–104	Week 0–52	Week 52–104
	BKZ 160 mg Q4W Total[a] n=702 595.6 PY	ADA 40 mg Q2W n=140 136.8 PY	ADA → BKZ 160 mg Q4W n=121 117.2 PY	BKZ 160 mg Q4W Total[a] n=773 738.0 PY	BKZ 160 mg Q4W Total[a] n=388 340.0 PY	BKZ 160 mg Q4W Total[a] n=361 335.2 PY
Fungal infections	15.3 (12.2, 18.9)	1.5 (0.2, 5.3)	12.0 (6.4, 20.4)	10.5 (8.3, 13.2)	12.2 (8.7, 16.7)	4.6 (2.6, 7.5)
Candida infections	9.8 (7.4, 12.7)	0.7 (0.0, 4.1)	4.4 (1.4, 10.2)	6.5 (4.8, 8.7)	8.0 (5.2, 11.7)	3.3 (1.7, 5.9)
Oral candidiasis	6.7 (4.8, 9.2)	0.7 (0.0, 4.1)	4.4 (1.4, 10.2)	5.5 (3.9, 7.5)	7.6 (4.9, 11.3)	3.3 (1.7, 5.9)
Vulvovaginal candidiasis	1.4 (0.6, 2.7)	0	0	0.8 (0.3, 1.8)	0	0
Oesophageal candidiasis	0.7 (0.2, 1.7)	0	0	0.1 (0.0, 0.8)	0.6 (0.1, 2.1)	0
Skin candida	0.7 (0.2, 1.7)	0	0	0.3 (0.0, 1.0)	0	0
Oropharyngeal candidiasis	0.3 (0.0, 1.2)	0	0	0.3 (0.0, 1.0)	0	0
Candida infection	0	0	0	0.1 (0.0, 0.8)	0	0
Otitis externa candida	0	0	0	0.1 (0.0, 0.8)	0	0
Fungal infections NEC	5.2 (3.5, 7.4)	0	8.1 (3.7, 15.4)	4.0 (2.7, 5.8)	3.6 (1.9, 6.3)	0.9 (0.2, 2.6)
Fungal skin infection	1.9 (0.9, 3.3)	0	2.6 (0.5, 7.6)	1.0 (0.4, 2.0)	1.2 (0.3, 3.0)	0.6 (0.1, 2.2)
Vulvovaginal mycotic infection	1.2 (0.5, 2.4)	0	0.9 (0.0, 4.8)	0.1 (0.0, 0.8)	1.2 (0.3, 3.0)	0
Oral fungal infection	1.7 (0.8, 3.1)	0	4.4 (1.4, 10.3)	1.9 (1.1, 3.2)	0.3 (0.0, 1.6)	0.3 (0.0, 1.7)
Eye infection, fungal	0	0	0	0	0.3 (0.0, 1.6)	0
Tongue fungal infection	0.5 (0.1, 1.5)	0	0	0.3 (0.0, 1.0)	0.6 (0.1, 2.1)	0
Fungal oesophagitis	0.2 (0.0, 0.9)	0	0	0.1 (0.0, 0.8)	0	0
Gastrointestinal fungal infection	0	0	0	0.1 (0.0, 0.8)	0	0
Oropharyngitis fungal	0	0	0	0.1 (0.0, 0.8)	0	0
Otitis media fungal	0	0	0	0.1 (0.0, 0.8)	0	0
Laryngitis fungal	0.2 (0.0, 0.9)	0	0	0	0	0

EAIR (95% CI) /100 PY	BE OPTIMAL (bDMARD-naïve)				BE COMPLETE (TNFi-IR)	
	Week 0–52		Week 52–104	Week 52–104	Week 0–52	Week 52–104
	BKZ 160 mg Q4W Total[a] n=702 595.6 PY	ADA 40 mg Q2W n=140 136.8 PY	ADA → BKZ 160 mg Q4W n=121 117.2 PY	BKZ 160 mg Q4W Total[a] n=773 738.0 PY	BKZ 160 mg Q4W Total[a] n=388 340.0 PY	BKZ 160 mg Q4W Total[a] n=361 335.2 PY
Onychomycosis	0.2 (0.0, 0.9)	0	0.9 (0.0, 4.8)	0.3 (0.0, 1.0)	0	0
Upper respiratory fungal infection	0.2 (0.0, 0.9)	0	0	0	0	0
Tinea infections	1.2 (0.5, 2.4)	0.7 (0.0, 4.1)	0	0.5 (0.1, 1.4)	1.5 (0.5, 3.5)	0.3 (0.0, 1.7)
Tinea versicolour	0.5 (0.1, 1.5)	0.7 (0.0, 4.1)	0	0	0.3 (0.0, 1.6)	0
Tinea capitis	0	0	0	0	0.3 (0.0, 1.6)	0
Body tinea	0.2 (0.0, 0.9)	0	0	0.1 (0.0, 0.8)	0.3 (0.0, 1.6)	0
Tinea infection	0.2 (0.0, 0.9)	0	0	0	0.3 (0.0, 1.6)	0
Tinea pedis	0.3 (0.0, 1.2)	0	0	0.3 (0.0, 1.0)	0.3 (0.0, 1.6)	0.3 (0.0, 1.7)
Tinea cruris	0	0	0	0.1 (0.0, 0.8)	0.3 (0.0, 1.6)	0
Serious fungal infections	0	0	0	0.1 (0.0, 0.8)	0	0
Fungal infections leading to patient discontinuation[b]	0.5 (0.1, 1.5)	0	0	0.5 (0.1, 1.4)	0.6 (0.1, 2.1)	0.6 (0.1, 2.2)

Safety set. [a] BKZ groups include PBO/BKZ Week 16 switchers, includes events after switch only; BE OPTIMAL Weeks 52–104 also includes ADA/BKZ switchers, events after switch only; [b] There were no documented cases of recurrent fungal infections leading to discontinuation. ADA: adalimumab; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; CI: confidence interval; EAIR: exposure-adjusted incidence rate; NEC: not elsewhere classified; PBO: placebo; PYs: patient-years; Q2W: every 2 weeks; Q4W: every 4 weeks; TNFi-IR: prior inadequate response or intolerance to tumour necrosis factor inhibitors.

Supplementary Table S3. Malignancies from Week 0–52 and Week 52–104

EAIR (95% CI) /100 PY	BE OPTIMAL (bDMARD-naïve)				BE COMPLETE (TNFi-IR)	
	Week 0–52		Week 52–104	Week 52–104	Week 0–52	Week 52–104
	BKZ 160 mg Q4W Total[a] n=702 595.6 PY	ADA 40 mg Q2W n=140 136.8 PY	ADA → BKZ 160 mg Q4W n=121 117.2 PY	BKZ 160 mg Q4W Total[a] n=773 738.0 PY	BKZ 160 mg Q4W Total[a] n=388 340.0 PY	BKZ 160 mg Q4W Total[a] n=361 335.2 PY
Malignancies excluding nonmelanoma skin cancer	0.7 (0.2, 1.7)	0	0	0.4 (0.1, 1.2)	0.9 (0.2, 2.6)	0.6 (0.1, 2.2)[b]
Breast cancer stage 1	0	0	0	0	0	0
Breast cancer	0	0	0	0.1 (0.0, 0.8)	0	0.3 (0.0, 1.7)
Colon cancer	0.2 (0.0, 0.9)	0	0	0	0	0
Chronic lymphocytic leukaemia stage 0	0.2 (0.0, 0.9)	0	0	0	0	0
Papillary thyroid cancer	0.2 (0.0, 0.9)	0	0	0	0	0
Ovarian cancer	0	0	0	0.1 (0.0, 0.8)	0	0
Bone cancer metastatic	0	0	0	0	0	0.3 (0.0, 1.7)
Endometrial cancer stage 1	0	0	0	0	0.3 (0.0, 1.6)	0
Gastric cancer	0	0	0	0	0	0.3 (0.0, 1.7)
Gastric cancer recurrent	0	0	0	0	0.3 (0.0, 1.6)	0
Prostate cancer	0	0	0	0	0.3 (0.0, 1.6)	0
Uterine cancer	0	0	0	0.1 (0.0, 0.8)	0	0

Safety set. [a] BKZ groups include PBO/BKZ Week 16 switchers (for both BE OPTIMAL and BE COMPLETE), includes events after switch only; BE OPTIMAL Weeks 52–104 also includes ADA/BKZ switchers, events after switch only; [b] One patient had both bone cancer and breast cancer. ADA: adalimumab; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; CI: confidence interval; EAIR: exposure-adjusted incidence rate; PBO: placebo; PYs: patient-years; Q2W: every 2 weeks; Q4W: every 4 weeks; TNFi-IR: prior inadequate response or intolerance to tumour necrosis factor inhibitors.

Supplementary Table S4. Adjudicated major adverse cardiovascular events from Week 0–52 and Week 52–104

	BE OPTIMAL (bDMARD-naïve)				BE COMPLETE (TNFi-IR)	
	Week 0–52		Week 52–104	Week 52–104	Week 0–52	Week 52–104
EAIR (95% CI) /100 PY	**BKZ 160 mg Q4W Total[a] n=702 595.6 PY**	**ADA 40 mg Q2W n=140 136.8 PY**	**ADA → BKZ 160 mg Q4W n=121 117.2 PY**	**BKZ 160 mg Q4W Total[a] n=773 738.0 PY**	**BKZ 160 mg Q4W Total[a] n=388 340.0 PY**	**BKZ 160 mg Q4W Total[a] n=361 335.2 PY**
Total	0.7 (0.2, 1.7)	0	1.7 (0.2, 6.2)	0.4 (0.1, 1.2)	0.6 (0.1, 2.1)	0
Acute myocardial infarction	0	0	0.9 (0.0, 4.8)	0.3 (0.0, 1.0)	0	0
Cerebrovascular accident	0.2 (0.0, 0.9)	0	0	0	0	0
Ischaemic stroke	0.2 (0.0, 0.9)	0	0.9 (0.0, 4.8)	0.1 (0.0, 0.8)	0	0
Myocardial infarction	0.2 (0.0, 0.9)	0	0	0	0	0
Thrombotic cerebral infarction	0.2 (0.0, 0.9)	0	0	0	0	0
Cerebral haemorrhage	0	0	0	0	0.3 (0.0, 1.6)	0
Sudden death	0	0	0	0	0.3 (0.0, 1.6)	0

Safety set. [a] BKZ groups include PBO/BKZ Week 16 switchers (for both BE OPTIMAL and BE COMPLETE), includes events after switch only; BE OPTIMAL Weeks 52–104 also includes ADA/BKZ switchers, events after switch only. ADA: adalimumab; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; CI: confidence interval; EAIR: exposure-adjusted incidence rate; PBO: placebo; PYs: patient-years; Q2W: every 2 weeks; Q4W: every 4 weeks; TNFi-IR: prior inadequate response or intolerance to tumour necrosis factor inhibitors.

Supplementary Table S5. Venous thromboembolism events from Week 0–52 and Week 52–104

	BE OPTIMAL (bDMARD-naïve)				BE COMPLETE (TNFi-IR)	
	Week 0–52		Week 52–104	Week 52–104	Week 0–52	Week 52–104
n (%) EAIR [95% CI] /100 PY	**BKZ 160 mg Q4W Total[a] n=702 595.6 PY**	**ADA 40 mg Q2W n=140 136.8 PY**	**ADA → BKZ 160 mg Q4W n=121 117.2 PY**	**BKZ 160 mg Q4W Total[a] n=773 738.0 PY**	**BKZ 160 mg Q4W Total[a] n=388 340.0 PY**	**BKZ 160 mg Q4W Total[a] n=361 335.2 PY**
Pulmonary embolism	0	0	0	1 (0.1) 0.1 (0.0, 0.8)	0	0
Deep vein thrombosis	1 (0.1) 0.2 (0.0, 0.9)	0	0	3 (0.4) 0.4 (0.1, 1.2)	0	0

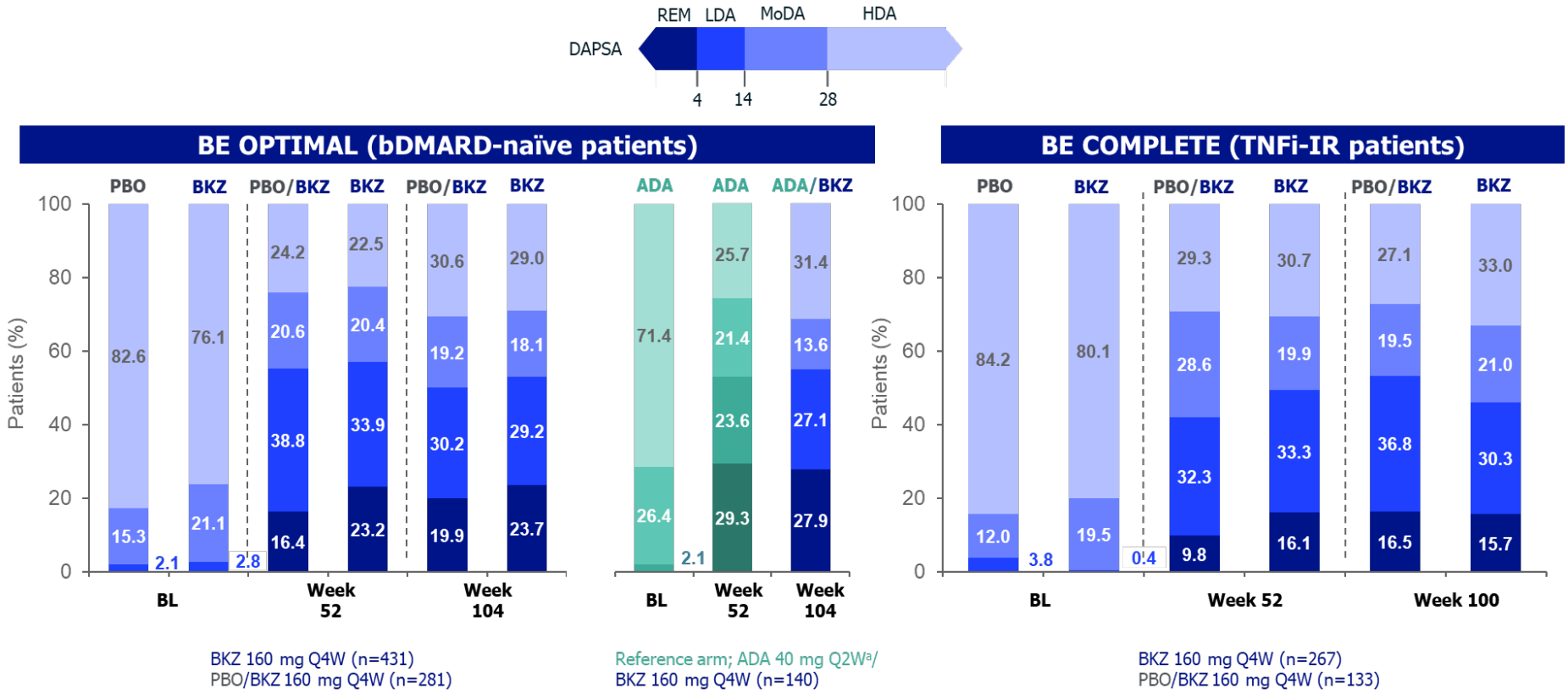
Safety set. Events reported by event type. [a] BKZ groups include PBO/BKZ Week 16 switchers (for both BE OPTIMAL and BE COMPLETE), includes events after switch only; BE OPTIMAL Weeks 52–104 also includes ADA/BKZ switchers in addition to PBO- and BKZ-randomised patients, events after switch only. bDMARD: biologic disease-modifying antirheumatic drug; ADA: adalimumab; BKZ: bimekizumab; CI: confidence interval; EAIR: exposure-adjusted incidence rate; PBO: placebo; PYs: patient-years; Q2W: every two weeks; Q4W: every four weeks; TNFi-IR: prior inadequate response or intolerance to tumour necrosis factor inhibitors.

Supplementary Table S6. Adjudicated suicidal ideation and behaviour events from Week 0–52 and Week 52–104

	BE OPTIMAL (bDMARD-naïve)				BE COMPLETE (TNFi-IR)	
	Week 0–52		Week 52–104	Week 52–104	Week 0–52	Week 52–104
EAIR (95% CI) /100 PY	**BKZ 160 mg Q4W Total[a] n=702 595.6 PY**	**ADA 40 mg Q2W n=140 136.8 PY**	**ADA → BKZ 160 mg Q4W n=121 117.2 PY**	**BKZ 160 mg Q4W Total[a] n=773 738.0 PY**	**BKZ 160 mg Q4W Total[a] n=388 340.0 PY**	**BKZ 160 mg Q4W Total[a] n=361 335.2 PY**
Total	0	0	0	0.1 (0.0, 0.8)	0	0
Psychiatric evaluation abnormal	0	0	0	0	0	0
Suicidal behaviour	0	0	0	0.1 (0.0, 0.8)	0	0

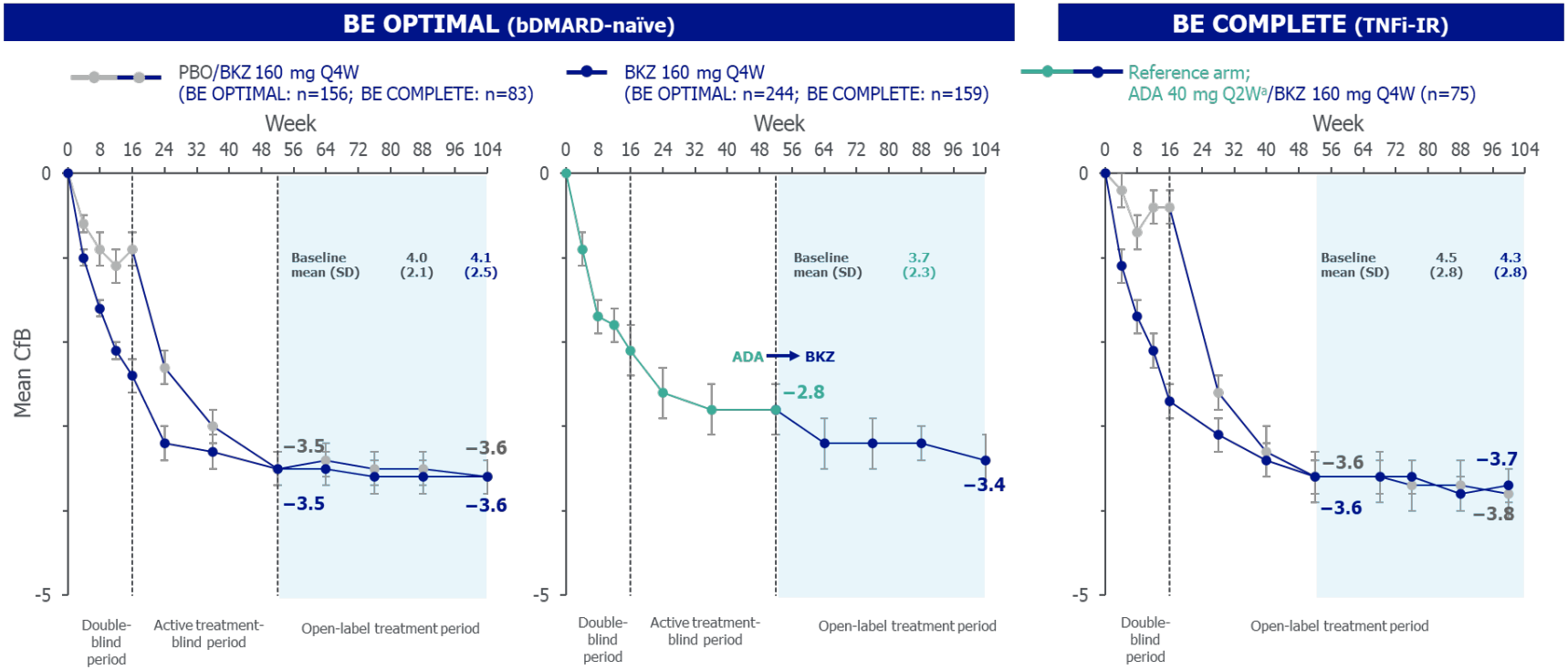
Safety set. [a] BKZ groups include PBO/BKZ Week 16 switchers (for both BE OPTIMAL and BE COMPLETE), includes events after switch only; BE OPTIMAL Weeks 52–104 also includes ADA/BKZ switchers, events after switch only. ADA: adalimumab; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; CI: confidence interval; EAIR: exposure-adjusted incidence rate; PBO: placebo; PYs: patient-years; Q2W: every 2 weeks; Q4W: every 4 weeks; TNFi-IR: prior inadequate response or intolerance to tumour necrosis factor inhibitors.

Supplementary Figure S2. DAPSA disease states to Week 104/100 (WCI)



Randomised set. In BE OPTIMAL, patients on ADA switched to BKZ 160 mg Q4W at Week 52. [a] Reference arm; study not powered for statistical comparisons between ADA and BKZ or PBO. ADA: adalimumab; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; BL: baseline; DAPSA: Disease Activity Index for Psoriatic Arthritis; HDA: high disease activity; LDA: low disease activity; MoDA: moderate disease activity; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks; REM: remission; TNFi-IR: prior inadequate response or intolerance to tumour necrosis factor inhibitors; WCI: worst category imputation.

Supplementary Figure S3. Nail psoriasis change from baseline to Week 104/100 (MI)



Randomised set, in patients with mNAPSI >0 at baseline. In BE OPTIMAL, patients on ADA switched to BKZ 160 mg Q4W at Week 52. [a] Reference arm; study not powered for statistical comparisons between ADA and BKZ or PBO. ADA: adalimumab; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; CfB: change from baseline; mNAPSI: modified Nail Psoriasis Severity Index; NRI: non-responder imputation; OC: observed case; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks; TNFi-IR: prior inadequate response or intolerance to tumour necrosis factor inhibitors.

1 **Supplementary Appendix S1.** Local institutional review board and independent ethics committee names for BE OPTIMAL and BE COMPLETE

BE OPTIMAL	BE COMPLETE
Australia	
Monash Medical Center 246 Clayton Road Level 4 Block 3168 Clayton Victoria Australia Site: 30002	CALHN Research Office - SA Health Government Level 3, Roma Mitchell House 136 North Terrace South Australia Site: 30006
CALHN Research Office - SA Health Government Level 3, Roma Mitchell House 136 North Terrace South Australia Site: 30006	Bellberry Limited 123 Glen Osmond Road Eastwood 5063 South Australia Sites: 30007, 30005
Bellberry Limited 123 Glen Osmond Road Eastwood 5063 South Australia Site 30003	–
Bellberry Limited 123 Glen Osmond Road Eastwood 5063 South Australia Site 30005	–
Bellberry Limited 123 Glen Osmond Road Eastwood 5063 South Australia Site 30007	–

Bellberry Limited 123 Glen Osmond Road Eastwood 5063 South Australia Site 30008	–
Belgium	
UZ Leuven - Campus Gasthuisberg Ethische Commissie Onderzoek UZ/KU Leuven Herestraat 49 3000 Leuven Belgium Site: 40002	–
CHU Ambroise Paré Comité d'éthique Boulevard Kennedy 2 7000 Mons Belgium Site: 40059	–
CHU de Liège – Sart Tilman Comité d'éthique Hospitalo-Facultaire Universitaire de Liège Domaine Universitaire du Sart Tilman, Bâtiment B35 4000 Liège Belgium Sites: 40060, 40003	–
Canada	
Advarra 372 Hollandview Trail Suite 300 Ontario L4G 0A5 Aurora Canada	Advarra 372 Hollandview Trail Suite 300 Ontario L4G 0A5 Aurora Canada

Sites: 50041, 50042, 50044	Sites: 50042, 50044
Nova Scotia Health Authority Research Ethics Board 5790 University Avenue Room 118 Nova Scotia B3H 1V7 Halifax Canada Site: 50043	Nova Scotia Health Authority Research Ethics Board 5790 University Avenue Room 118 Nova Scotia B3H 1V7 Halifax Canada Site: 50043
Czech Republic	
CTCenter MaVe s.r.o. Eticka komise Na Sibeniku 914/1 779 00 Olomouc Czech Republic Site: 40064	Fakultni nemocnice v Motole Eticka komise (Central Ethic Committee) V Uvalu 84 Praha 5 150 06 Praha 5 Czech Republic Sites: 40009, 40012, 40063, 40066
Fakultni nemocnice v Motole Eticka komise V Uvalu 84 Praha 5 150 06 Praha 5 Czech Republic Sites: 40009, 40010, 40012, 40013, 40014, 40015, 40061, 40062, 40063, 40064, 40065, 40066	Revmatologicky ustav Eticka komise Na Slupi 4 128 50 Praha 2 Czech Republic Site: 40066
Revmatologicky ustav Eticka komise Na Slupi 4 128 50 Praha 2 Czech Republic Site: 40066	–
France	
CPP Sud Est III Bâtiment Pinel (Central Ethic Committee) 59 Boulevard Pinel Bron 69500 France Sites: 40019, 40067, 40068, 40069, 40070	–

Germany	
Ethikkommission an der Medizinischen Fakultät der Universität Leipzig Ethic Committee Käthe-Kollwitz-Straße 82 Karl-Sudhoff-Institut Sachsen 4109 Leipzig Germany Site: 40078	Ethikkommission an der Medizinischen Fakultät der Universität Leipzig Ethic Committee Käthe-Kollwitz-Straße 82 Karl-Sudhoff-Institut Sachsen 4109 Leipzig Germany Site: 40078
Ethikkommission der Ärztekammer Hamburg Ethic Committee Weidestraße 122b Hamburg 22083 Hamburg Germany Sites: 40029, 40071	Ethikkommission der Ärztekammer Hamburg Ethic Committee Weidestraße 122b Hamburg 22083 Hamburg Germany Sites: 40029, 40071
Ethikkommission an der Medizinischen Fakultät Ernst-Moritz-Arndt-Universität Greifswald Institut für Pharmakologie Felix-Hausdorff-Str. 3 Mecklenburg-Vorpommern 17487 Greifswald Germany Site: 40074	Ethikkommission der Ärztekammer Nordrhein Ethics Committee Tersteegenstraße 9 Nordrhein-Westfalen 40474 Düsseldorf Germany Site: 40026
Ethikkommission der Ärztekammer Nordrhein Ethics Committee Tersteegenstraße 9 Nordrhein-Westfalen 40474 Düsseldorf Germany Site: 40026 Ethikkommission der Ärztekammer Westfalen-Lippe und der medizinischen Fakultät der WWU Münster Ethics Committee Gartenstr. 210 - 214 Nordrhein-Westfalen 48147 Münster	Ethikkommission der Medizinischen Fakultät der Friedrich-Alexander-Universität Erlangen-Nürnberg Krankenhausstraße 12 Bayern 91054 Erlangen Germany Sites: 40023, Central EC

Germany Site: 40027	
Ethikkommission der Ärztekammer Sachsen-Anhalt - IRB/IEC IRB/IEC Am Kirchtor 9 Sachsen-Anhalt 06108 Halle (Saale) Germany Site: 40348	Ethikkommission der Landesärztekammer Brandenburg Dreifertstraße 12 03044 Cottbus Germany Site: 40076
Ethikkommission der Medizinischen Fakultät der Friedrich-Alexander-Universität Erlangen-Nürnberg Krankenhausstraße 12 Bayern 91054 Erlangen Germany Site: 40023 (Central EC)	Ethikkommission des Fachbereichs Medizin der Goethe- Universität Ethic Committee Theodor-Stern-Kai 7 Haus 1, 2. OG, Zi. 207 Hessen 60596 Frankfurt am Main Germany Site: 40117
Ethikkommission der Landesärztekammer Brandenburg Dreifertstraße 12 03044 Cottbus Germany Site: 40076	–
Ethikkommission des Landes Berlin, Landesamt für Gesundheit und Soziales Ethics Committe Turmstraße 21 Haus A Berlin 10559 Berlin Germany Sites: 40025, 40028	–
Ethikkommission des Fachbereichs Medizin der Goethe-Universität Ethic Committee	–

Theodor-Stern-Kai 7 Haus 1, 2. OG, Zi. 207 Hessen 60596 Frankfurt am Main Germany Site: 40117	
Hungary	
Debreceni Egyetem Klinikai Központ, Regionális Intézményi és Kutatásetikai Bizottság 40332 Debrecen Nagyerdei krt. 98. Pf. 34. Hungary Site: 40032	Csongrád Megyei Dr. Bugyi István Kórház Mozgasszervi Rehabil. Osztaly Sima F. u. 44-58 Csongrád 6600 Szentes Hungary Site: 40079
Csongrád Megyei Dr. Bugyi István Kórház Mozgasszervi Rehabil. Osztaly Sima F. u. 44-58 Csongrád 6600 Szentes Hungary Site: 40079	Markhot Ferenc Oktatokorhaz es Rendelointezet - Rheumatology Rheumatology Furdo u. 4. Heves 3300 Eger Hungary Site: 40030
Markhot Ferenc Oktatokorhaz es Rendelointezet - Rheumatology Rheumatology Furdo u. 4. Heves 3300 Eger Hungary Site: 40030	Pest Megyei Flór Ferenc Kórház Intézményi, Kutatásetikai Bizottság2143, Kistarcsa Semmelweis tér 1. Hungary Site: 40082
Vasútegészségügyi Kft. Intézeti Kutatásetikai Bizottság 1062 Budapest Podmaniczky utca 109 Hungary Site: 40080	–
Fejér Megyei Szent György Egyetemi Oktató Kórház, Kutatásetikai Bizottság,	–

8000, Szekesfehervar Seregelyesi ut 3 Hungary Site: 40033	
Pest Megyei Flór Ferenc Kórház Intézményi, Kutatásetikai Bizottság 2143 Kistarcsa Semmelweis tér 1 Hungary Site: 40082	–
Medical Research Council Ethics Committee for Clinical Pharm Alkotmány u. 25. Budapest 1054 Budapest Hungary Sites: 40081, 40083	–
Italy	
Comitato Etico Catania 1 (Central Ethics Committee) A.O.U. Policlinico Vittorio Emanuele Di Catania Via Santa Sofia, 78 95123 Catania Italy Site: 40084	Comitato Etico Catania 1 (Central Ethic Committee) A.O.U. Policlinico Vittorio Emanuele Di Catania Via Santa Sofia, 78 95123 Catania Italy Site: 40084
COMITATO ETICO DELL'AREA VASTA EMILIA NORD - Segreteria Locale di Reggio Emila c/o AUSL – IRCCS di Reggio Emilia Edificio Spallanzani Viale Umberto I, 50 42100 Reggio Emilia Italy Site: 40086	COMITATO ETICO DELL'AREA VASTA EMILIA NORD - Segreteria Locale di Reggio Emila c/o AUSL – IRCCS di Reggio Emilia Edificio Spallanzani Viale Umberto I, 50 42100 Reggio Emilia Italy Site: 40086
Comitato Etico Area 1	Comitato Etico Area 1

ASST Fatebenefratelli Sacco Via GB Grassi 74 20157 Milano Italy Site: 40087	ASST Fatebenefratelli Sacco, Via GB Grassi 74 20157 Milano Italy Site: 40087
Japan	
Hokkaido University Hospital Institutional Review Board Kita 14, Nishi 5, Kita-ku Sapporo, Hokkaido, 060-8648 Japan Site: 20031	Hokkaido University Hospital Institutional Review Board Kita 14, Nishi 5, Kita-ku Sapporo, Hokkaido, 060-8648 Japan Site: 20031
Nagoya City University Institutional Review Board 1 Kawasumi, Mizuhocho, Mizuho-ku Nagoya, Aichi, 467-8602 Japan Site: 20033	Nagoya City University Institutional Review Board 1 Kawasumi, Mizuhocho, Mizuho-ku Nagoya, Aichi, 467-8602, Japan Site: 20033
Juntendo University Hospital Institutional Review Board 3-1-3, Hongo Bunkyo-ku, Tokyo, 113-8431 Japan Site: 20035	Saitama medical University Hospital Institutional Review Board 38 Morohongo, Moroyama-machi, Iruma-gun, Saitama, 350-0495, Japan Site: 20039
Kochi Medical School Hospital Institutional Review Board 185-1 Kohasu, Oko-cho Nankoku-shi, Kochi, 783-8505 Japan Site: 20038	Kochi Medical School Hospital Institutional Review Board 185-1 Kohasu, Oko-cho, Nankoku-shi, Kochi, 783-8505 Japan Site: 20038

Kagawa University Hospital Institutional Review Board 1750-1 Ikenobe, Miki-cho Kita-gun, Kagawa, 761-0793 Japan Site: 20045	Kagawa University Hospital Institutional Review Board 1750-1 Ikenobe, Miki-cho Kita-gun, Kagawa, 761-0793 Japan Site: 20045
Jichi Medical University Saitama Medical Center Institutional Review Board 1-847, Amanumacho, Omiya-ku Saitama, Saitama, 330-8503 Japan Site: 20048	Jichi Medical University Saitama Medical Center Institutional Review Board 1-847, Amanumacho, Omiya-ku, Saitama, Saitama, 330-8503, Japan Site: 20048
Hospital of the University of Occupational and Environmental Health, Japan Institutional Review Board 1-1 Iseigaoka, Yahatanishi-ku Kitakyushu, Fukuoka, 807-8556 Japan Site: 20049	Hospital of the University of Occupational and Environmental Health, Japan Institutional Review Board 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu, Fukuoka, 807-8556 Japan Site: 20049
St. Luke's International Hospital Institutional Review Board 9-1 Akashicho Chuo-ku, Tokyo, 104-8560 Japan Site: 20030	St. Luke's International Hospital Institutional Review Board 9-1 Akashicho, Chuo-ku, Tokyo, 104-8560 Japan Site: 20030
Osaka University Hospital Institutional Review Board 2-15 Yamadaoka Suita, Osaka, 565-0871 Japan Site: 20032	Osaka University Hospital Institutional Review Board 2-15 Yamadaoka, Suita, Osaka, 565-0871, Japan Site: 20032
National Hospital Organization Osaka Minami Medical	National Hospital Organization Osaka Minami Medical

Center Institutional Review Board 2-1 Kidohigashimachi Kawachinagano, Osaka, 586-8521 Japan Site: 20036	Center Institutional Review Board 2-1 Kidohigashimachi, Kawachinagano, Osaka, 586-8521, Japan Site: 20036
Osaka City University Hospital Institutional Review Board 1-5-7 Asahimachi, Abeno-ku Osaka, Osaka, 545-8586 Japan Site: 20041	Osaka Metropolitan University Hospital Institutional Review Board 1-5-7 Asahimachi, Abeno-ku Osaka, Osaka, 545-8586, Japan Site: 20041
Sasebo Chuo Hospital Institutional Review Board 15 Yamato-cho Sasebo, Nagasaki, 857-1195 Japan Site: 20042	Sasebo Chuo Hospital Institutional Review Board 15 Yamato-cho, Sasebo, Nagasaki, 857-1195, Japan Site: 20042
Nihon University Hospital's Joint Institutional Review Board 30-1 Oyaguchi, Kami-cho Itabashi-ku, Tokyo, 173-8610 Japan Site: 20043	Nihon University Hospital's Joint Institutional Review Board 30-1 Oyaguchi, Kami-cho Itabashi-ku, Tokyo, 173-8610, Japan Site: 20043
The Jikei University Hospital Institutional Review Board 3-19-18, Nishi-Shinbashi, Minato-ku, Tokyo, 105-8471 Japan Site: 20044	The Jikei University Hospital Institutional Review Board 3-19-18, Nishi-Shinbashi, Minato-ku, Tokyo, 105-8471, Japan Site: 20044
Nippon Life Hospital Institutional Review Board 2-1-54 Enokojima, Nishi-ku	Nippon Life Hospital Institutional Review Board 2-1-54 Enokojima, Nishi-ku,

Osaka, Osaka, 550-0006 Japan Site: 20046	Osaka, Osaka, 550-0006, Japan Site: 20046
Poland	
Komisja Bioetyczna przy Okregowej Radzie Lekarskiej Wielkopolskiej Izby Lekarskiej Ul. Nowowiejskiego 51 61-734 Poznan Poland Sites: 40037, 40038, 40039, 40041, 40042, 40043, 40044, 40088, 40090, 40091, 40092, 40093, 40094, 40095, 40096, 40097, 40098, 40118, 40119	Komisja Bioetyczna przy Okregowej Radzie Lekarskiej Wielkopolskiej Izby Lekarskiej Ul. Nowowiejskiego 51 61-734 Poznan Poland Sites: 40037, 40038, 40039, 40041, 40043, 40044, 40090, 40091,40097, 40098, 40118, 40119
Russian Federation	
Leningrad Regional Clinical Hospital Ethics Committe 45-49 Prospect Lunacharskogo 194291 Saint-Petersburg Russian Federation Site: 20001	Leningrad Regional Clinical Hospital Ethics Committe 45-49 Prospect Lunacharskogo 194291 Saint-Petersburg Russian Federation Site: 20001
Clinical Rheumatological Hospital #25 Ethics Committe Liter A, 30 Bolshaya Podyacheskaya Ulitsa 190068 Saint-Petersburg Russian Federation Site: 20003	Indepentent Ethics Committee "Pharmexpert" 8/2, prospekt Nauki Sankt-Peterburg 195257 Saint-Petersburg Russian Federation Site: 20004
Indepentent Ethics Committee "Pharmexpert" 8/2, prospekt Nauki Sankt-Peterburg 195257 Saint-Petersburg Russian Federation	LLC Family Outpatient Clinic 4 Local Ethic Committee 33, Stantsionnaya st 141060 Korolev Russian Federation

Site: 20004	Site: 20005
LLC Family Outpatient Clinic 4 Local Ethic Committee 33, Stantsionnaya str 141060 Korolev Russian Federation Site: 20005	LLC "BioMed" - Administration Administration 6, Nikitina street 600005 Vladimir Russian Federation Site: 20006
LLC "BioMed" - Administration Administration 6, Nikitina street 600005 Vladimir Russian Federation Site: 20006	LLC Clinic of private security guards and detectives 84, Borovaya str Sankt-Peterburg 192007 Saint Petersburg Russian Federation Site: 20009
LLC Clinic of private security guards and detectives 84, Borovaya str Sankt-Peterburg 192007 Saint Petersburg Russian Federation Site: 20009	City Clinical Hospital # 1 n.a. N.I. Pirogov Ethics Committee 8, Leninsky Prospect Moskva 119049 Moscow Russian Federation Site: 20010
City Clinical Hospital # 1 n.a. N.I. Pirogov Ethics Committee 8, Leninsky Prospect Moskva 119049 Moscow Russian Federation Site: 20010	Clinical Hospital Of Emergency Care N.V. Soloviev Ethics Committe 11 Ulitsa Zagorodnyj Sad 150003 Yaroslavl Russian Federation Site: 20015
Clinical Hospital of Emergency Care N.V. Soloviev Ethics Committe 11 Ulitsa Zagorodnyj Sad	Rheumatology Research Institute Of Russian Academy Of Medica

150003 Yaroslavl Russian Federation Site: 20015	Ethics Committe Kashirskoe Shosse, 34 115522 Moscow Russian Federation Sites: 20002
Rheumatology Research Institute of Russian Academy of Medica Ethics Committe Kashirskoe Shosse, 34 115522 Moscow Russian Federation Sites: 20002, 20017	Saratov Regional Clinical Hospital rheumatology 1, Smirnovskoe uschelye Saratovskaya oblast' 410053 Saratov Russian Federation Site: 20007
Saratov Regional Clinical Hospital Rheumatology 1, Smirnovskoe uschelye Saratovskaya oblast 410053 Saratov Russian Federation Site: 20007	SBHI of Yaroslavl Region "Clinical Hospital n.a. N.A. Semashko" 12, Gagarina street Yaroslavskaya oblast' 150023 Yaroslavl Russian Federation Site: 20008
SBHI of Yaroslavl Region "Clinical Hospital n.a. N.A. Semashko 12, Gagarina street Yaroslavskaya oblast 150023 Yaroslavl Russian Federation Site: 20008	The Republican Hospital N.A. V.A. Baranov Ethics Committe 3 Ulitsa Pirogova 185019 Petrozavodsk Russian Federation Site: 20013
Ryazan State Medical University I.P. Pavlov Ethics Committe 9, Vysokovoltnaya Ulitsa 390026 Ryazan Russian Federation	Ulyanovsk Regional Clinical Hospital Rheumatology 7, Tretyego Internatsionala ul. 432063 Ulyanovsk Russian Federation

Site: 20012	Site: 20014
The Republican Hospital N.A. V.A. Baranov Ethics Committe 3 Ulitsa Pirogova 185019 Petrozavodsk Russian Federation Site: 20013	–
Ulyanovsk Regional Clinical Hospital Rheumatology 7, Tretyego Internatsionala ul. 432063 Ulyanovsk Russian Federation Site: 20014	–
Ryazan Regional Clinical Cardiological Dispensary Local Ethics Committee 96 Stroikova Ulitsa 390026 Ryazan Russian Federation Site: 20016	–
The Llc Institute of Medical Trials Lec 25 Koli Tomchaka Ul. Liter A3 196084 Saint-Petersburg Russian Federation Site: 20083	–
Spain	
CEIC Corporació Sanitària Parc Taulí Fundació Parc Taulí Edifici Santa Fe Ala izquierda, 2ª planta C/ Parc Taulí, 1 Barcelona 08208	–

Sabadell Spain Sites: 40045, 40049, 40099, 40101, 40102, 40103, 40104, 40105, 40106	
United Kingdom	
New Cross hospital Rheumatology New Cross hospital Wolverhampton WV10 0QP Wolverhampton United Kingdom Site: 40107	Nuffield Orthopaedic Centre ND07, NDORMS Windmill Road, Headington Oxfordshire OX3 7HE Oxford United Kingdom Site: 40109
Nuffield Orthopaedic Centre ND07, NDORMS Windmill Road, Headington Oxfordshire OX3 7HE Oxford United Kingdom Site: 40109	Bradford Royal Infirmary Rheumatology Duckworth Lane BD9 6RJ Bradford United Kingdom Site: 40111
Royal Cornwall Hospital Treliske Truro Cornwall TR1 3LJ Cornwall United Kingdom Site: 40112	Stamford and Rutland hospital Ryhall Road PE9 1UA Stamford United Kingdom Site: 40116
Barnsley Hospital NHS Foundation Trust Gawber Road S75 2EP Barnsley	–

United Kingdom Site: 40115	
United States	
Advarra IRB/IEC 6100 Merriweather Drive, Suite 600 Maryland 21044 Columbia United States Sites: 50001, 50002, 50004, 50006, 50007, 50008, 50009, 50012, 50015, 50016, 50017, 50020, 50028, 50029, 50033, 50035, 50036, 50037, 50039, 50040, 50049, 50050, 50051, 50125	Advarra IRB/IEC 6100 Merriweather Drive, Suite 600 Maryland 21044 Columbia United States Sites: 50001, 50002, 50004, 50005, 50006, 50008, 50009, 50011 50012, 50015, 50016, ,50017, 50019, 50020, 50021, 50024, 50026, 50028, 50029, 50031, 50033, 50034, 50035, 50036, 50037, 50039, 50040, ,50047 50050, 50064, 50125
WCG IRB IRB/EC 1019 39th Avenue SE Suite 120 Washington 98374 Puyallup United States Site: 50010	WCG IRB IRB/EC 1019 39th Avenue SE Suite 120 Washington 98374 Puyallup United States Site: 50010
–	Ochsner Institutional Review Board Institutional Review Board 1514 Jefferson Highway Louisiana 70121 New Orleans UNITED STATES Site: 50023

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