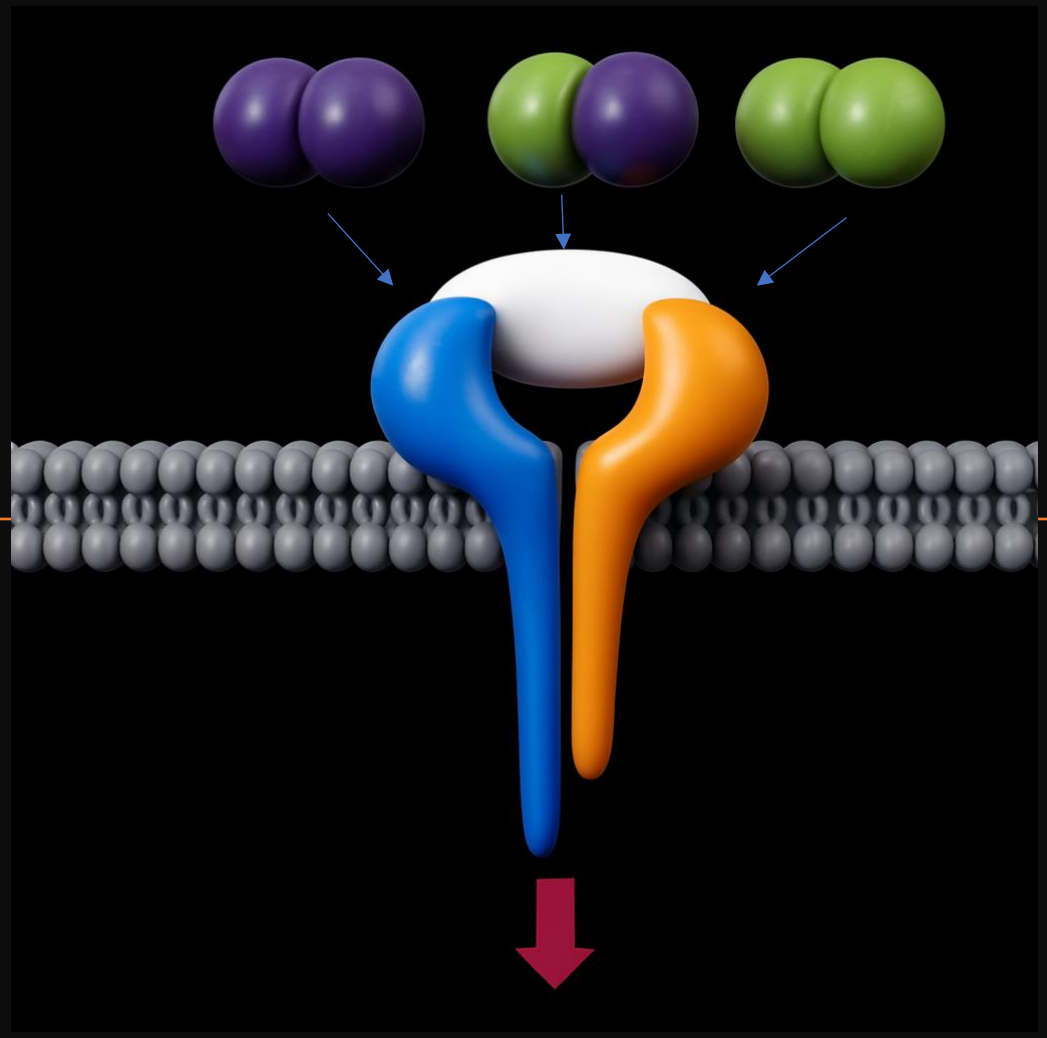
Διπλή αναστολή των IL-17A & F σε PsA και axSpA:
3 χρόνια δεδομένων, 1 χρόνος ελληνικής εμπειρίας



Αναστάσιος Καραμανάκος

Ρευματολόγος

ΓΝ «Ο Ευαγγελισμός»

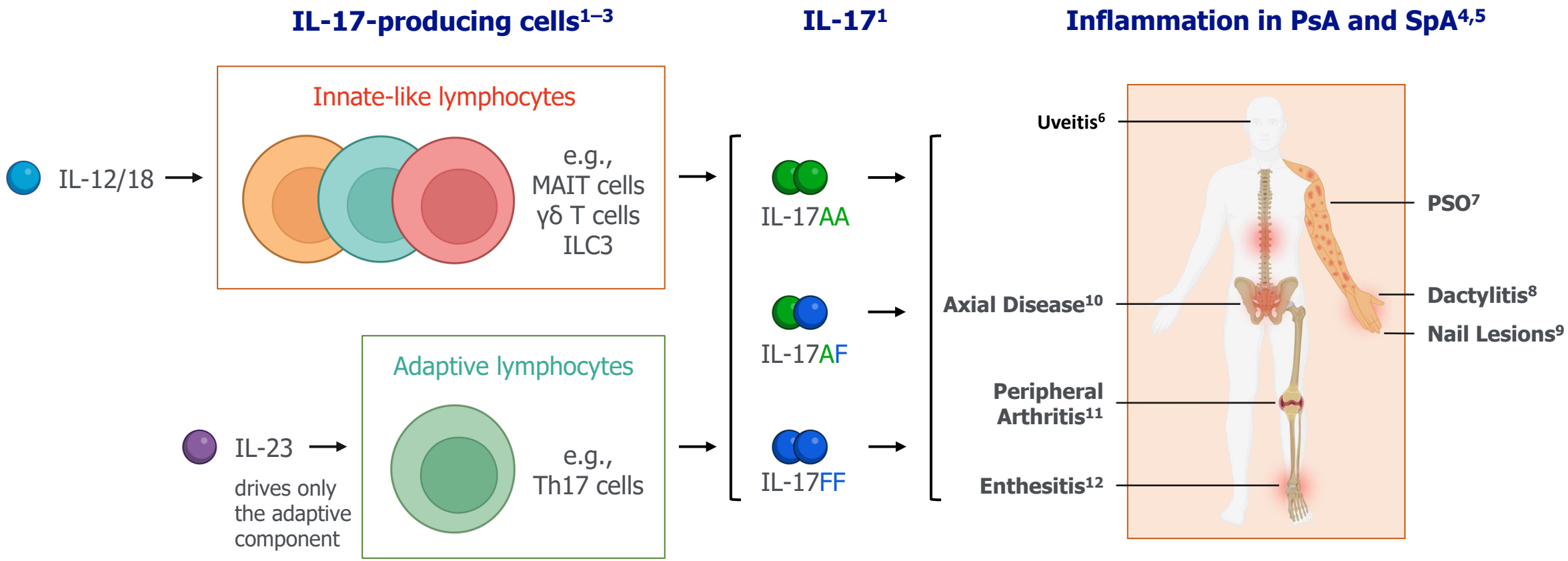
GR-BK-2500080

Σύγκρουση συμφερόντων

Έχω λάβει τιμητική αμοιβή από την εταιρεία UCB

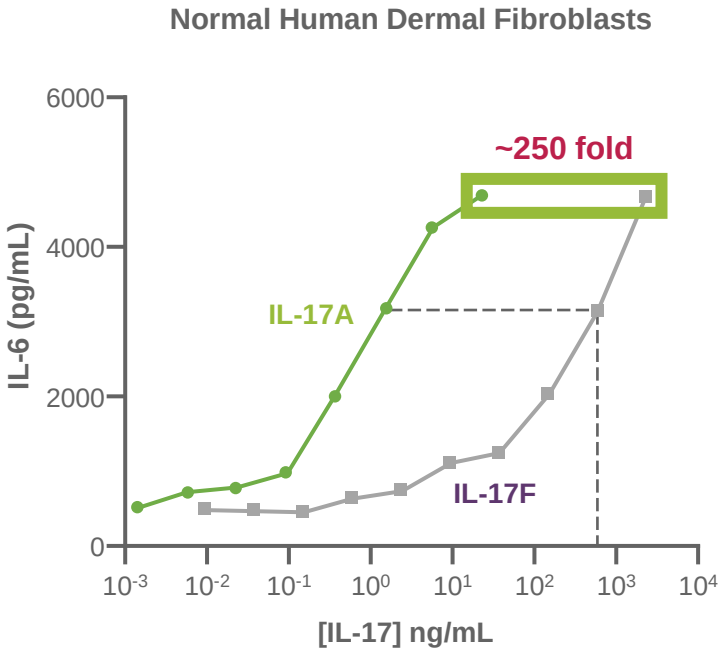
Το παρόν υλικό προορίζεται αποκλειστικά για επιστημονική ενημέρωση επαγγελματιών υγείας. Περιλαμβάνει ανασκόπηση δημοσιευμένων δεδομένων και δεν αποτελεί προωθητικό υλικό. Η χρήση της δραστικής ουσίας bimekizumab δεν προβάλλεται για σκοπούς συνταγογράφησης.

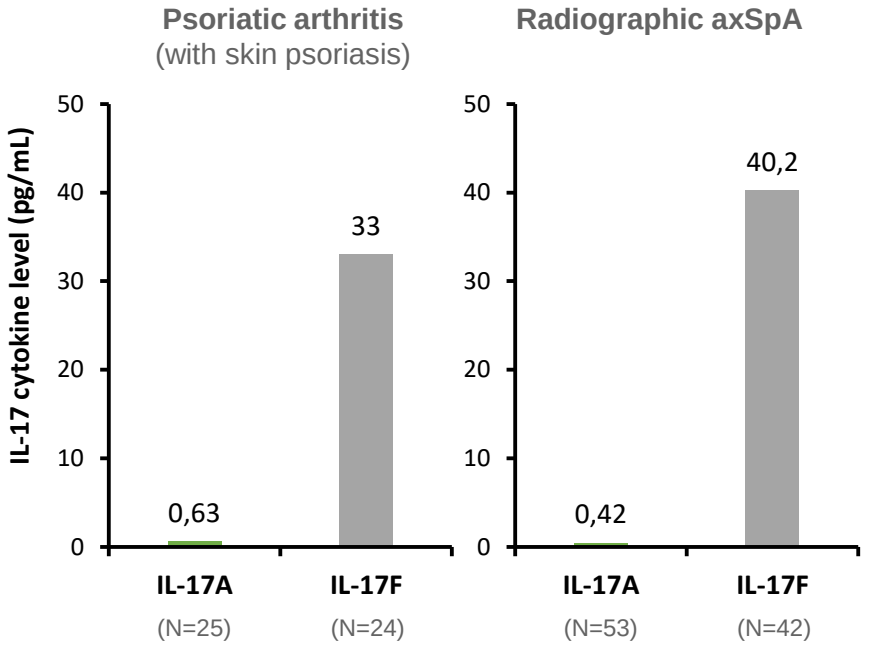
IL-17A and IL-17F are Produced by a Range of Lymphocytes[1]



1. Tsukazaki H, Kaito T. Int J Mol Sci. 2020;21(17):6401. 2. Cole S, et al. Front Immunol. 2020;11:585134. 3. Łukasik Z, et al. Rheumatology (Oxford). 2021;60(Suppl 4):iv16–27. 4. Shah M, et al. RMD Open. 2020;6(2):e001306. 5. Wang EA, et al. Eur J Rheumatol. 2017;4(4):272–77. 6. De Vicente Delmás A, et al. RMD Open. 2023;9:e002781. 7. Kane D, et al. Rheumatology (Oxford). 2003;42(12):1460–68. 8. Helliwell PS, et al. J Rheumatol. 2005;32(9):1745–50. 9. Sobolewski P, et al. Reumatologia. 2017;55(3):131–35. 10. McGagh D, Coates LC. Rheumatology (Oxford). 2020;59(Suppl 1):i29–36. 11. Helliwell PS, Taylor WJ. Ann Rheum Dis. 2005;64(Suppl 2):ii3–8. 12. Kaeley GS, et al. Semin Arthritis Rheum. 2018;48(1):35–43. γδ T cell: gamma delta T cell; IL: interleukin; ILC3: type 3 innate lymphoid cell; MAIT: mucosal-associated invariant T cell; PsA: psoriatic arthritis; PSO: psoriasis; Th17: IL-17-producing type 17 T cell; SpA: spondyloarthritis.

IL-17F is Less Potent But More Abundantly Expressed Than IL-17A in PsA and axSpA[1,2]





IL-17A is ~250-fold more potent than IL-17F[1]

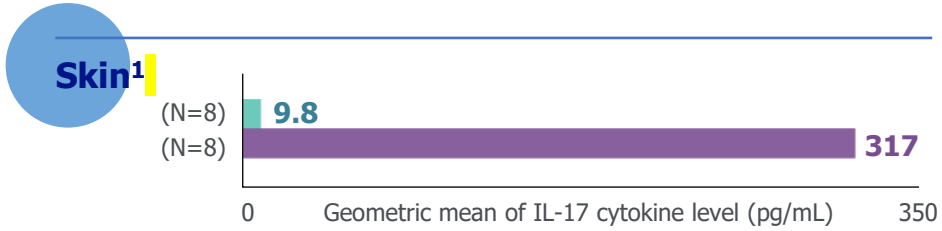
Serum* IL-17F levels are at least 50-fold higher than IL-17A in patients with PsA and AS[2]

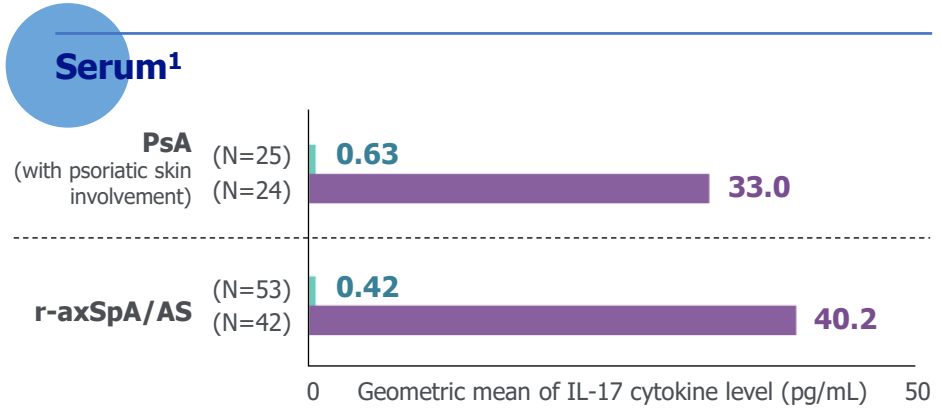
AS: Ankylosing spondylitis

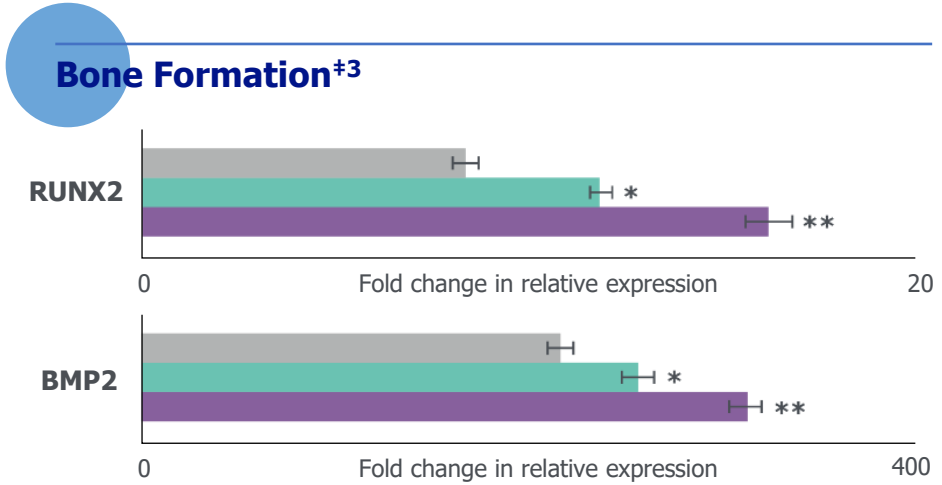
*Systemic biomarkers of inflammation. Data are mean ± SEM.

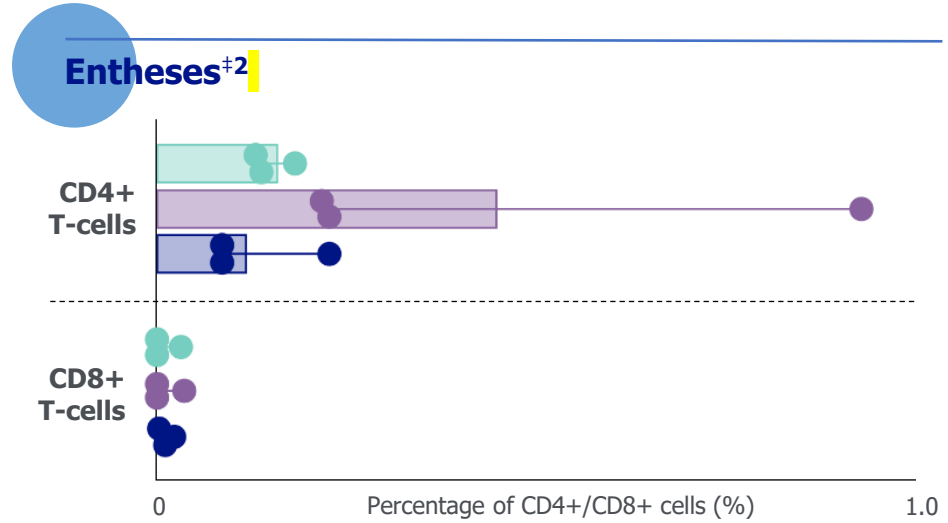
1. Adapted from Maroof et al. ESDR 2017. Poster P426.
2. Adapted from Kolbinger et al. J Allergy Clin Immunol. 2017;139:923–932.

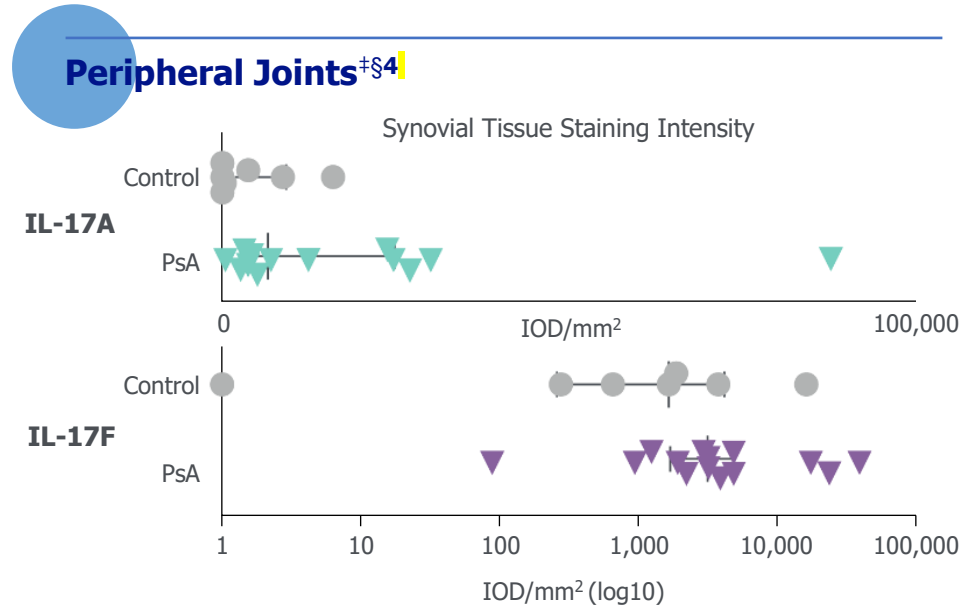
IL-17A and IL-17F in Tissues and Sites of Interest in SpA









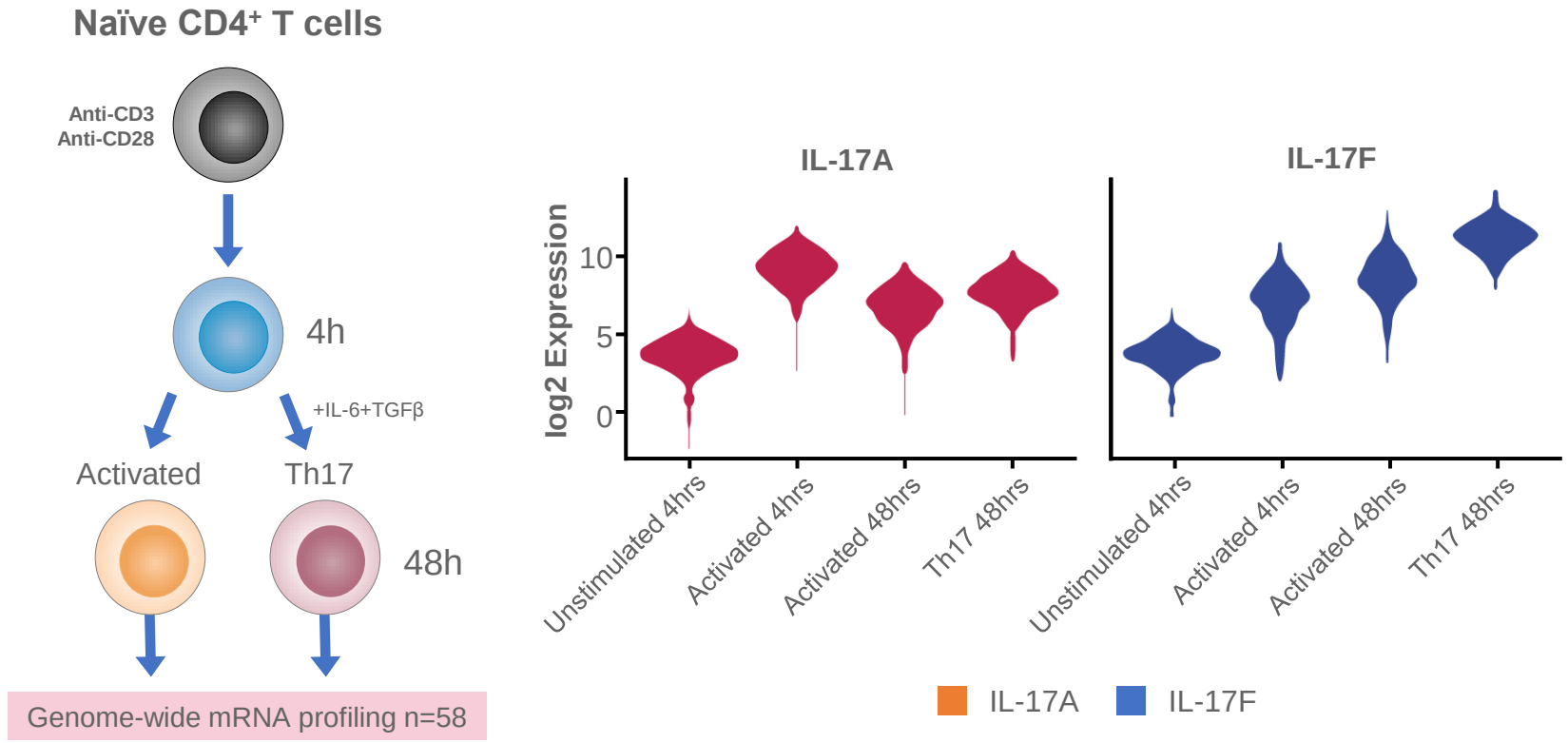


IL-17A
IL-17F
IL-17A/F
Control/DM

- *p<0.01; **p<0.001. ‡Estimated value based on graph visualiser software. §IL-17F data presented on a logarithmic scale; IL-17A data presented on a linear scale. BMP2: bone morphogenetic protein 2; CD: cluster of differentiation; DM: differentiation medium; IL: interleukin; PsA: psoriatic arthritis; RUNX2: runt-related transcription factor 2; r-axSpA: radiographic axial spondyloarthritis; SpA: spondyloarthritis.

1. Kolbinger F et al. J Allergy Clin Immunol. 2017;139:923–32. 2. McDermott N et al. Ann Rheum Dis. 2023;82(Suppl 1):1184. 3. Shah M et al. RMD Open. 2020;6(2):e001306. 4. van Baarsen LG et al. Arthritis Res Ther. 2014;16(4):426

Evidence of Temporal Transcription Disconnect Between IL-17A and IL-17F



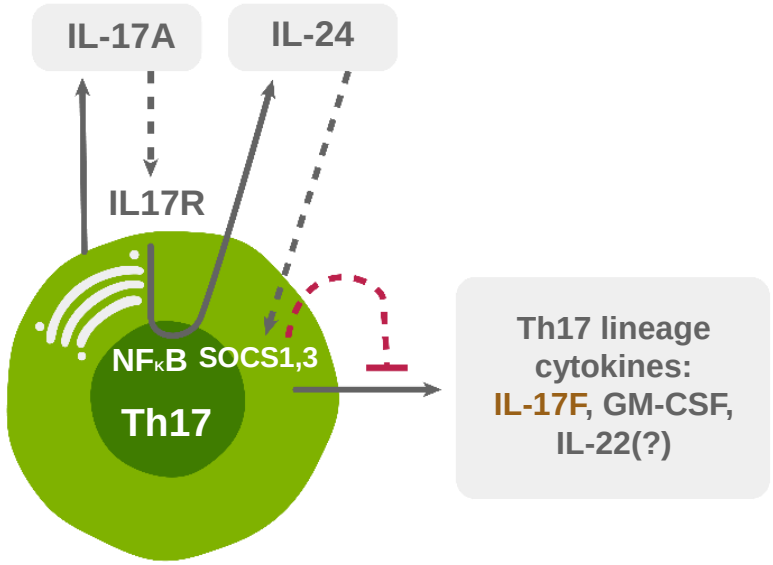
Transcript analysis shows early IL-17A expression after stimulation, followed by a later IL-17F response

TGFβ: Transforming growth factor beta; Th17: T-helper 17 cells

Adapted from Ye et al. Science. 2014;12;345(6202):1254665

Bimekizumab is the First Biologic that Selectively Inhibits IL-17F in Addition to IL-17A[1]

- IL-17A binds to its receptor on Th17 cells, activating NF-κB, inducing IL-24 and repressing the Th17 cytokine program through SOCS1/3
- IL-17A deficiency does not reduce the pathogenicity of Th17 cells in uveitis
- **Loss of IL-17A elevates Th17 expression** of cytokines GM-CSF and **IL-17F** and possibly IL-22
- Th17 lineage cytokines may be implicated in uveitis



GM-CSF: granulocyte-macrophage colony-stimulating factor; NF-κB: nuclear factor-kB; Th17: IL-17-producing type 17 T cell; SOCS: suppressor of cytokine signalling.

Adapted from Chong WP, et al. Immunity. 2020;53(2):384–97.

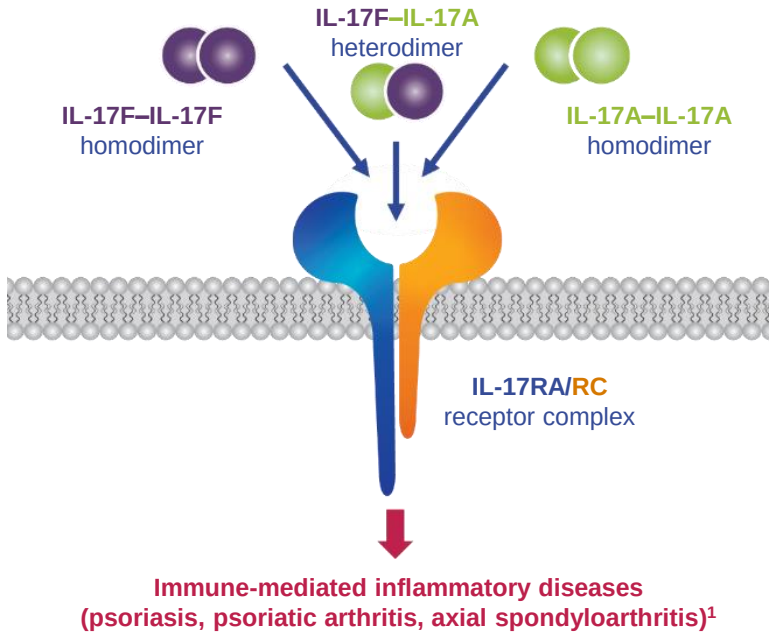
Rationale for Neutralising IL-17F in Addition to IL-17A

Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A[1]

IL-17A and IL-17F are key mediators of inflammation[2,3]

Signalling through the IL-17 receptor complex, IL-17A and IL-17F share >50% structural homology and form homodimers and heterodimers (IL-17A/A; 17 A/F; 17 F/F) that can promote inflammation and pathological bone formation/damage[1,4,5]

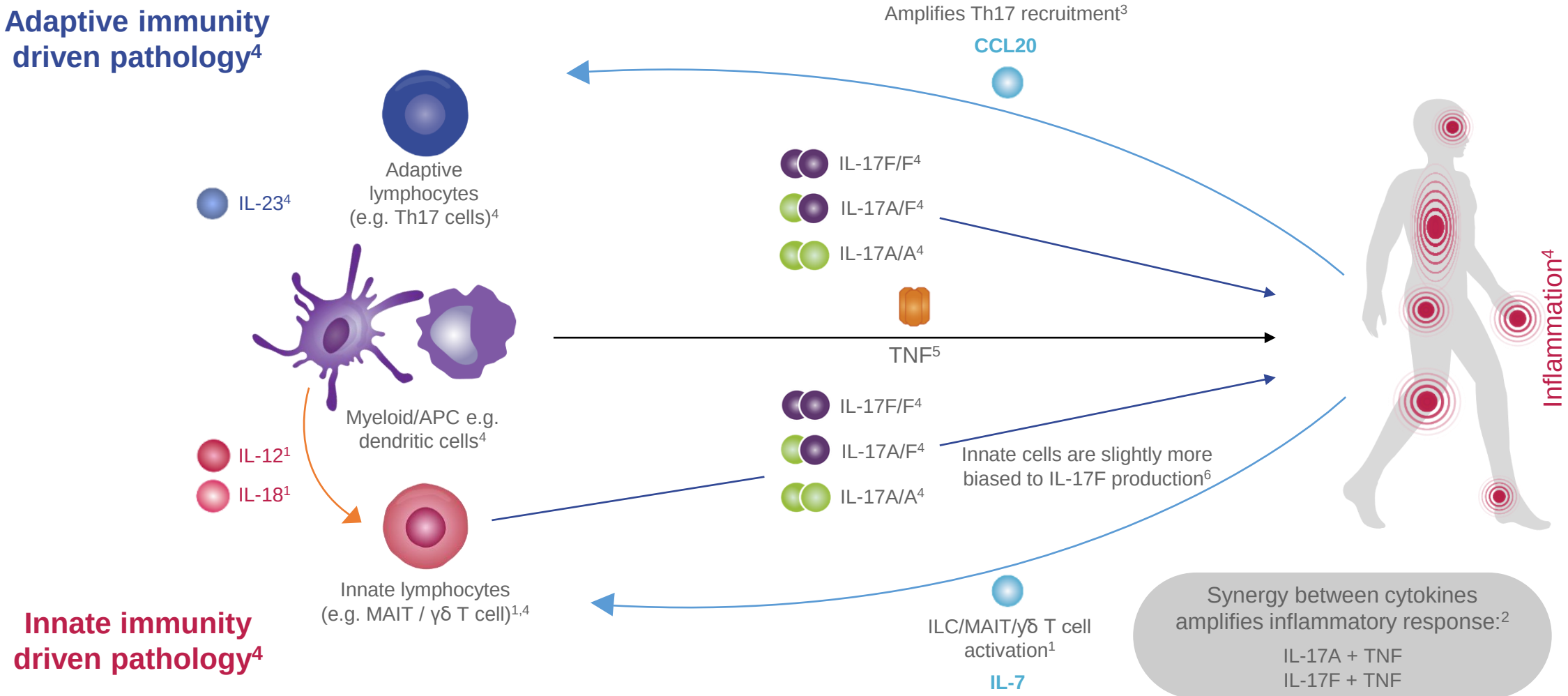
IL-17A and IL-17F[6]



Preclinical data comparing bimekizumab with IL-17A-specific inhibition suggest dual inhibition of IL-17A and IL-17F may lead to more effective suppression of inflammation[1,5,7,8]

1. Glatt S et al. Ann Rheum Dis. 2018;77(4):523–532. 2. Navarro-Compán V et al. Ann Rheum Dis. 2021;80: 1511–1521. 3. Sieper J et al. Nat Rev Rheumatol. 2019;15:747–757. 4. Pappu R et al. Immunology. 2011;134:8–16. 5. Shah M et al. RMD Open. 2020;6:e001306. 6. Yang XO et al. J Exp Med. 2008;205(5):1063–1075. 7. Adams R et al. Front Immunol. 2020;11:1894. 8. Reich K et al. N Engl J Med. 2021;385:142–152.

Synergy Between Cytokines and Additional Feedback Loops Amplify the Inflammatory Response[1–3]

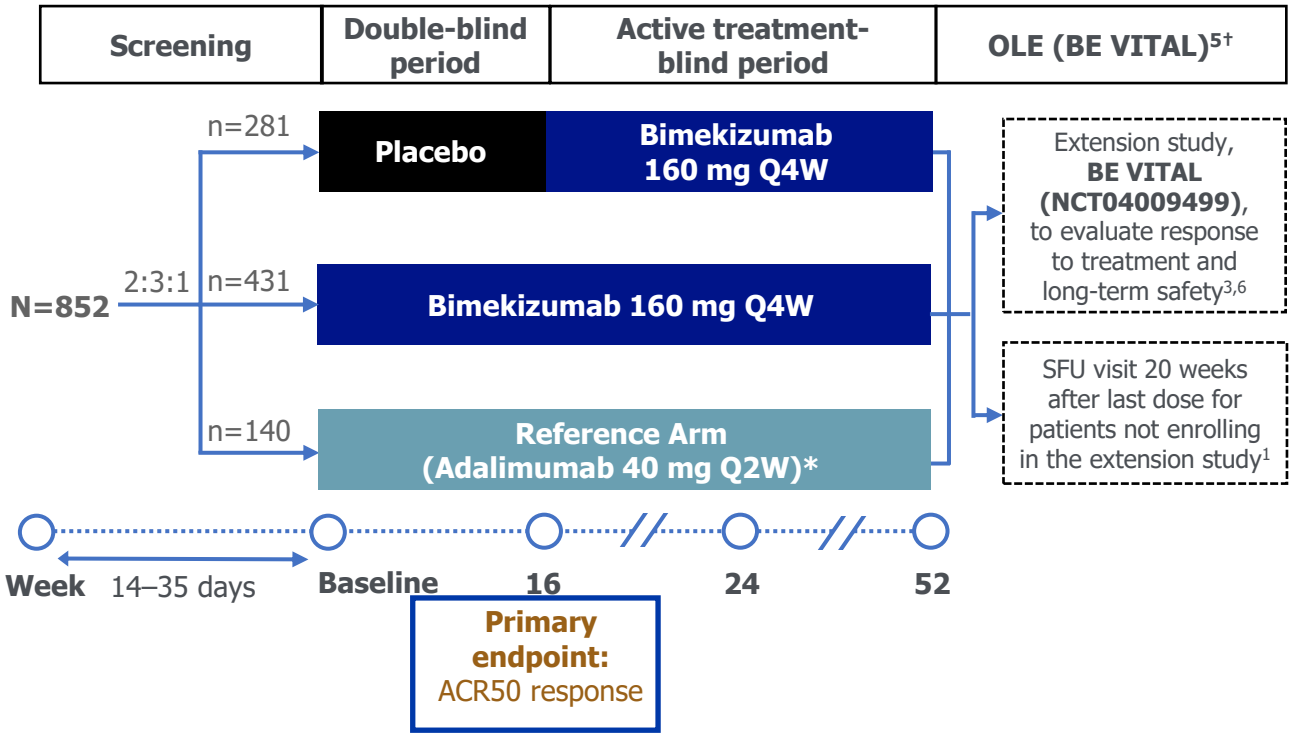


- Example cell types are shown; not an exhaustive list. APC: antigen-presenting cell; CCL20: C-C motif chemokine ligand 20; ILC: innate lymphoid cell; MAIT: mucosal-associated invariant T cell; Th17: T helper 17 cell; TNF: tumour necrosis factor; γδT: gamma delta T cell.

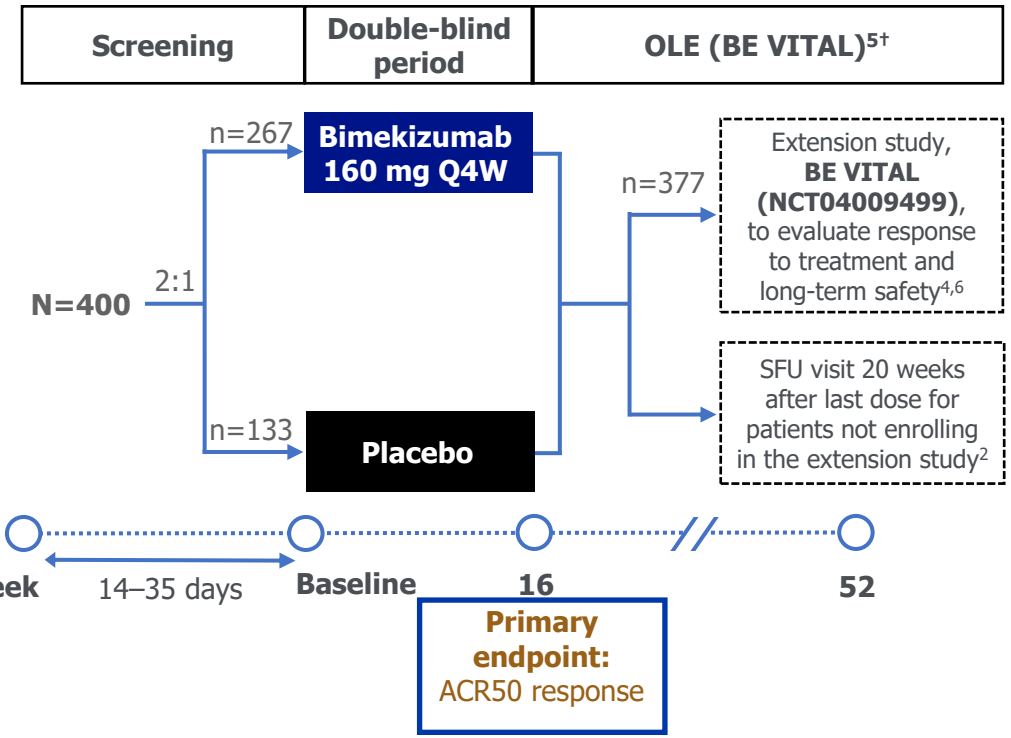
1. Rosine N, Miceli-Richard C. Front Immunol. 2021;11:553742. 2. Glatt S et al. Ann Rheum Dis. 2018;77:523–532. 3. Russell T et al. Cells. 2021;10(2):341. 4. Tsukazaki H, Kaito T. Int J Mol Sci. 2020;21(17):6401. 5. Blanco P et al. Cytokine Growth Factor Rev. 2008;19(1):41–52. 6. Cole S et al. Front Immunol. 2020;11:585134.2

BE OPTIMAL and BE COMPLETE Study Designs

BE OPTIMAL (bDMARD-naïve patients)[3]



BE COMPLETE (TNFi-IR patients)[4]



BKZ-treated patients were eligible to receive rescue therapy from Week 16 at the discretion of the investigator, while continuing to receive BKZ.[1,5] *The adalimumab 40 mg Q2W treatment arm served as an active reference.[1] †Response to treatment to 140 weeks and safety to 212 weeks from BE VITAL entry visit.[6] The BE OPTIMAL study was not powered for statistical comparisons of adalimumab to bimekizumab or adalimumab to placebo.[1] CASPAR: classification criteria for psoriatic arthritis.

1. McInnes IB et al. Lancet. 2023;401(10370):25–37. 2. Merola JF et al. Lancet. 2023;401(10370):38–48. 3. Adapted from McInnes IB et al. Lancet. 2023;401(10370):Suppl. 4. Adapted from Merola JF et al. Lancet. 2023;401(10370):Suppl. 5. Coates LC et al. EULAR 2023. Presentation POS0231. 6. PA0012, https://clinicaltrials.gov/ct2/show/NCT04009499. Accessed January 2024.

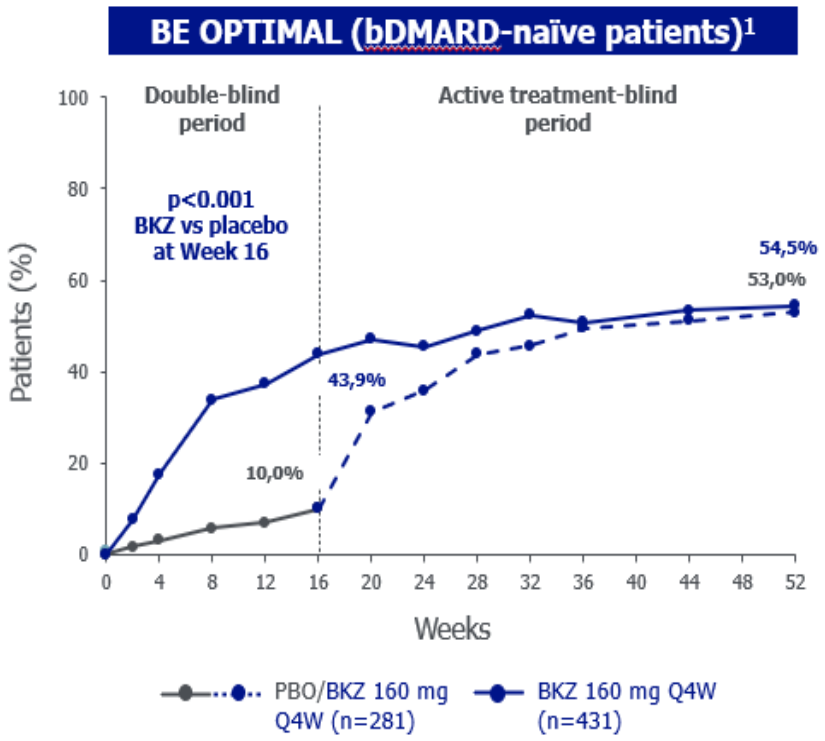
BE OPTIMAL and BE COMPLETE: Baseline characteristics

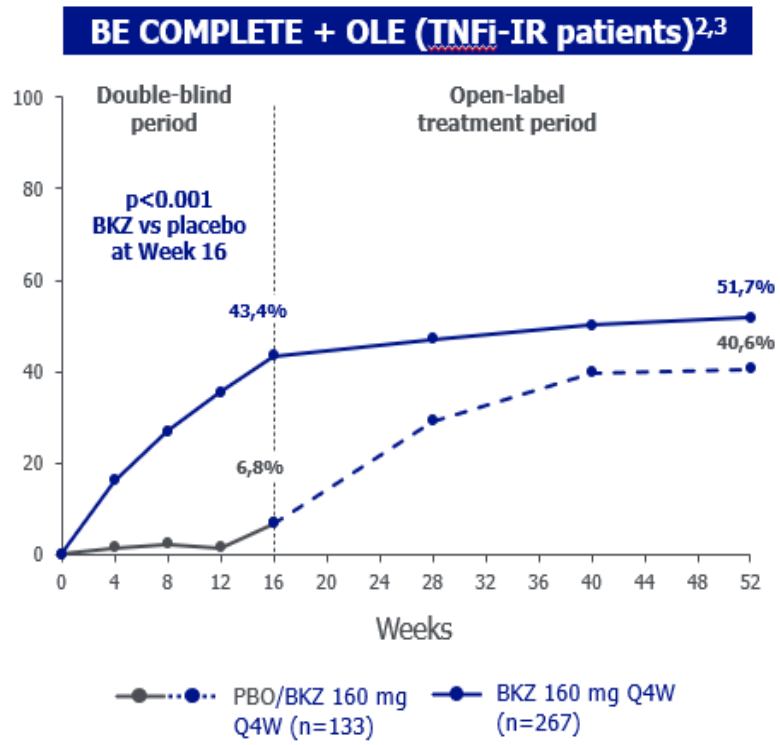
	BE OPTIMAL[1]			BE COMPLETE[2]	
	Placebo (n=281)	BKZ 160 mg Q4W (n=431)	Reference Arm (ADA 40 mg Q2W; n=140)	Placebo (n=133)	BKZ 160 mg Q4W (n=267)
Age, years, mean (SD)	48.7 (11.7)	48.5 (12.6)	49.0 (12.8)	51.3 (12.9)	50.1 (12.4)
Sex, male, n (%)	127 (45)	201 (47)	71 (51)	60 (45)	130 (49)
BMI, kg/m^2, 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,* years, mean (SD)	5.6 (6.5)	6.0 (7.3)	6.1 (6.8)	9.2 (8.1)	9.6 (9.9)
csDMARDs at baseline, n (%)	194 (69)	301 (70)	99 (71)	63 (47)	139 (52)
Concomitant methotrexate, n (%)	163 (58)	252 (59)	82 (59)	51 (38)	119 (45)
Prior TNFi exposure, n (%)					
Inadequate response to 1 TNFi	-	-	-	103 (77)	204 (76)
Inadequate response to 2 TNFi	-	-	-	15 (11)	29 (11)
Intolerance to TNFi	-	-	-	15 (11)	34 (13)
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)	9.7 (7.1)	10.3 (8.2)	9.7 (7.5)
hs-CRP ≥6 mg/L, n (%)	121 (43)	158 (37)	44 (31)	59 (44)	118 (44)

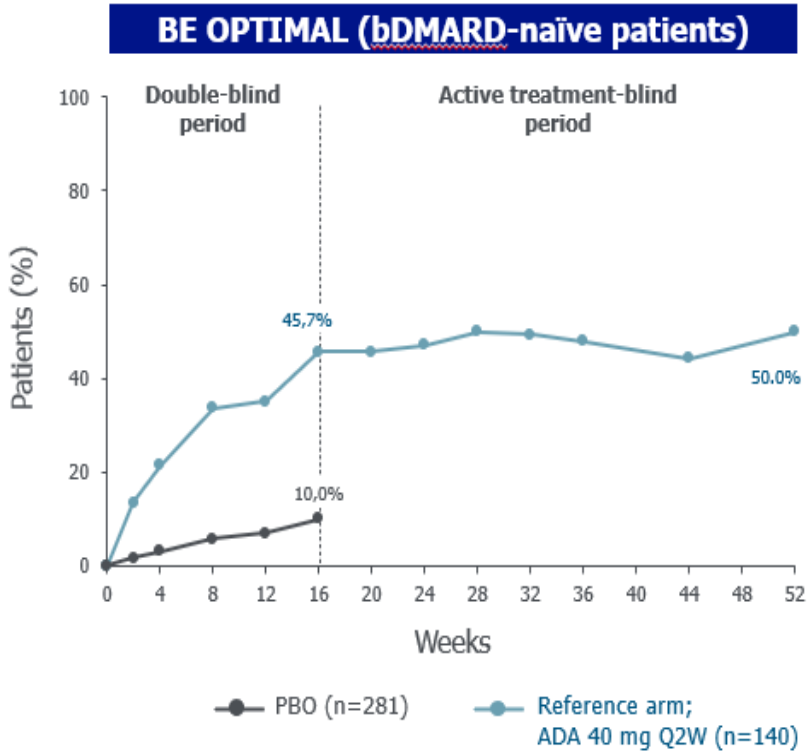
- Randomised set. BE OPTIMAL: the study was not powered for statistical comparisons of ADA to BKZ or ADA to PBO. *BE OPTIMAL: data missing for 2 placebo patients, 8 BKZ patients and 1 ADA patient; BE COMPLETE: data missing for 1 placebo patient and 1 BKZ patient.

1. Adapted from Ritchlin CT et al. Ann Rheum Dis. 2023;82(11):1404–1414.
2. Adapted from Merola JF et al. Lancet. 2023;401(10370):38–48.

ACR50 Responses with BKZ to Week 52 (NRI)





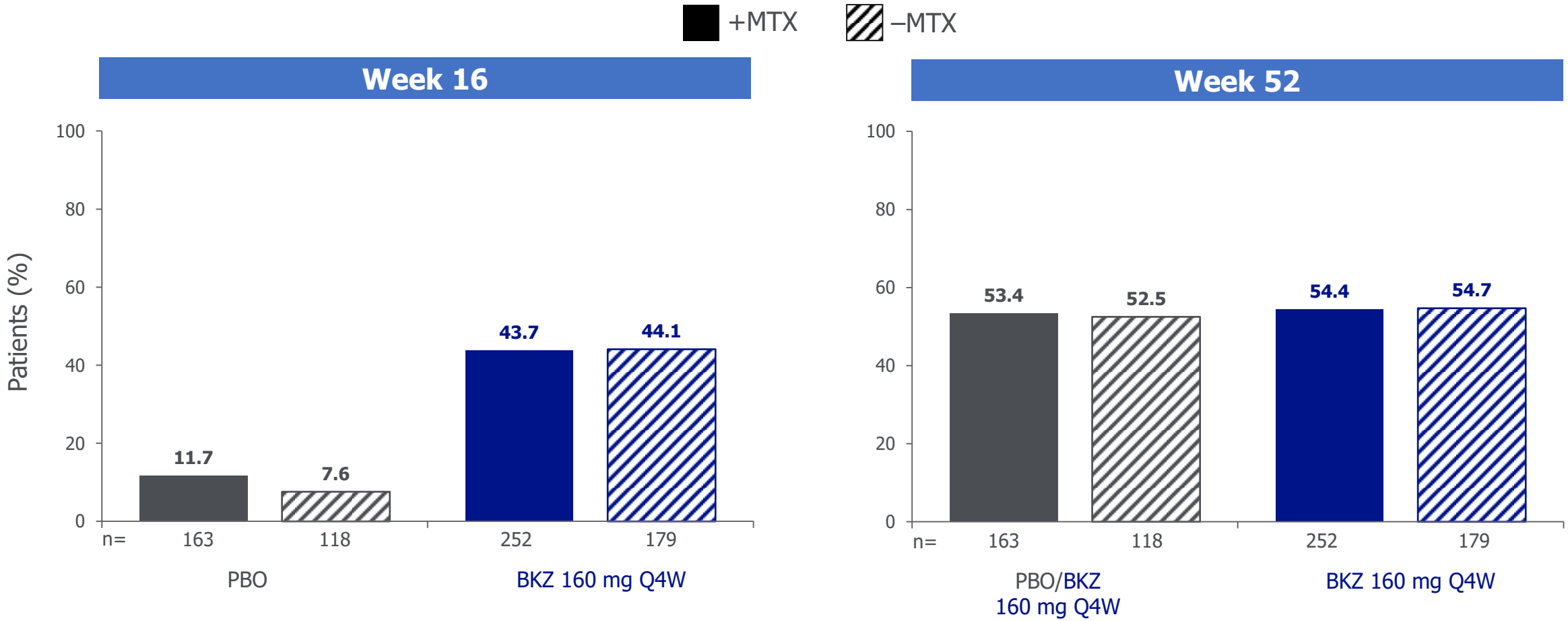


- **Non-responder imputation.** Randomised set. Primary endpoint: ACR50 at Week 16. BE OPTIMAL: p value for BKZ vs placebo was calculated using a logistic regression model with treatment, bone erosion at baseline and region as stratification factors. BE COMPLETE: p value calculated using a logistic regression model with treatment, prior TNFi exposure, and region as stratification factors.[2,3]

1. Adapted from Ritchlin CT et al. Ann Rheum Dis. 2023;82(11):1404–1414 2024. 2. Adapted from Coates L et al. Arthritis Rheumatol. 2023;75(Suppl 9). Abstract 2230. 3. Adapted from Merola JF et al. Lancet. 2023;401(10370):38–48.

Adapted from Ritchlin CT et al. Ann Rheum Dis. 2023;82(11):1404–1414.

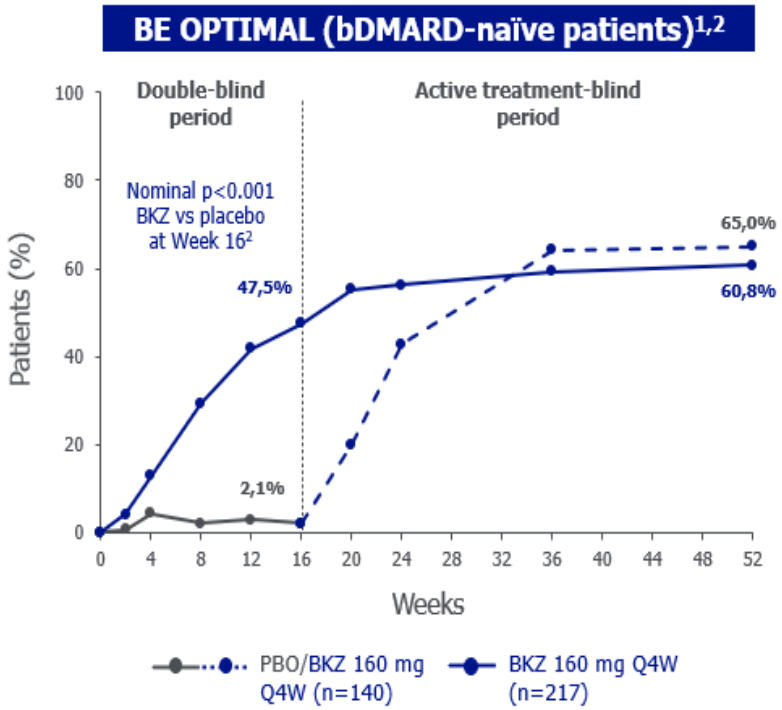
BE OPTIMAL: ACR50 Response +/– MTX to Week 52 (NRI)

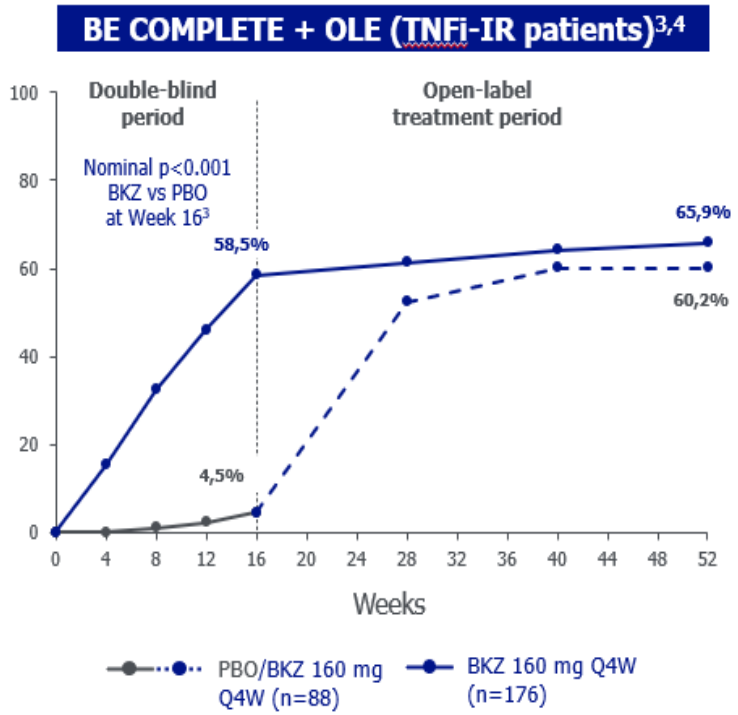


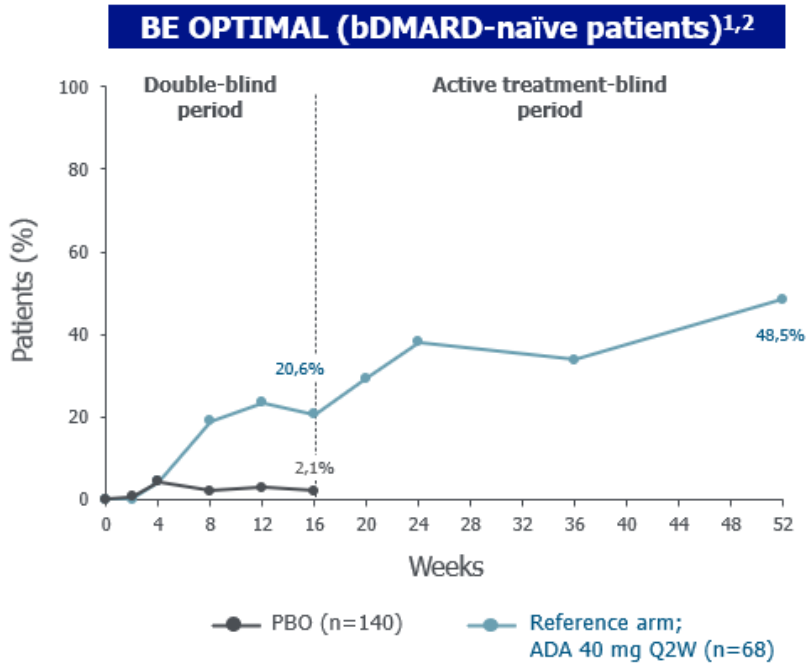
In BE OPTIMAL, bDMARD-naïve patients treated with BKZ achieved consistent clinical efficacy to Week 52, irrespective of concomitant MTX

Adapted from McInnes IB et al. EULAR 2023. Presentation POS1537

PASI100 Responses with BKZ to Week 52 (NRI)





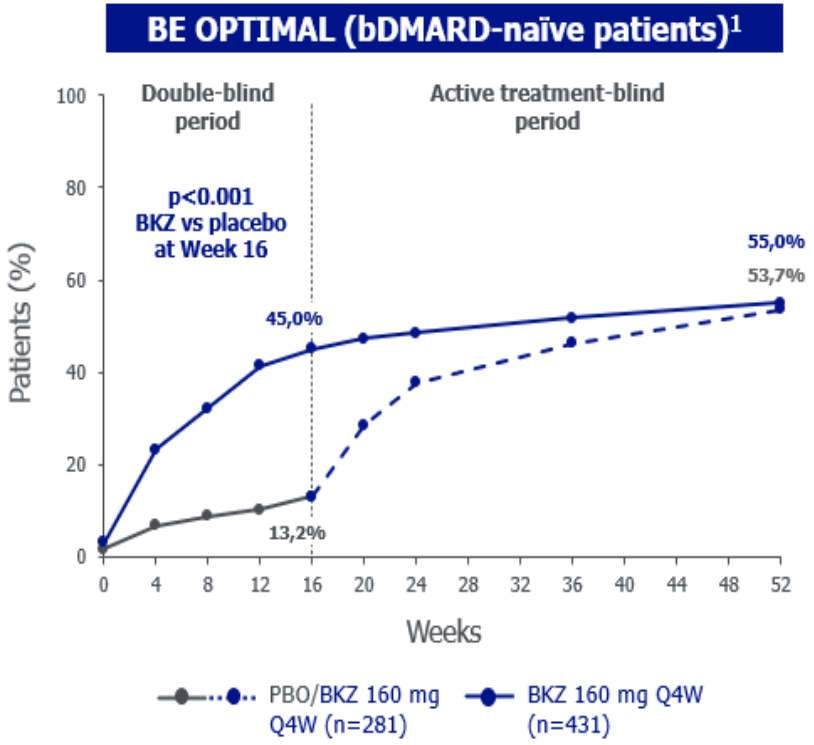


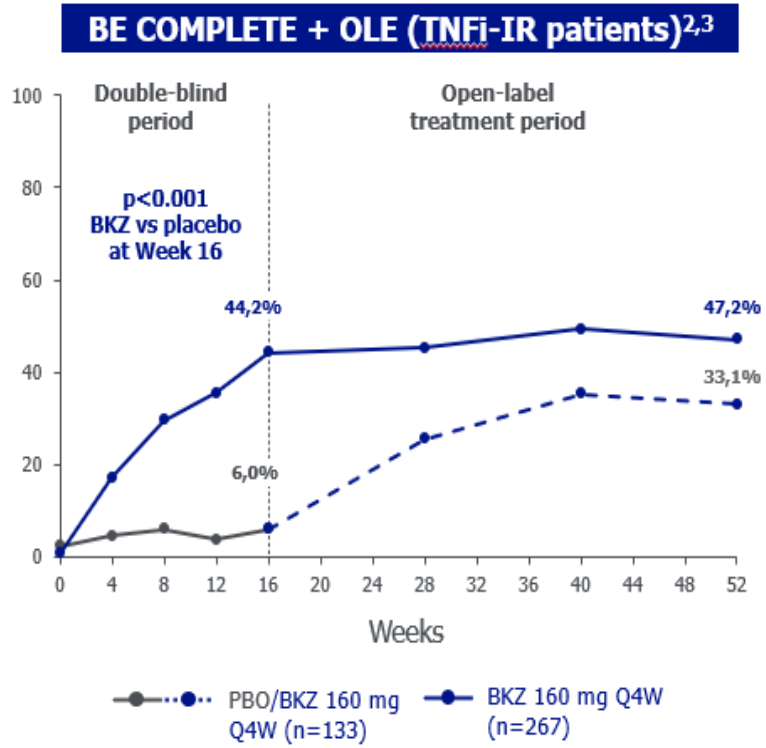
- **Non-responder imputation.** Randomised set. Primary endpoint: ACR50 at Week 16. BE OPTIMAL: p value for BKZ vs placebo was calculated using a logistic regression model with treatment, bone erosion at baseline and region as stratification factors. BE COMPLETE: p value calculated using a logistic regression model with treatment, prior TNFi exposure, and region as stratification factors.[2,3]

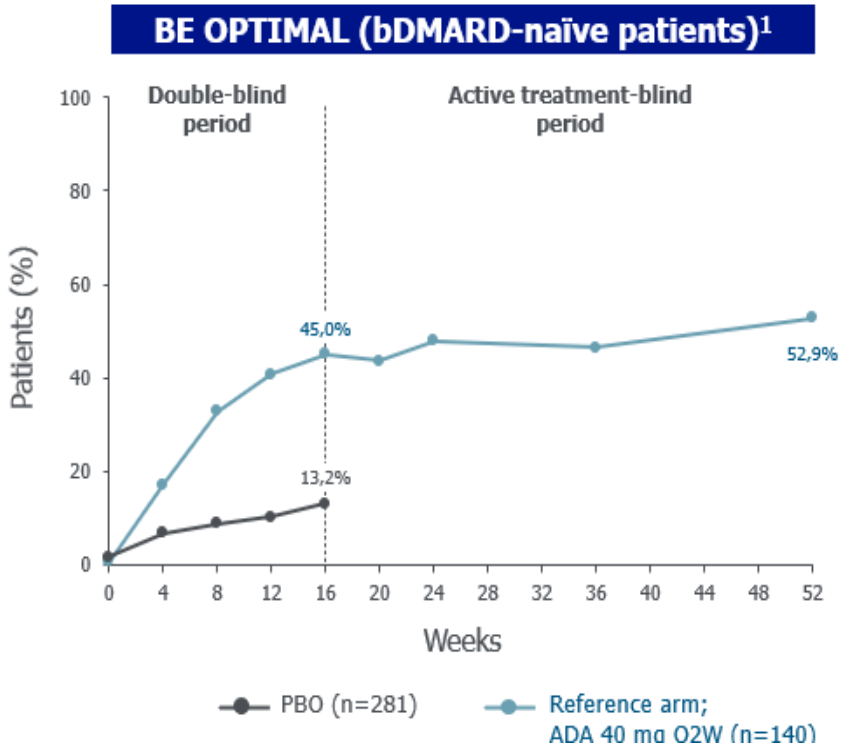
1. Adapted from Ritchlin CT et al. Ann Rheum Dis. 2023;82(11):1404–1414. 2. Ritchlin CT et al. Arthritis Rheumatol. 2022;74(Suppl 9). Abstract L02. 3. Adapted from Coates L et al. Arthritis Rheumatol. 2023;75(Suppl 9). Abstract 2230. 4. Adapted from Merola JF et al. Lancet. 2023;401(10370):38–48. 5. Ritchlin CT et al. ACR 2022. Presentation L02. .

1.Adapted from Ritchlin CT et al. Ann Rheum Dis. 2023;82(11):1404–1414. 2. Ritchlin CT et al. Arthritis Rheumatol. 2022;74(Suppl 9). Abstract L02.

MDA Response with BKZ to Week 52 (NRI)





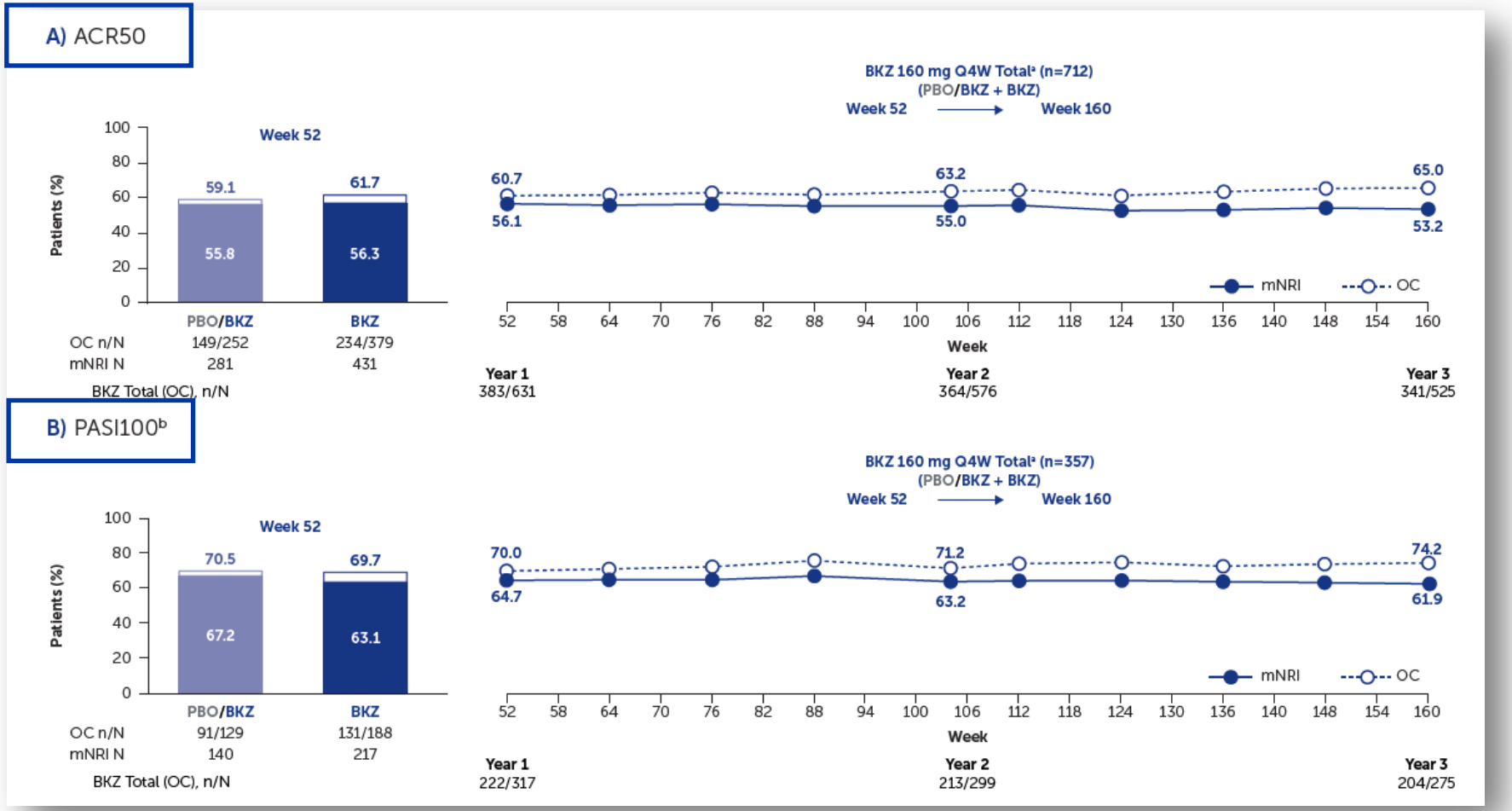


- **Non-responder imputation.** Randomised set. Primary endpoint: ACR50 at Week 16. BE OPTIMAL: p value for BKZ vs placebo was calculated using a logistic regression model with treatment, bone erosion at baseline and region as stratification factors. BE COMPLETE: p value calculated using a logistic regression model with treatment, prior TNFi exposure, and region as stratification factors.[2,3]

1. Adapted from Ritchlin CT et al. Ann Rheum Dis. 2023;82(11):1404–1414. 2. Adapted from Coates L et al. Arthritis Rheumatol. 2023;75(Suppl 9). Abstract 2230. 3. Merola JF et al. Lancet. 2023;401(10370): 38–48. 4. Ritchlin CT et al. ACR 2022. Presentation L02.

1.Adapted from Ritchlin CT et al. Ann Rheum Dis. 2023;82(11):1404–1414. 2. Ritchlin CT et al. ACR 2022. Presentation L02.

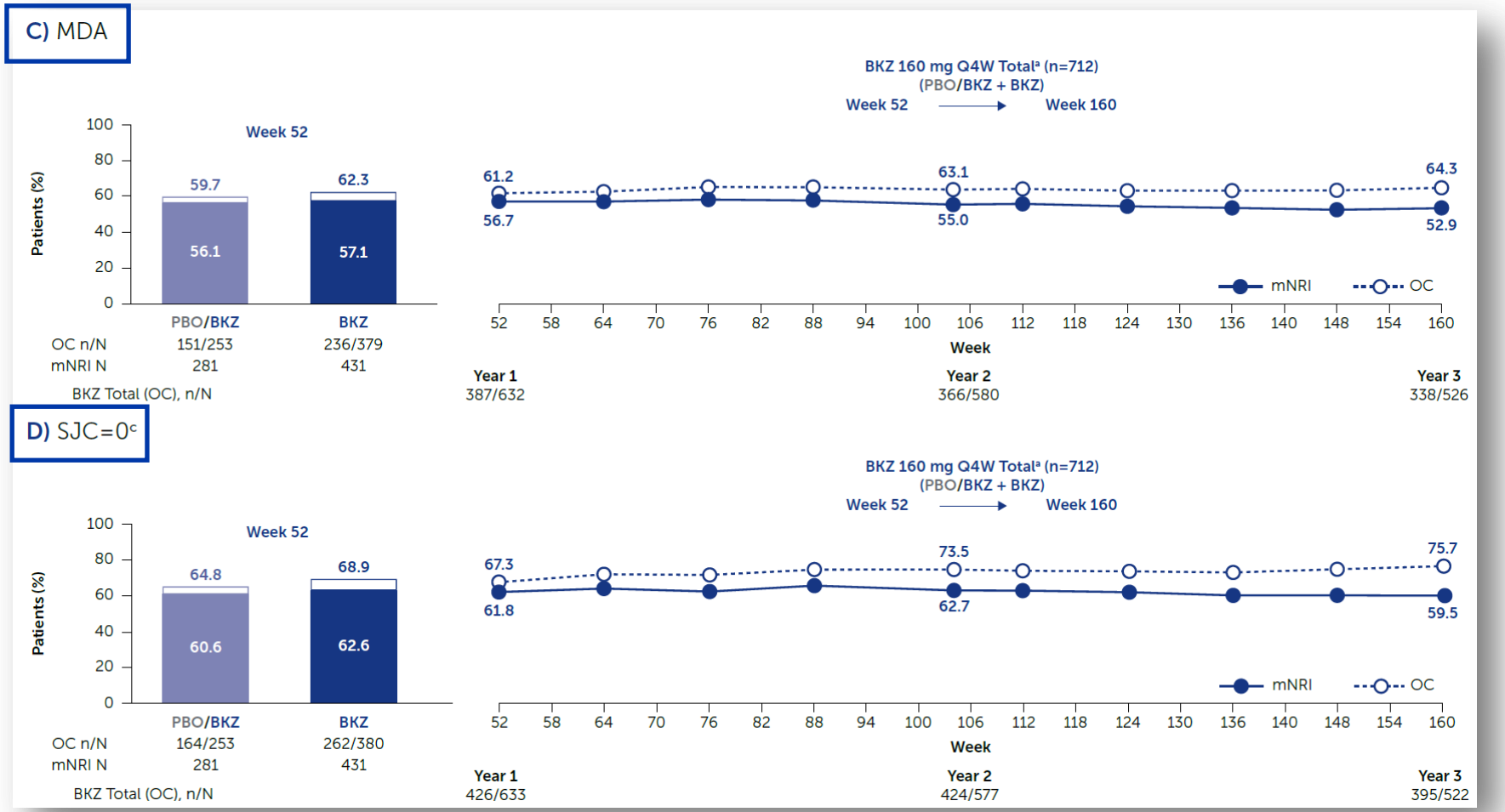
ACR50 and PASI100 Over Time to Week 160 in BE OPTIMAL (mNRI, OC)



Randomised set. Efficacy data reported from Year 1 (Week 52) through Year 2 (Week 104) and Year 3 (Week 160). [a]BKZ Total group includes BKZ-randomised patients and PBO-randomised patients who switched to BKZ at Week 16; [b]In patients with psoriasis involving ≥3% BSA at baseline (n=357). ACR50: ≥50% improvement from baseline in American College of Rheumatology response criteria; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; BSA: body surface area; mNRI: modified non-responder imputation; OC: observed case; PASI100: 100% improvement from baseline in Psoriasis Area and Severity Index; PBO: placebo; Q4W: every 4 weeks.

Gossec L, et al. EULAR 2025. Poster POS1294.

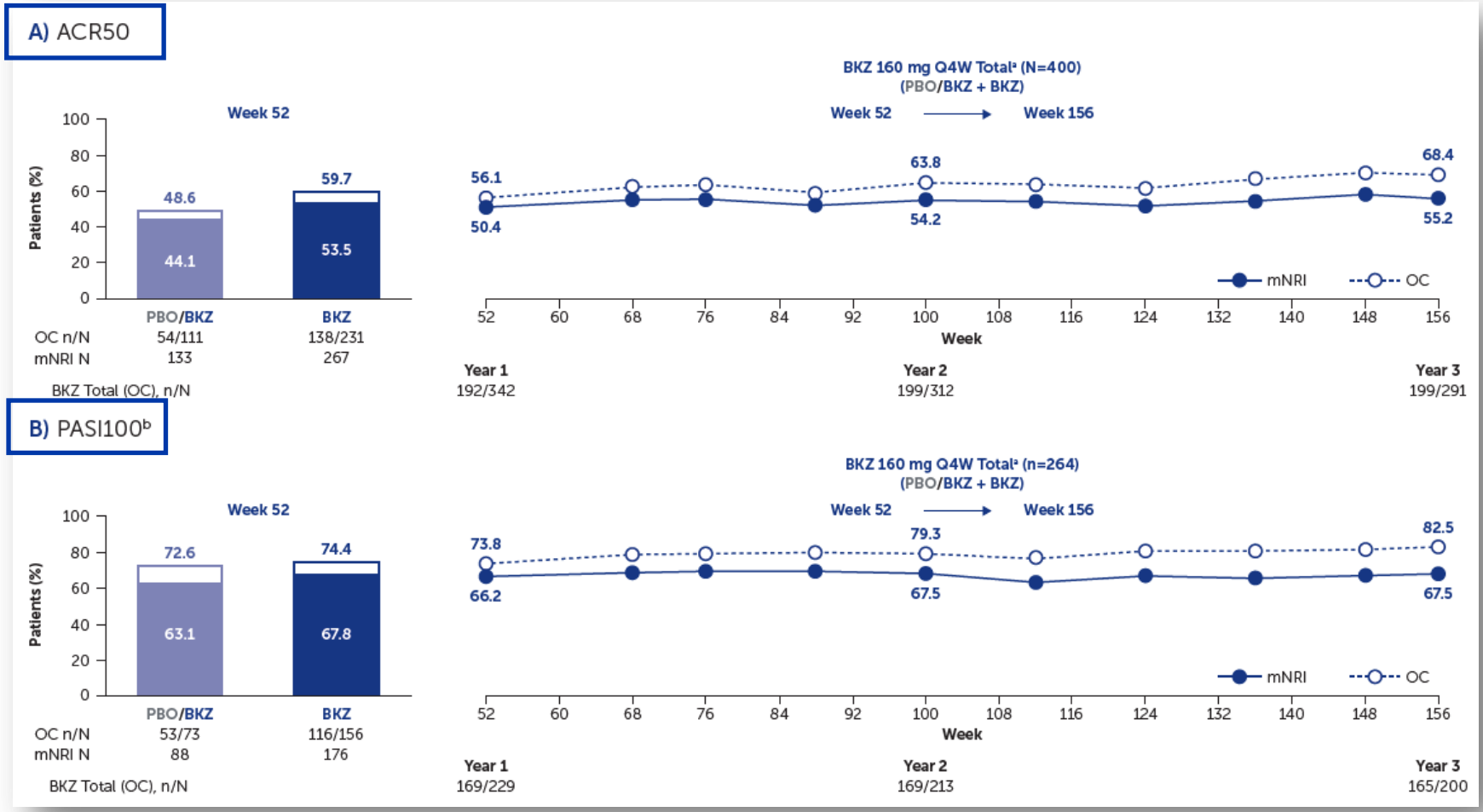
MDA and SJC=0 Over Time to Week 160 in BE OPTIMAL (mNRI, OC)



Randomised set. Efficacy data reported from Year 1 (Week 52) through Year 2 (Week 104) and Year 3 (Week 160). [a]BKZ Total group includes BKZ-randomised patients and PBO-randomised patients who switched to BKZ at Week 16; [c]Resolution of swollen joint count (SJC=0) was assessed in 66 joints. bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; MDA: minimal disease activity; mNRI: modified non-responder imputation; OC: observed case; PBO: placebo; Q4W: every 4 weeks; SJC: swollen joint count.

Gossec L, et al. EULAR 2025. Poster POS1294.

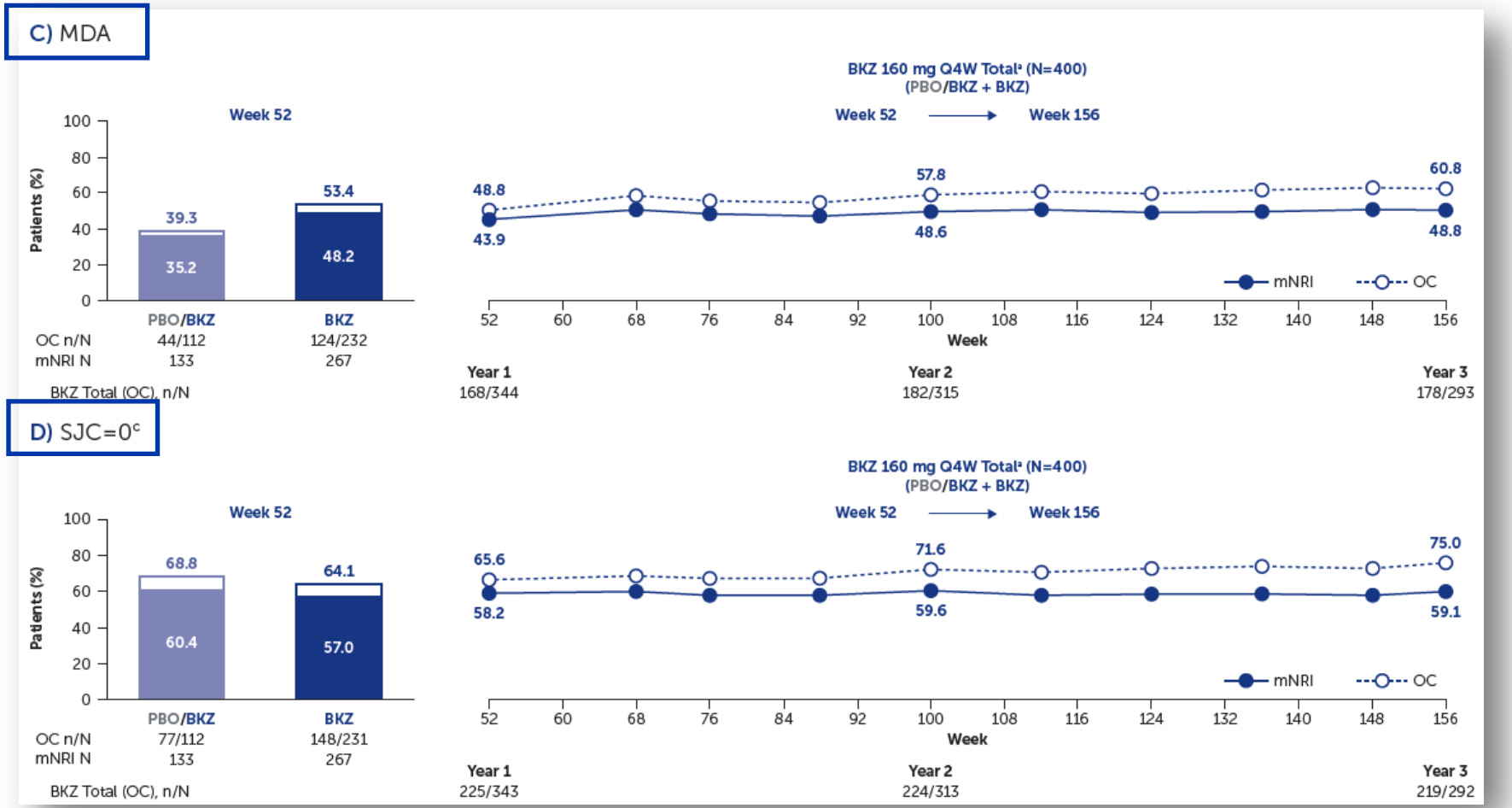
ACR50 and PASI100 Over Time to Week 156 in BE COMPLETE (mNRI, OC)



Randomised set. Data reported through Year 1 (Week 52) to Year 2 (Week 100) and Year 3 (Week 156). [a]BKZ Total group includes BKZ-randomised patients and PBO-randomised patients who switched to BKZ at Week 16; [b]In patients with psoriasis involving ≥3% BSA at baseline (n=264). ACR50: ≥50% improvement from baseline in American College of Rheumatology response criteria; BKZ: bimekizumab; BSA: body surface area; mNRI: modified non-responder imputation; OC: observed case; PASI100: 100% improvement from baseline in Psoriasis Area and Severity Index; PBO: placebo; Q4W: every four weeks; TNFi-IR: inadequate response or intolerance to tumour necrosis factor inhibitors.

McInnes IB, et al. EULAR 2025. Poster POS0105.

MDA and SJC=0 Over Time to Week 160 in BE COMPLETE (mNRI, OC)



Randomised set. Data reported through Year 1 (Week 52) to Year 2 (Week 100) and Year 3 (Week 156). [c]SJC=0 was assessed in 66 joints. BKZ: bimekizumab; MDA: minimal disease activity; mNRI: modified non-responder imputation; OC: observed case; PBO: placebo; Q4W: every four weeks; SJC: swollen joint count; TNFi-IR: inadequate response or intolerance to tumour necrosis factor inhibitors.

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Safety at Week 156

n (%) [EAIR/100 PY]	BE OPTIMAL (bDMARD-naïve) BKZ 160 mg Q4W Total[a] (n=702); 1794.3 PY	BE OPTIMAL (bDMARD-naïve) All Patients[a] (N=823); 2022.1 PY
Any TEAEs	650 (92.6) [168.1]	755 (91.7) [164.2]
Serious TEAEs	114 (16.2) [6.9]	122 (14.8) [6.5]
Study discontinuation due to TEAEs	60 (8.5) [3.4]	65 (7.9) [3.3]
Drug-related TEAEs[b]	324 (46.2) [27.4]	365 (44.3) [26.9]
Severe TEAEs	61 (8.7) [3.5]	66 (8.0) [3.4]
Deaths	2 (0.3) [0.1][c]	3 (0.4) [0.2][c,d]
Most frequent TEAEs[e]		
SARS-CoV-2 (COVID-19) infection	191 (27.2) [12.2]	223 (27.1) [12.7]
Nasopharyngitis	125 (17.8) [8.0]	139 (16.9) [7.8]
Upper respiratory tract infection	102 (14.5) [6.2]	113 (13.7) [6.1]
Safety topics of interest		
Serious infections	25 (3.6) [1.4]	28 (3.4) [1.4]
Opportunistic infections	20 (2.8) [1.1]	21 (2.6) [1.1]
Active tuberculosis	0	0
Fungal infections	144 (20.5) [9.2]	163 (19.8) [9.2]
Candida infections	97 (13.8) [5.9]	106 (12.9) [5.7]
Oral candidiasis	73 (10.4) [4.3]	82 (10.0) [4.3]
Fungal infections NEC	61 (8.7) [3.6]	71 (8.6) [3.7]
Tinea infections	11 (1.6) [0.6]	12 (1.5) [0.6]
Neutropenia	22 (3.1) [1.3][f]	22 (2.7) [1.1][f]
Serious hypersensitivity reaction	0	0
Administration/injection site reaction[g]	24 (3.4) [1.4]	28 (3.4) [1.4]
Definite or probable adjudicated IBD	5 (0.7) [0.3]	7 (0.9) [0.4]
Uveitis[h]	4 (0.6) [0.2][i]	4 (0.5) [0.2][i]
Adjudicated suicidal ideation and behaviour	2 (0.3) [0.1][j]	2 (0.2) [0.1][j]
Adjudicated MACE	7 (1.0) [0.4]	9 (1.1) [0.5]
Elevated liver enzymes[k]	71 (10.1) [4.3]	80 (9.7) [4.2]
>3x ULN ALT or AST, n/N (%) [EAIR]	34/701 (4.9) [2.0]	39/822 (4.7) [2.0]
Malignancies, excluding non-melanoma skin cancer	9 (1.3) [0.5]	9 (1.1) [0.5]

n (%) [EAIR/100 PY]	BE COMPLETE (TNFi-IR) BKZ-Treated Patients (BKZ 160 mg Q4W)[a] (n=388); 985.3 PY
Any TEAEs	318 (82.0) [88.6]
Serious TEAEs	52 (13.4) [5.7]
Study discontinuation due to TEAEs	27 (7.0) [2.8]
Drug-related TEAEs[b]	130 (33.5) [17.1]
Severe TEAEs	35 (9.0) [3.7]
Deaths	1 (0.3) [0.1][c]
Most frequent TEAEs[d]	
SARS-CoV-2 (COVID-19) infection	68 (17.5) [7.6]
Nasopharyngitis	44 (11.3) [4.8]
Upper respiratory tract infection	38 (9.8) [4.1]
Safety topics of interest	
Serious infections	13 (3.4) [1.3]
Opportunistic infections	3 (0.8) [0.3]
Active tuberculosis	0
Fungal infections	52 (13.4) [5.8]
Candida infections	37 (9.5) [4.0]
Oral candidiasis	34 (8.8) [3.6]
Fungal infections NEC	18 (4.6) [1.9]
Tinea infections	6 (1.5) [0.6]
Neutropenia	13 (3.4) [1.4][e]
Serious hypersensitivity reaction	1 (0.3) [0.1][f]
Administration/injection site reaction[g]	8 (2.1) [0.8]
Definite or probable adjudicated IBD	1 (0.3) [0.1]
Uveitis	0
Adjudicated suicidal ideation and behaviour	0
Adjudicated MACE	2 (0.5) [0.2]
Elevated liver enzymes[h]	37 (9.5) [4.0]
>3x ULN ALT or AST	17 (4.4) [1.8]
Malignancies, excluding non-melanoma skin cancer	10 (2.6) [1.0]

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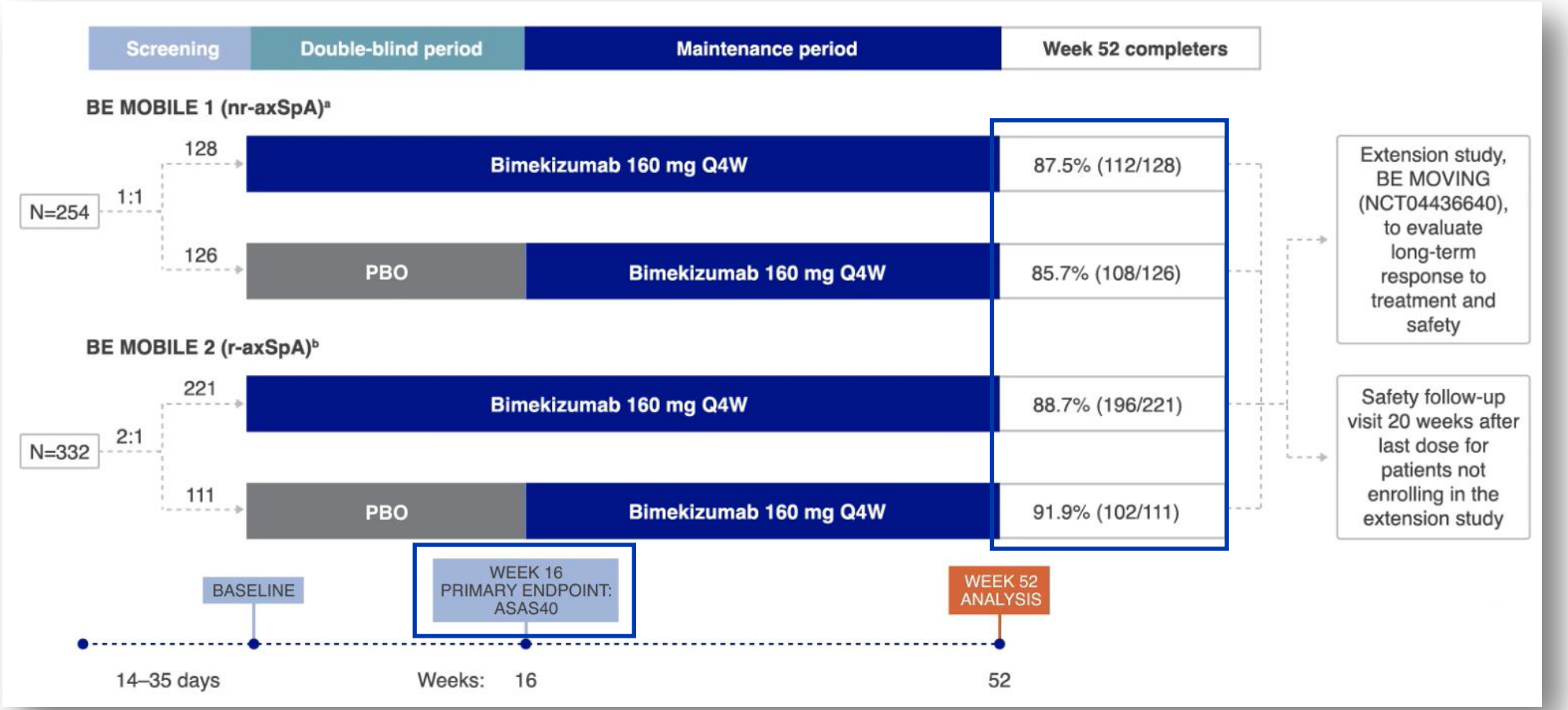
BE MOBILE Study Design



Patients were eligible to receive non-biologic rescue therapy from Week 20 at the discretion of the investigator while continuing to receive BKZ. [a]Included patients had adult-onset nr-axSpA fulfilling ASAS classification criteria and objective signs of inflammation (active sacroiliitis on MRI and/or elevated CRP [≥6 mg/L]); [b]Included patients had radiographic evidence of nr-axSpA fulfilling modified New York criteria. ASAS: Assessment of SpondyloArthritis international Society; ASAS40: ASAS 40% response; CRP: C-reactive protein; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.

Baraliakos X et al. Ann Rheum Dis. 2024
van der Heijde D et al. Ann Rheum Dis. 2023

Inclusion and exclusion criteria

Key inclusion criteria[a]

- ≥18 years of age with active nr-axSpA or r-axSpA at baseline (BASDAI ≥4 and spinal pain ≥4)
- **BE MOBILE 1:** nr-axSpA fulfilling ASAS classification criteria and objective inflammation at screening, specifically active sacroiliitis on MRI fulfilling ASAS criteria and/or elevated CRP (≥6.0 mg/L)
- **BE MOBILE 2**: r-axSpA[b] fulfilling modified New York criteria including documented radiographic evidence of sacroiliitis (grade ≥2 bilateral or grade ≥3 unilateral)
- Prior failure to respond to two different NSAIDs, or history of intolerance or contraindication to NSAIDs

Key exclusion criteria[a]

- Received >TNFi, >2 additional biologic response modifiers or any IL-17 response modifier; patients who had previously received a TNFi must have been intolerant or experienced an inadequate response
- Patients with inflammatory conditions other than nr-axSpA/r-axSpA were excluded
- Active, symptomatic IBD at baseline or screening (prior history was not an exclusion criteria)
- Anterior uveitis within 6 weeks of baseline visit

[a]van der Heijde D. Ann Rheum Dis 2023;82:515–526; 2. [b]All patients in BE MOBILE 2 also fulfilled ASAS criteria. ASAS: Assessment of Spondyloarthritis international Society; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; IBD: inflammatory bowel disease; IL: interleukin; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; NSAID: non-steroidal anti-inflammatory drug; r-axSpA: radiographic axial spondyloarthritis; TNFi: tumour necrosis factor inhibitor.

BE MOBILE 1 and BE MOBILE 2: Baseline characteristics

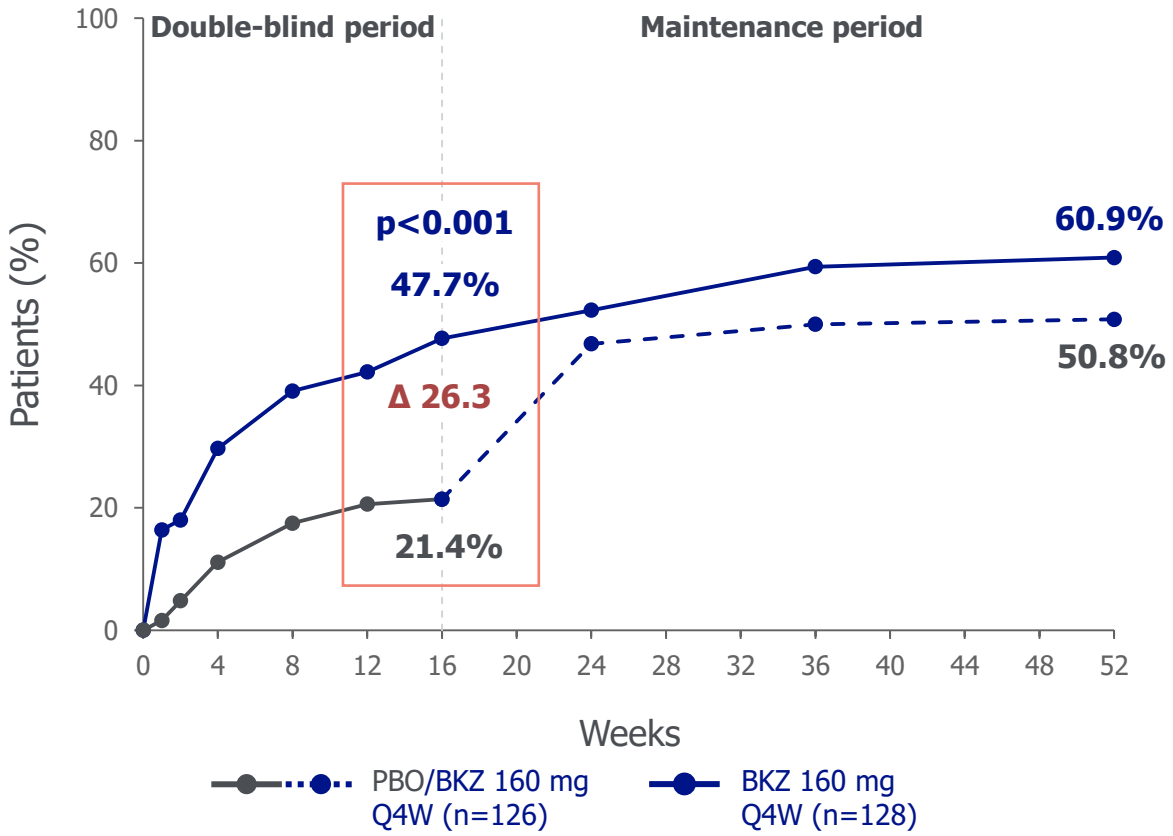
	BE MOBILE 1 (nr-axSpA)[1]		BE MOBILE 2 (r-axSpA/AS)[1]	
	PBO (n=126)	BKZ 160 mg Q4W (n=128)	PBO (n=111)	BKZ 160 mg Q4W (n=221)
Sex (male), n (%)	65 (51.6)	73 (57.0)	80 (72.1)	160 (72.4)
Age, years, mean (SD)	39.4 (11.8)	39.5 (11.1)	39.2 (12.6)	41.0 (12.1)
HLA-B27, positive, n (%)	94 (74.6)	103 (80.5)	93 (83.8)	191 (86.4)
Prior TNFi exposure, n (%)	17 (13.5)	10 (7.8)	17 (15.3)	37 (16.7)
Symptom duration, years, mean (SD)	9.0 (9.0)	9.1 (8.7)	11.9 (8.6)	14.2 (11.0)
Time since first diagnosis, years, mean (SD)	3.6 (5.4)	3.7 (6.2)	5.7 (6.9)	6.7 (8.3)
hs-CRP, mg/L Geometric mean Median (min, max)	 5.0 6.5 (0.1, 56.1)[2]	 4.6 6.1 (0.1, 79.1)[2]	 6.7 6.3 (0.3, 104.3)[3]	 6.5 8.2 (0.1, 105.4)[3]
hs-CRP >ULN,* n (%)	71 (56.3)	70 (54.7)	67 (60.4)	137 (62.0)
ASDAS, mean (SD)	3.7 (0.7)	3.7 (0.8)	3.7 (0.8)	3.7 (0.8)[†]
BASDAI, mean (SD)	6.7 (1.3)	6.9 (1.2)	6.5 (1.3)	6.5 (1.3)
Morning stiffness (BASDAI Q5 and 6),[‡] mean (SD)	6.9 (1.6)	7.0 (1.8)	6.8 (1.6)	6.7 (1.9)
Total spinal pain,[‡] mean (SD)	7.1 (1.6)	7.3 (1.5)	7.2 (1.2)	7.1 (1.6)
Nocturnal spinal pain, mean (SD)	6.7 (2.1)	6.9 (2.0)	6.8 (1.8)	6.6 (1.9)

- Randomised set. *ULN value for hs-CRP is 5 mg/L. [†]n=220.
  [‡]Part of the primary outcome measure

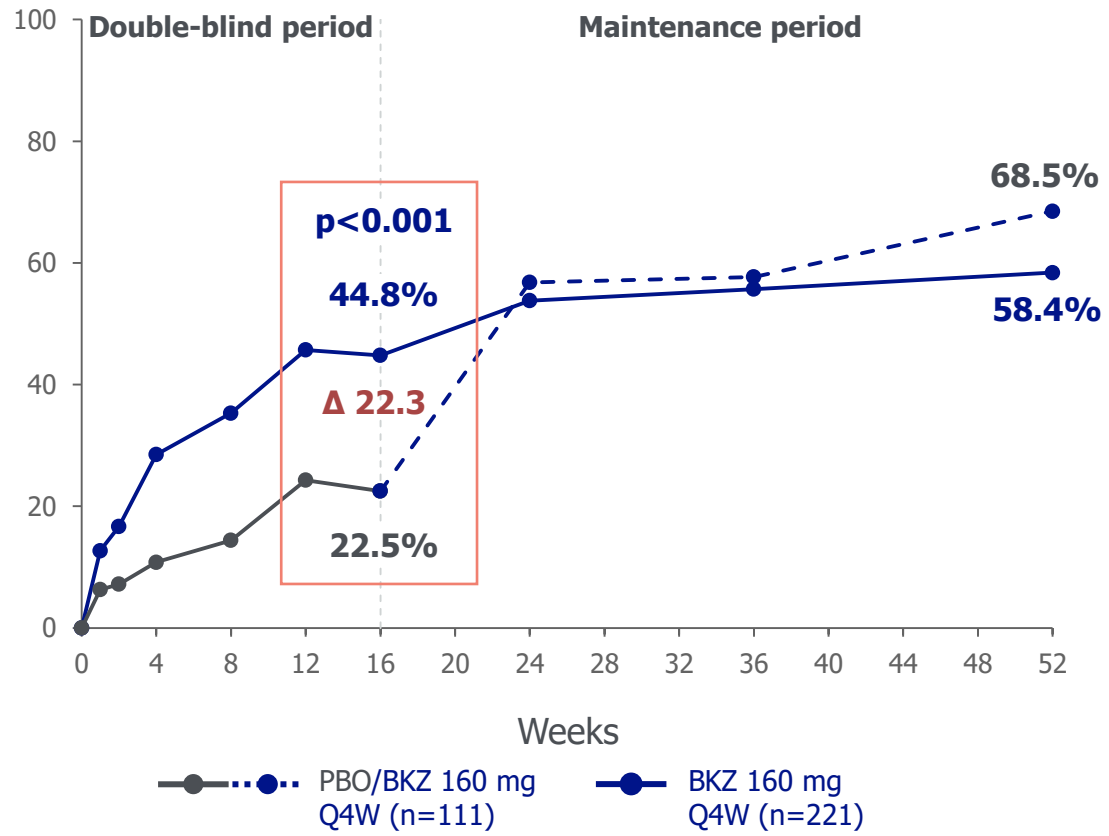
1. van der Heijde D et al. Ann Rheum Dis. 2023. doi:10.1136/ard-2022-223595.
2. Deodhar A et al. ACR 2022. Presentation 0544. 3. van der Heijde D et al. ACR 2022. Poster 0411

ASAS40 Responses Over Time to Week 52 (NRI)

BE MOBILE 1 (nr-axSpA)



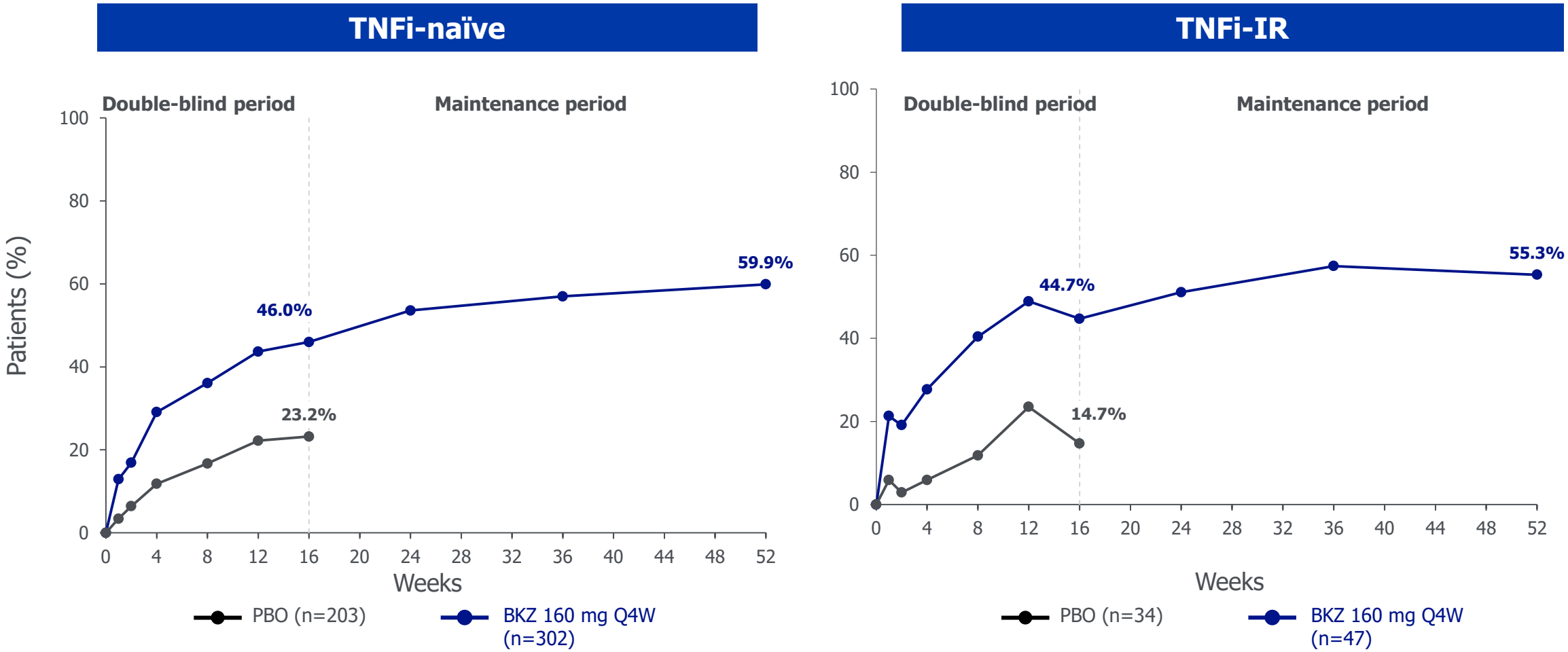
BE MOBILE 2 (r-axSpA/AS)



- **Non-responder imputation**. Randomised set. p values calculated by logistic regression with treatment, region, MRI/CRP classification (BE MOBILE 1) and prior TNFi exposure (BE MOBILE 2 only) as factors. **Delta values manually calculated as the difference between the corresponding Week 16 values reported.**

Adapted from Baraliakos X et al. Ann Rheum Dis. 2024;83(2):199–213

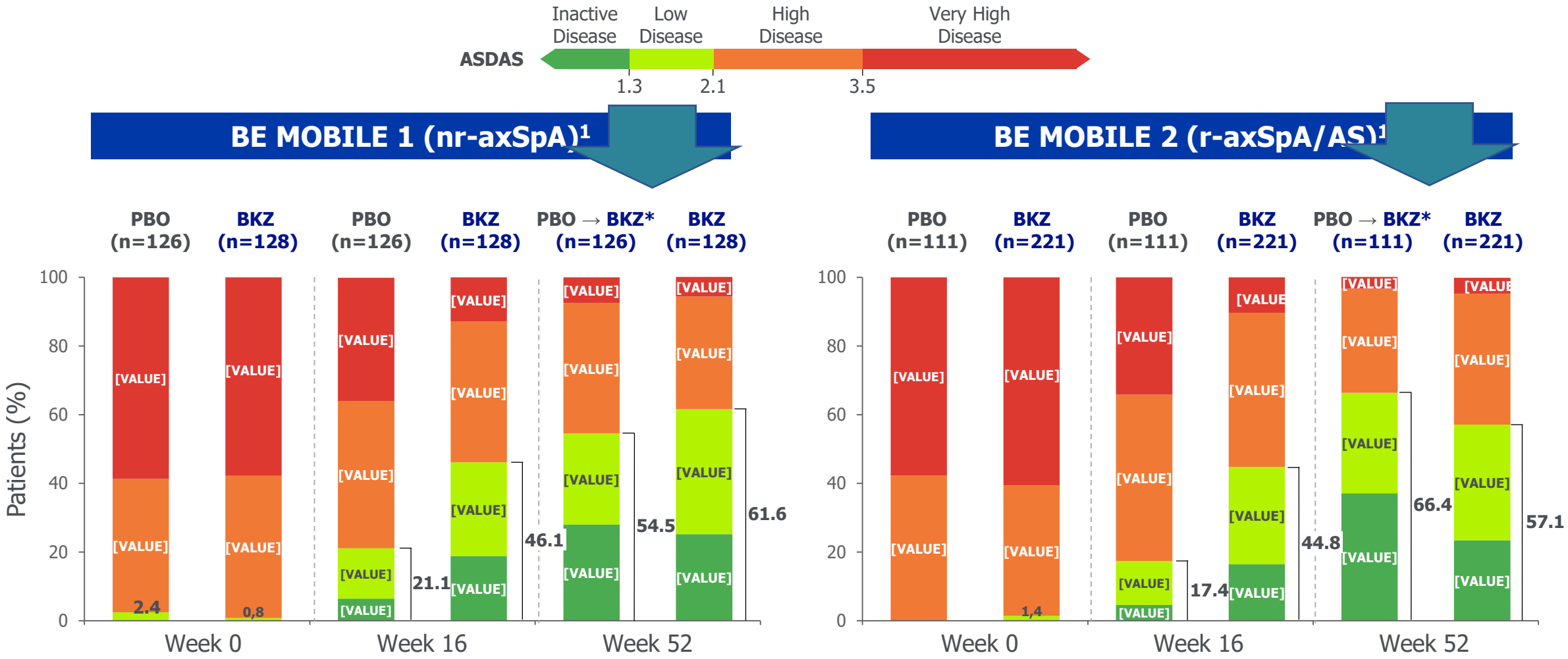
ASAS40 Responses in TNFi-Naïve and TNFi-IR



- **Non-responder imputation.** Data are pooled from BE MOBILE 1 and BE MOBILE 2.

Adapted from Magrey M et al. Arthritis Rheumatol. 2023;75(Suppl 9).

ASDAS <2.1 at Week 52 Across the axSpA Spectrum[1,2]



- **Data reported using multiple imputation** where patients that discontinued treatment due to loss of efficacy or safety were considered as non-responders.[3] Randomised set. *At Week 16, patients on PBO switched to BKZ.[1,4]

Baraliakos X et al. ACR 2022. Poster L14.
Baraliakos X et al. EULAR 2023. Poster POS1103.
Machado P et al. Ann Rheum Dis. 2018. 77(10):1539–1540.
Adapted from Baraliakos X et al. Ann Rheum Dis. 2023;82(Suppl 1):873

Pooled efficacy endpoints across BE MOBILE 1 and 2 in TNFi-naïve and -IR patients

	Week 16				Week 52	
	BE MOBILE 1 and 2 TNFi-naïve		BE MOBILE 1 and 2 TNFi-IR		BE MOBILE 1 and 2 TNFi-naïve	BE MOBILE 1 and 2 TNFi-IR
	PBO N=203	BKZ 160 mg Q4W N=302	PBO N=34	BKZ 160 mg Q4W N=47	BKZ 160 mg Q4W N=302	BKZ 160 mg Q4W N=47
ASDAS-CRP CfB [MI] mean (SE)	−0.7 (0.1)	−1.5 (0.1)	−0.6 (0.1)	−1.6 (0.1)	−1.8 (0.1)	−1.9 (0.2)
BASDAI CfB [MI] mean (SE)	−1.7 (0.1)	−3.0 (0.1)	−1.6 (0.4)	−2.7 (0.3)	−3.6 (0.1)	−3.7 (0.3)
SPARCC MRI SIJ CfB [OC][a] mean (SD)	−0.9 (7.3)[b]	−5.3 (8.4)[c]	1.4 (6.0)[d]	−5.6 (13.4)[e]	−5.9 (9.1)[f]	−6.9 (12.2)[e]
Berlin MRI Spine CfB [OC][a] mean (SD)	−0.2 (1.5)[g]	−1.4 (3.2)[h]	0.4 (1.3)[i]	−0.5 (1.9)[e]	−1.7 (3.6)[j]	−1.2 (2.1)[e]
BASFI CfB [MI] mean (SE)	−1.1 (0.1)	−2.3 (0.1)	−0.5 (0.3)	−2.2 (0.3)	−2.8 (0.1)	−2.9 (0.3)
Nocturnal spinal pain CfB [MI] mean (SE)	−1.7 (0.2)	−3.4 (0.2)	−2.1 (0.5)	−3.3 (0.3)	−4.1 (0.2)	−3.9 (0.3)
ASQoL CfB [MI] mean (SE)	−2.8 (0.3)	−5.1 (0.3)	−2.4 (0.6)	−4.2 (0.6)	−5.8 (0.3)	−4.7 (0.6)

Data are pooled from BE MOBILE 1 and 2. Data reported using OC or MI. Data from PBO-randomized patients not included from Wk 16 onwards. [a] Only patients enrolled in the SIJ and spine MRI substudy and with ≥1 post-baseline record for the respective variable are included; [b] n=95; [c] n=144; [d] n=13; [e] n=15; [f] n=130; [g] n=94; [h] n=140; [i] n=12; [j] n=127. ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score C-reactive protein; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; CfB: change from baseline; IR: inadequate responders; MI: multiple imputation; MRI: magnetic resonance imaging; OC: observed case; PBO: placebo; Q4W: every four weeks; SD: standard deviation; SE: standard error; SIJ: sacroiliac joints; SPARCC: Spondylarthritis Research Consortium of Canada; TNFi: tumor necrosis factor inhibitor.

Adapted from Magrey M et al. Arthritis Rheumatol. 2023;75(Suppl 9).

Safety Overview: Weeks 0-52

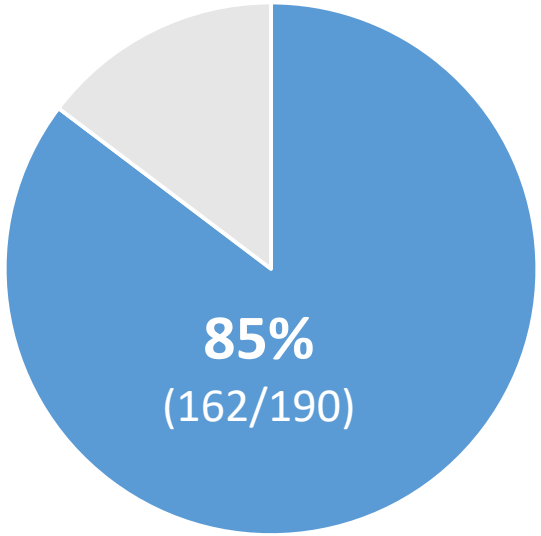
n (%), overall period: [EAIR/100 PY]		Double-blind treatment period Weeks 0–16		Maintenance period Weeks 16–52	Overall Weeks 0–52
		PBO	BKZ 160 mg Q4W	BKZ 160 mg Q4W	BKZ 160 mg Q4W[a]
nr-axSpA (BE MOBILE 1) / r-axSpA (BE MOBILE 2)		n=126 (38.1 PYAR) / n=111 (34.6 PYAR)	n=128 (40.4 PYAR) / n=221 (68.3 PYAR)	n=242 (167.8 PYAR) / n=319 (220.0 PYAR)	n=244 (208.2 PYAR) / n=330 (290.9 PYAR)
Pre-specified safety topics of interest and other important TEAEs					
Serious infections	nr-axSpA	0	0	4 (1.7)	4 (1.6) [1.9]
	r-axSpA	1 (0.9)	1 (0.5)	5 (1.6)	6 (1.8) [2.1]
Opportunistic infections	nr-axSpA	0	1 (0.8)	4 (1.7)	5 (2.0) [2.4]
	r-axSpA	0	0	3 (0.9)	3 (0.9) [1.0]
Any fungal infections	nr-axSpA	0	9 (7.0)	32 (13.2)	37 (15.2) [19.6]
	r-axSpA	0	14 (6.3)	31 (9.7)	40 (12.1) [14.9]
Candida infections	nr-axSpA	0	5 (3.9)	23 (9.5)	25 (10.2) [12.8]
	r-axSpA	0	11 (5.0)	15 (4.7)	23 (7.0) [8.3]
Hypersensitivity[b]	nr-axSpA	3 (2.4)	3 (2.3)	17 (7.0)	18 (7.4) [9.1]
	r-axSpA	2 (1.8)	17 (7.7)	28 (8.8)	41 (12.4) [15.3]
Adjudicated MACE	nr-axSpA	0	0	0	0
	r-axSpA	0	0	0	0
Adjudicated IBD[c]	nr-axSpA	1 (0.8)	0	2 (0.8)	2 (0.8) [1.0]
	r-axSpA	0	2 (0.9)	1 (0.3)	3 (0.9) [1.0]
Uveitis[d]	nr-axSpA	6 (4.8)	2 (1.6)	3 (1.2)	3 (1.2) [1.5]
	r-axSpA	5 (4.5)	0	7 (2.2)	7 (2.1) [2.4]

Safety set. MedDRA (Version 19.0). Overall period includes all data available up to the last Week 52 visit, including data for patients treated beyond Week 24. [a]Includes patients who switched from PBO to BKZ (events after switch only); [b]Hypersensitivity events were identified using the MedDRA standardised medical query 'Hypersensitivity (SMQ)'; [c]Definite or probable IBD reported per external adjudication committee; [d]Includes the preferred terms autoimmune uveitis, uveitis, iridocyclitis and iritis. BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; IBD: inflammatory bowel disease; MACE: major adverse cardiac event; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; PY: patient years; PYAR: patient years at risk; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; SMQ: standardised medical query.

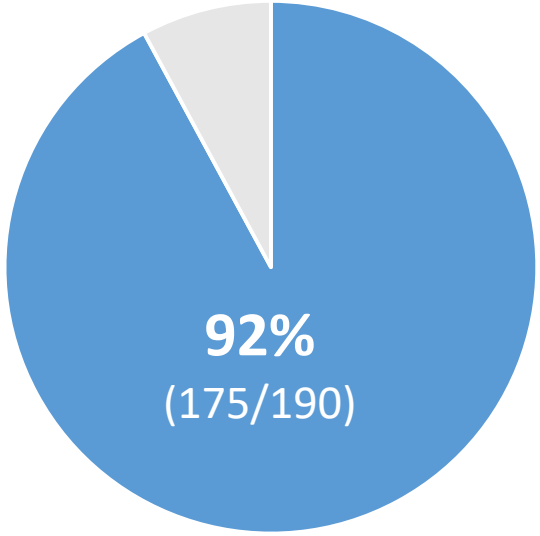
Baraliakos X et al. Ann Rheum Dis. 2024

Proportion of Non-Progressors at Week 104 (OC)

Non-progression defined as mSASSS CfB ≤0.5



Non-progression defined as mSASSS CfB <2



Patients with **no** spinal radiographic progression

Patients with spinal radiographic progression

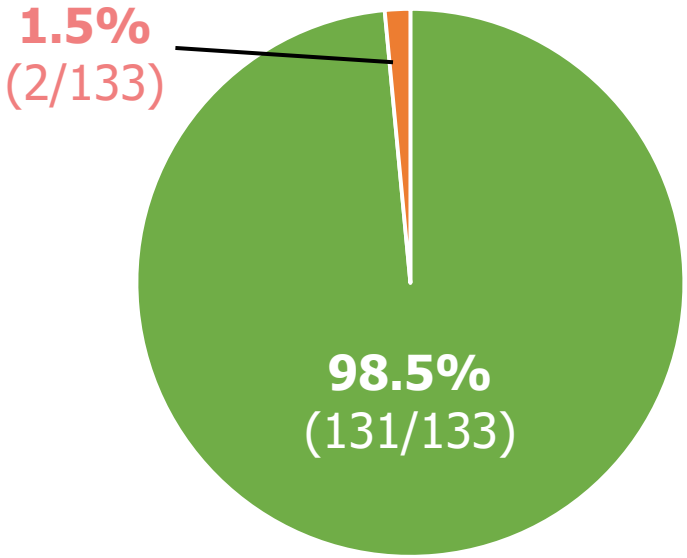
Non-progressors at Week 104 included 83.1% (69/83) of the patients who had existing structural damage (mSASSS ≥2) at baseline

Includes patients in the X-ray sub-study with valid X-ray assessments at baseline and Week 104 (n=190). All patients received bimekizumab 160 mg Q4W from Week 16. mSASSS ranges from 0–72, with lower scores indicating less structural damage. CfB: change from baseline; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score; OC: observed case; Q4W; every 4 weeks.

New Syndesmophytes at Week 104 (OC)

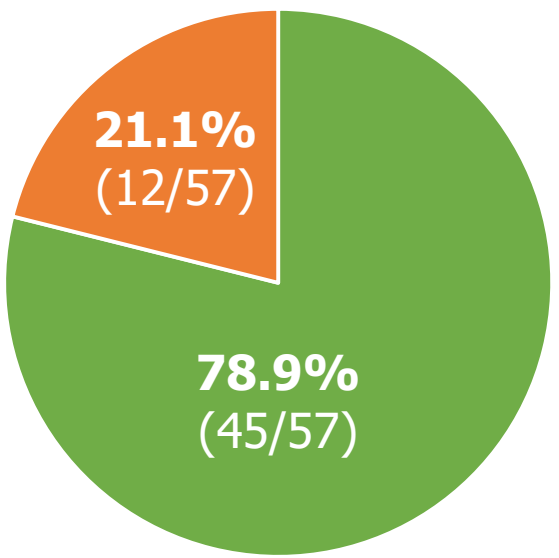
New syndesmophytes in patients without syndesmophytes at baseline

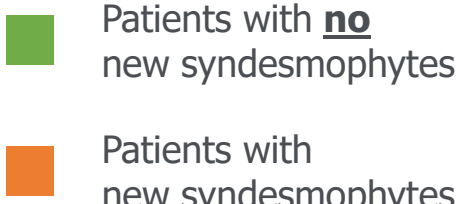
At baseline, 133/190 patients (70.0%) had **no** syndesmophytes present



New syndesmophytes in patients with syndesmophytes at baseline

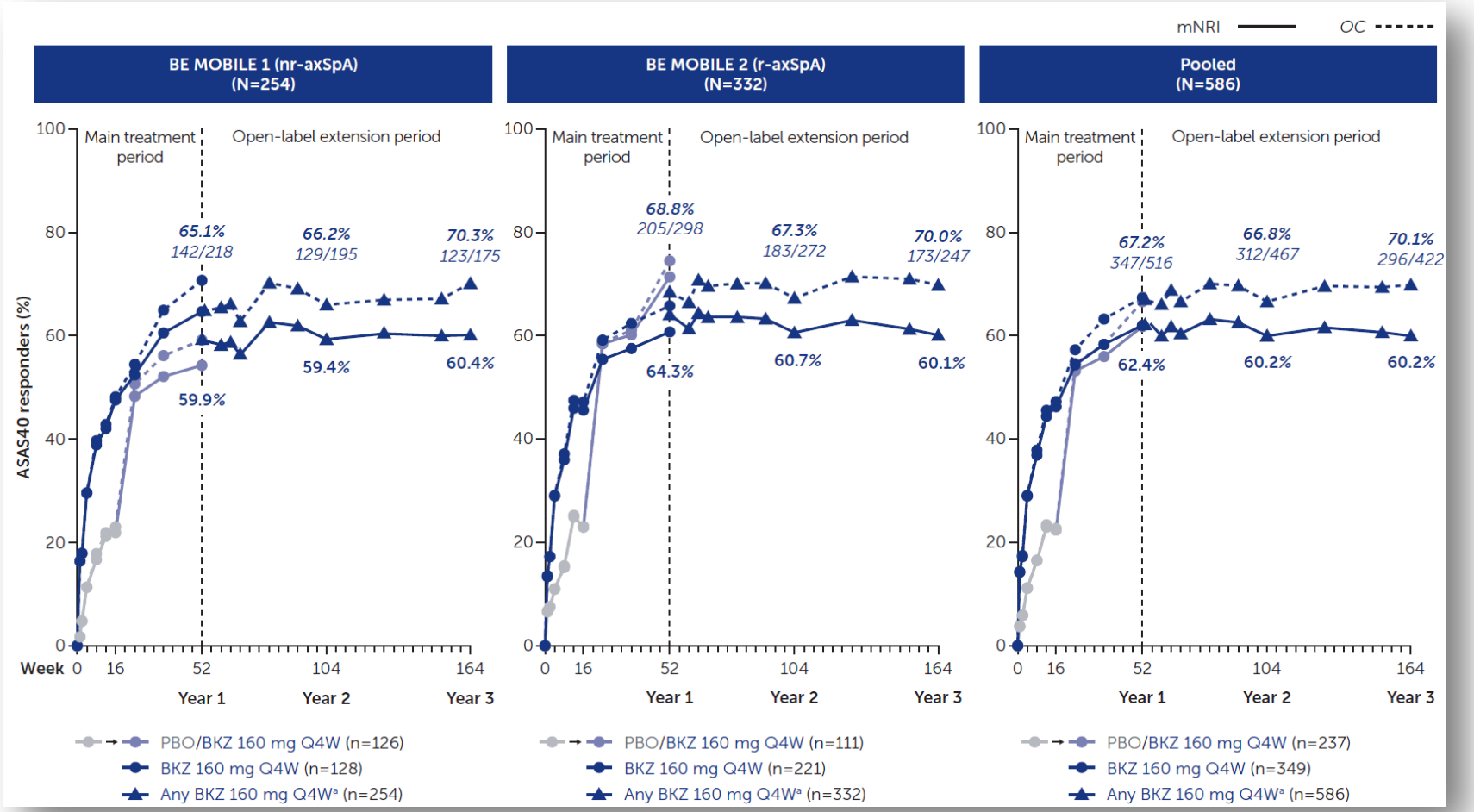
At baseline, 57/190 patients (30.0%) had syndesmophytes present





Includes patients in the X-ray sub-study with valid X-ray assessments at baseline and Week 104 (n=190). New syndesmophytes were defined as syndesmophytes declared present at Week 104 but not at baseline at the same site. OC: observed case.

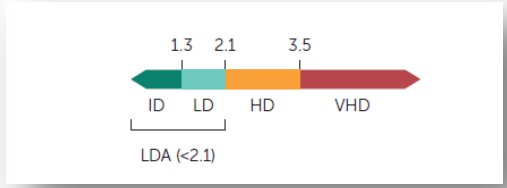
Achievement of ASAS40 to 3 Years (mNRI, OC)



Randomised sets. mNRI considered all visits following discontinuation due to adverse events or lack of efficacy as non-response; all other missing data were imputed with MI and the response derived from the imputed values. Data labels at Week 52 are related to the Any BKZ group. [a]Includes patients originally randomised to placebo; all patients were treated with BKZ 160 mg Q4W from Week 16. ASAS: Assessment of SpondyloArthritis international Society; ASAS40: ASAS 40% response; axSpA: axial spondyloarthritis; BKZ: bimekizumab; MI: multiple imputation; mNRI: modified non-responder imputation; nr-axSpA: non-radiographic axSpA; OC: observed case; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axSpA.

Baraliakos X, et al. EULAR 2025. Poster POS0788.

ASDAS States Over Time to Week 164 (MI)



Randomised sets. Includes patients originally randomised to placebo; all patients were treated with BKZ 160 mg Q4W from Week 16. ASDAS: Axial Spondyloarthritis Disease Activity Score; axSpA: axial spondyloarthritis; BKZ: bimekizumab; HD: high disease; ID: inactive disease; LD: low disease; LDA: low disease activity; MI: multiple imputation; nr-axSpA: non-radiographic axSpA; Q4W: every 4 weeks; r-axSpA: radiographic axSpA; VHD: very high disease.

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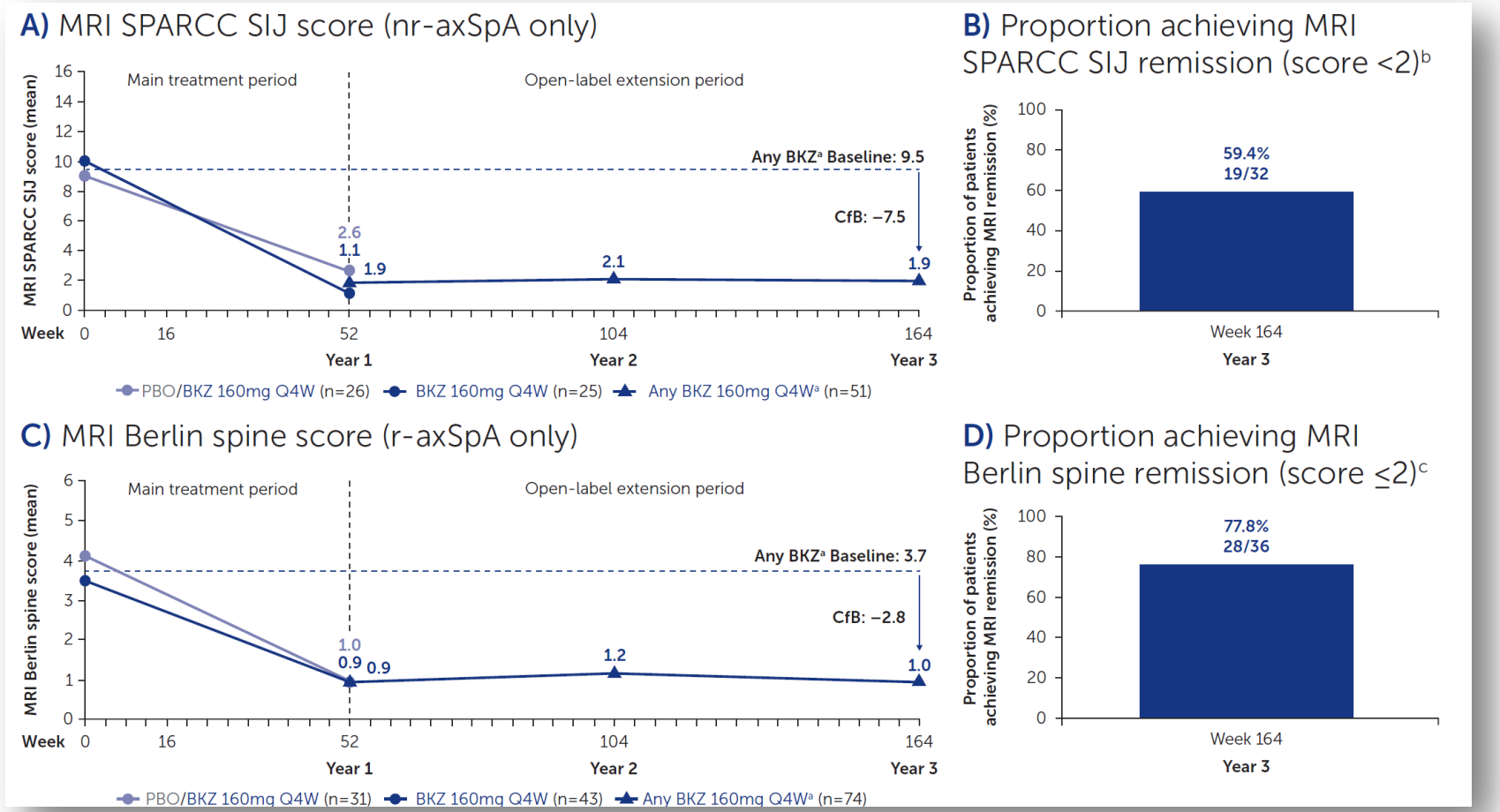
Absolute MRI Inflammation Scores and Remission Rates to 3 Years (OC)



Only study participants enrolled in the respective MRI sub-study with recorded data at each of the timepoints shown are included in this analysis. MRI remission is defined as having a SPARCC <2 or Berlin MRI spine score ≤2. [a]Includes patients originally randomised to placebo; all patients were treated with BKZ 160 mg Q4W from Week 16; [b]SPARCC SIJ score <2, in patients with SPARCC SIJ score ≥2 at baseline and MRI assessments at the remaining 3 timepoints (Week 52, 104 and 164) in the MRI sub-study (nr-axSpA only); [c]Berlin spine ≤2, in patients with Berlin spine score >2 at baseline and MRI assessments at the remaining 3 timepoints (Week 52, 104 and 164) in the MRI sub-study (r-axSpA only). axSpA: axial spondyloarthritis; BKZ: bimekizumab; CfB: change from baseline; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axSpA; OC: observed case; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axSpA; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada.

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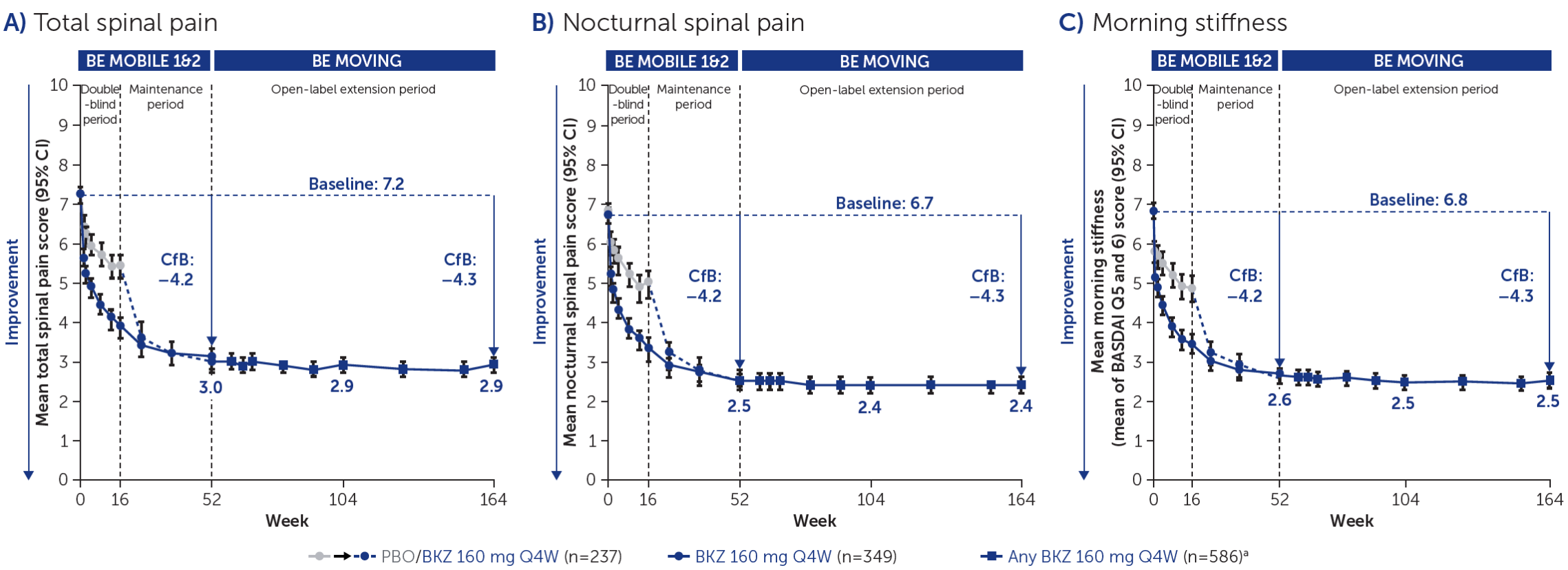
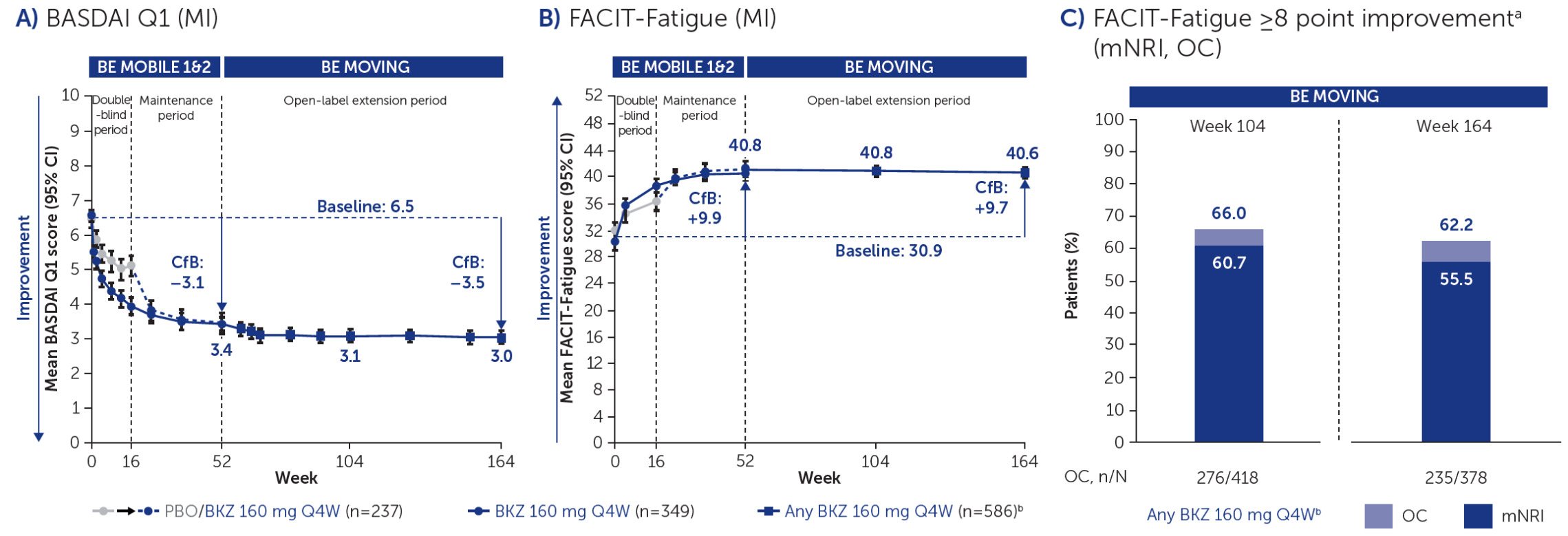
Spinal Pain and Morning Stiffness to Week 164 (MI)



Pooled randomised set (N=586). Error bars represent 95% CI scores. Baseline scores are from Week 0 of BE MOBILE 1 or 2. From Week 16, all patients received BKZ 160 mg Q4W. Morning stiffness was assessed as the mean of BASDAI Q5 and Q6. Total score range for spinal pain and morning stiffness: 0–10. [a]Includes patients originally randomised to placebo in BE MOBILE 1 or 2. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; CfB: change from baseline; CI: confidence interval; MI: multiple imputation; PBO: placebo; Q4W: every 4 weeks.

Navarro-Compán V, et al. EULAR 2025. Poster POS0921

Fatigue to Week 164, and FACIT-Fatigue Score ≥8-Point Improvement at Week 104 and Week 164 (mNRI, MI, OC)



Pooled randomised set (N=586). Error bars represent 95% CI scores. Baseline scores are from Week 0 of BE MOBILE 1 or 2. From Week 16, all patients received BKZ 160 mg Q4W. Improvement is indicated by reduced scores for BASDAI Q1 (total score range: 0–10) and increased scores for FACIT-Fatigue (total score range: 0–52). mNRI considered all visits following discontinuation due to adverse events or lack of efficacy as non-response; all other missing data were imputed with MI and the response derived from the imputed values. [a]In patients with FACIT-Fatigue score ≤44 at baseline (N=520);[3] [b]Includes patients originally randomised to placebo in BE MOBILE 1 or 2. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; CfB: change from baseline; CI: confidence interval; FACIT: Functional Assessment of Chronic Illness Therapy; MI: multiple imputation; mNRI: modified non-responder imputation; OC: observed case; PBO: placebo; Q4W: every 4 weeks.

Cella D. J Patient Rep Outcomes. 2024;8:92.
Navarro-Compán V, et al. EULAR 2025. Poster POS0921

Safety Overview to 3 Years (Week 164)

n (%) [EAIR/100 PY]	BKZ 160 mg Q4W[a] (N=574; 1,664.7 PY)
Any TEAE	519 (90.4) [139.0]
Serious TEAEs	76 (13.2) [4.9]
Study discontinuation due to TEAEs	36 (6.3) [2.2]
Drug-related TEAEs[b]	290 (50.5) [28.7]
Severe TEAEs	47 (8.2) [3.0]
Death	0
Most frequent TEAEs[c]	
SARS-CoV-2 (COVID-19) infection[d]	195 (34.0) [14.5]
Nasopharyngitis	139 (24.2) [9.9]
Upper respiratory tract infection	88 (15.3) [5.8]
Safety topics of interest	
Serious infections	20 (3.5) [1.2]
Opportunistic infections	14 (2.4) [0.9]
Active tuberculosis	0
Fungal infections	131 (22.8) [9.4]
Candida infections	80 (13.9) [5.3]
Oral candidiasis	66 (11.5) [4.3]
Fungal infections NEC	52 (9.1) [3.3]
Tinea infections	21 (3.7) [1.3]
Neutropenia[e]	10 (1.7) [0.6]
Serious hypersensitivity reactions	0
Administration/injection site reactions[f]	26 (4.5) [1.6]
Adjudicated suicidal ideation and behavior	2 (0.3) [0.1]
Adjudicated MACE	0
Elevated liver enzymes[g]	55 (9.6) [3.6]
>3X ULN ALT or AST	31 (5.4) [1.9]
Malignancies, excluding non melanoma skin cancer	8 (1.4) [0.5]
Adjudicated IBD (definite or probable)	9 (1.6) [0.5]
With prior history[h]	1 (12.5) [4.5]
Without prior history	8 (1.4) [0.5]
Uveitis[i]	25 (4.4) [1.5]
With prior history[j]	18 (18.9) [7.0]
Without prior history	7 (1.5) [0.5]

Baraliakos X, et al. EULAR 2025. Poster POS0788.

Δεδομένα από το τμήμα μας

	Characteristics	mean±SD *or* N (%)
Demographics	Males/Females	7 (44)/ 9 (56)
	Age, *yrs*	50.5 ± 12
	BMI	29 ± 6
	Disease Duration, *yrs*	4.7 ± 6
	Follow up, *months*	7.3 ± 4
Disease	AxSpA	8 (50)
	- rAxSpA	5 (31)
	PsA	8 (50)
Previous – concurrent treatment	csDMARDs	6 (38)
	b/tsDMARDs	13 (81)
	b/tsDMARDs ≥ 2	9 (56)
	Previous antiIL-17	7 (44)
	Glucocorticoids	2 (13)
	NSAIDs	3 (19)

Disease activity (switch)		
- AxSpA (ASDAS-CRP)	- Moderate	-
	- High	4 (25)
	- Very high	4 (25)
- PsA (DAPSA)	- Moderate	5 (31)
	- High	3 (19)
Disease activity (LFU)		
- AxSpA (ASDAS-CRP)	- Inactive/LDA	7 (44)
	- High	1 (6)
	- Very high	-
- PsA (DAPSA)	- REM/LDA	6 (38)
	- Moderate	2 (13)
	- High disease activity	-
Adverse Events	URTI	2 (13)
	Fungal infections	1 (6)
	IBD (new onset/flare)	1 (6)/-
	Uveitis (new onset/flare)	-/-

Take home messages

- ✓ Προκλινικά δεδομένα υποστηρίζουν πως η διπλή αναστολή της IL17A & F παρέχει καλύτερο έλεγχο της φλεγμονής
- ✓ Η θεραπεία με Bimekizumab προσφέρει άμεση και μακροχρόνια αποτελεσματικότητα στην ΨΑ και σε όλο το φάσμα της ΑξΣπΑ
- ✓ Η μακροχρόνια θεραπεία με Bimekizumab χαρακτηρίζεται από άριστη ανοχή και ασφάλεια


Σας Ευχαριστώ