Bimekizumab in patients with active non-radiographic and radiographic axial spondyloarthritis: 52-week efficacy and safety from the BE MOBILE phase 3 studies

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Objective

To report efficacy and safety of bimekizumab in patients with active non-radiographic and radiographic axial spondyloarthritis to Week 52 in the pivotal phase 3 studies, BE MOBILE 1 and 2, respectively.

Background

- Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, met all primary and ranked secondary endpoints at Week 16 in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) and radiographic axSpA (r-axSpA; i.e., ankylosing spondylitis), in the parallel phase 3 BE MOBILE 1 and 2 studies, respectively.[1]

Methods

- BE MOBILE 1 (NCT03928704; nr-axSpA) and 2 (NCT03928743; r-axSpA) each comprised a 16-week double-blind, placebo (PBO)-controlled period followed by a 36-week maintenance period (**Figure 1**).[1]
- Primary and secondary efficacy endpoints were assessed at Week 16 and are presented in this analysis to Week 52 (randomised set).
- Treatment-emergent adverse events (TEAEs; MedDRA v19.0) following first BKZ exposure are reported at Week 52 for patients who received ≥1 dose of BKZ (safety set).

Results

Patients

- Of randomised patients, 220/254 (86.6%) with nr-axSpA and 298/332 (89.8%) with r-axSpA completed Week 52.
- Baseline characteristics were reflective of a patient population with moderate to severe nr-axSpA and r-axSpA (**Table 1**).

Efficacy

- In both studies, in BKZ-randomised patients, the primary and ranked secondary efficacy outcomes were sustained to Week 52 (**Table 2**); among patients who switched from PBO to BKZ at Week 16 (PBO/BKZ), efficacy at Week 52 was similar to that seen in BKZ-randomised patients.
  - ASAS40 responses in BKZ-randomised patients further increased from Week 16 to Week 52 (**Figure 2**; **Table 2**).
- The proportion of BKZ-randomised patients achieving ASAS40 increased from baseline to Week 52 irrespective of prior TNFi exposure. Week 52 responses in PBO/BKZ patients approached or exceeded that of BKZ-randomised patients (**Figure 3**).
- At Week 16, ASDAS low disease activity (<2.1) was achieved by 46.1% and 44.8% of BKZ-randomised patients with nr-axSpA and r-axSpA, respectively; this was sustained or improved to Week 52, reaching >54% in all groups (**Table 2**).[1]
- Reductions from baseline in objective signs of inflammation (MRI, hs-CRP; **Figure 4**) and improvements in spinal mobility (BASMI), physical function (BASFI), enthesitis (MASES) and health-related quality of life (ASQoL), at Week 16, were maintained through 52 weeks.

Safety

- At Week 52, 183/244 (75.0%) of patients with nr-axSpA and 249/330 (75.5%) of patients with r-axSpA had ≥1 TEAE (**Table 3**).
- The most frequent TEAEs were nasopharyngitis and upper respiratory tract infection.
- Most incidences of fungal infection were candidiasis, with the most frequent preferred term being oral candidiasis, and were mild to moderate (none were serious or systemic); two patients with nr-axSpA and two with r-axSpA discontinued the study due to *Candida* infections.
- Few COVID-19 infections were reported (nr-axSpA: 7.0%; r-axSpA: 2.1%); none were serious and none led to study discontinuation.
- No major adverse cardiovascular events, severe psoriasis, active tuberculosis cases or deaths were reported; incidence of inflammatory bowel disease, uveitis and adjudicated suicidal ideation behaviour were low (**Table 3**).

Conclusions

Across the full axSpA disease spectrum, bimekizumab treatment resulted in deep levels of efficacy, including suppression of inflammation and improvements in physical function and health-related quality of life, to Week 52.

No new safety signals were observed, consistent with the previously reported safety profile of bimekizumab.[1]

Summary

In patients with active non-radiographic and radiographic axial spondyloarthritis, dual inhibition of IL-17F in addition to IL-17A, with subcutaneous bimekizumab 160 mg Q4W treatment:

Week 16
Led to achievement of the primary and all ranked secondary endpoints

Week 52
Showed sustained efficacy with no new safety signals observed

Bimekizumab resulted in clinically meaningful and sustained improvements in:

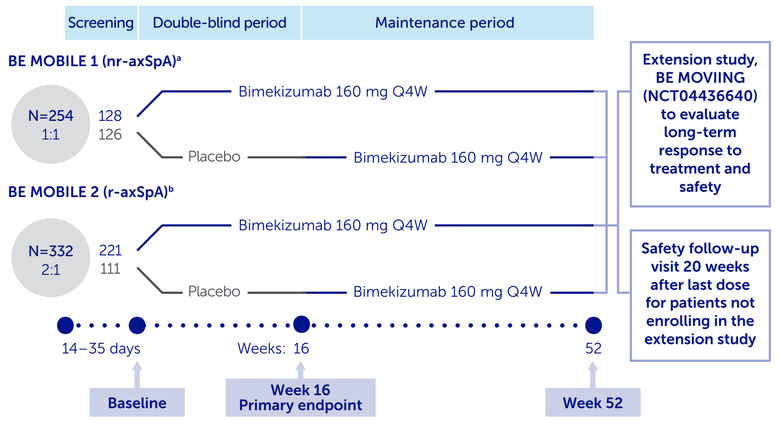
Signs and symptoms
Nocturnal spinal pain, enthesitis (MASES), spinal mobility (BASMI)

Disease activity and clinical responses
ASAS40, ASAS40 in TNFi-naïve and TNFi-IR patients, ASAS20, ASAS 5/6, ASAS Partial Remission, ASDAS, ASDAS-MI, ASDAS <2.1, BASDAI

Physical functioning, HRQoL
BASFI, SF-36 PCS, ASQoL

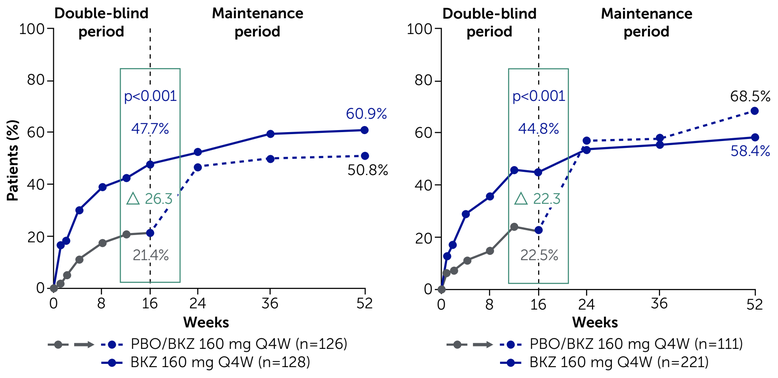
Objective signs of inflammation
MRI of SIJ (SPARCC) and spine (Berlin), hs-CRP

Figure 1 BE MOBILE 1 and 2 study designs



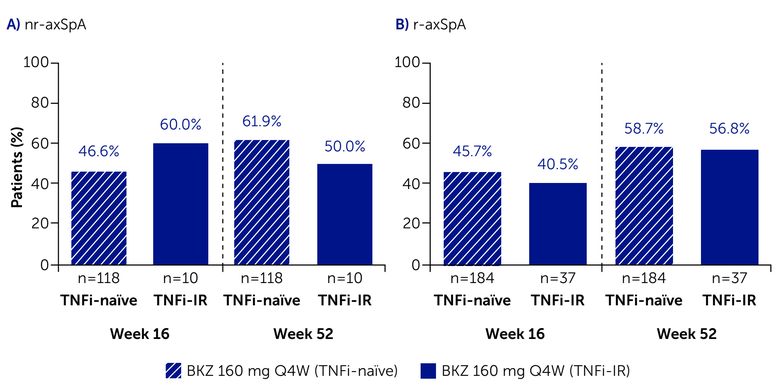
Patients were eligible to receive non-biologic rescue therapy from Week 20 at the discretion of the investigator, while continuing to receive BKZ. All patients had active nr-axSpA or r-axSpA at baseline (BASDAI ≥4 and spinal pain ≥4). [a]Included patients with adult-onset nr-axSpA fulfilling ASAS classification criteria and objective signs of inflammation (active sacroiliitis on MRI and/or elevated CRP [≥6 mg/L]); [b]Included patients with radiographic evidence of r-axSpA, fulfilling Modified New York criteria and ASAS classification criteria.

Figure 2 ASAS40 to Week 52 (NRI)



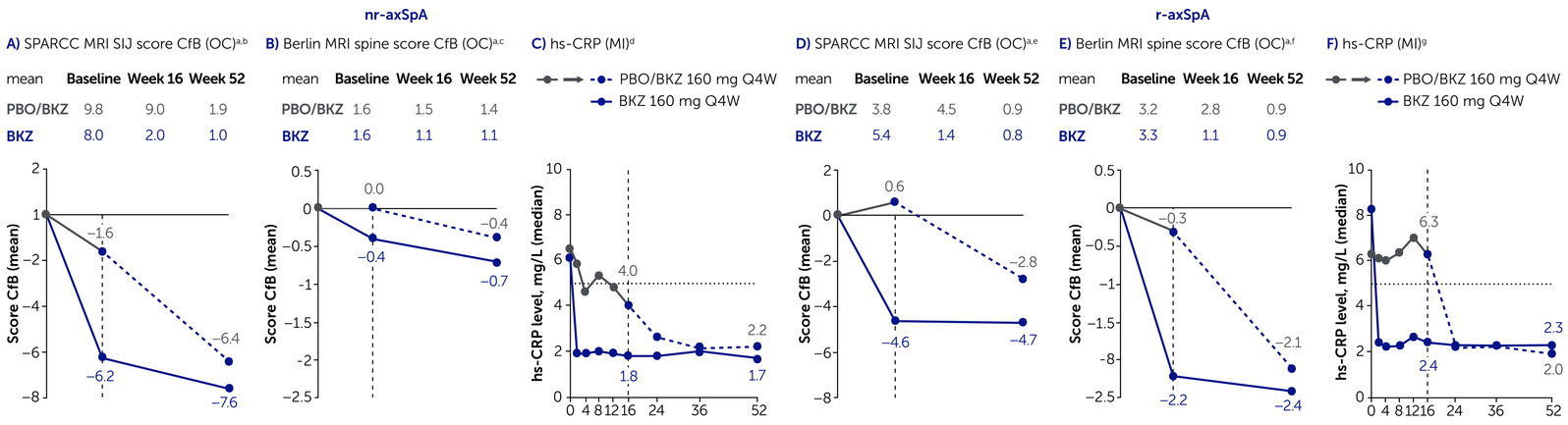
Randomised set. Missing data were imputed using NRI. p values were calculated using logistic regression with treatment, prior MRI/CRP status (BE MOBILE 1) or TNFi exposure (BE MOBILE 2), and region as factors.

Figure 3 ASAS40 to Week 52 in TNFi-naïve and TNFi-IR patients (NRI)



Randomised set. Missing data imputed using NRI. ASAS40 in TNF-naïve patients was a ranked secondary endpoint in BE MOBILE 2 only.

Figure 4 Objective signs of inflammation to Week 52 (OC and MI)



Randomised set. Data reported using OC (SPARCC MRI SIJ; Berlin MRI spine score) or MI, where patients that discontinued treatment due to loss of efficacy or safety were considered as non-responders (hs-CRP). Tables report mean absolute values. [a]Only includes patients enrolled in the SIJ and spine MRI sub-study; [b]At baseline n=70 (PBO/BKZ), n=82 (BKZ); [c]At baseline n=67 (PBO/BKZ), n=79 (BKZ); [d]n=126 (PBO/BKZ), n=128 (BKZ); [e]At baseline n=48 (PBO/BKZ), n=90 (BKZ); [f]At baseline n=48 (PBO/BKZ), n=89 (BKZ); [g]n=111 (PBO/BKZ), n=221 (BKZ).

Table 1 Baseline characteristics

	BE MOBILE 1 (nr-axSpA) N=254	BE MOBILE 2 (r-axSpA) N=332
Age, years, mean (SD)	39.4 (11.5)	40.4 (12.3)
Sex, male, n (%)	138 (54.3)	240 (72.3)
HLA-B27 positive, n (%)	197 (77.6)	284 (85.5)
Symptom duration, years, mean (SD)	9.0 (8.8)	13.5 (10.3)
Time since first diagnosis, years, mean (SD)	3.6 (5.8)	6.4 (7.9)
ASDAS, mean (SD)	3.7 (0.7)	3.7 (0.8)[a]
BASDAI, mean (SD)	6.8 (1.3)	6.5 (1.3)
BASMI, mean (SD)	3.0 (1.3)	3.9 (1.6)[b]
hs-CRP, mg/L, geometric mean (geometric CV, %)	4.8 (261.8)	6.6 (246.3)
hs-CRP >ULN,[c] n (%)	141 (55.5)	204 (61.4)
Total spinal pain score, mean (SD)	7.2 (1.5)	7.2 (1.5)
BASFI, mean (SD)	5.4 (2.3)	5.2 (2.1)
ASQoL, mean (SD)	9.4 (4.5)	8.9 (4.6)
SF-36 PCS, mean (SD)	33.4 (8.5)	34.4 (8.5)
Prior TNFi exposure, n (%)	27 (10.6)	54 (16.3)
Psoriasis,[d] n (%)	16 (6.3)	25 (7.5)

Randomised set. [a]n=331; [b]n=328; [c]ULN value for hs-CRP is 5 mg/L; [d]Includes any previous medical conditions that were resolved prior to study entry and ongoing medical conditions that were still on-going at the time of study entry.

Table 2 Efficacy endpoints at Week 52

	BE MOBILE 1 (nr-axSpA) Week 52		BE MOBILE 2 (r-axSpA) Week 52	
	PBO→BKZ 160 mg Q4W n=126	BKZ 160 mg Q4W n=128	PBO→BKZ 160 mg Q4W n=111	BKZ 160 mg Q4W n=221
ASAS40,* [NRI] n (%)	64 (50.8)	78 (60.9)	76 (68.5)	129 (58.4)
ASAS40 in TNFi-naïve,† [NRI] n (%)	58 (53.2)[a]	73 (61.9)[b]	67 (71.3)[c]	108 (58.7)[d]
ASAS40 in TNFi-IR,‡ [NRI] n (%)	6 (35.3)[f]	5 (50.0)[g]	9 (52.9)[f]	21 (56.8)[h]
ASAS20,†† [NRI] n (%)	88 (69.8)	94 (73.4)	89 (80.2)	158 (71.5)
ASAS PR,†† [NRI] n (%)	38 (30.2)	38 (29.7)	41 (36.9)	66 (29.9)
ASAS 5/6,†† [NRI] n (%)	65 (51.6)	71 (55.5)	74 (66.7)	124 (56.1)
BASDAI CfB,†† [MI] mean (SE)	−3.5 (0.2)	−3.9 (0.2)	−4.0 (0.2)	−3.6 (0.1)
BASFI CfB,†† [MI] mean (SE)	−2.6 (0.2)	−3.0 (0.2)	−2.8 (0.2)	−2.8 (0.1)
BASMI CfB,† [MI] mean (SE)	−0.4 (0.1)	−0.6 (0.1)	−0.7 (0.1)	−0.7 (0.1)
ASDAS CfB, [MI] mean (SE)	−1.6 (0.1)	−1.8 (0.1)	−1.9 (0.1)	−1.7 (0.1)
ASDAS-MI,†† [NRI] n (%)	37 (29.4)	47 (36.7)	49 (44.1)	71 (32.1)
ASDAS <2.1, [MI] %	54.5	61.6	66.4	57.1
Nocturnal spinal pain CfB,†† [MI] mean (SE)	−4.1 (0.2)	−4.3 (0.3)	−4.6 (0.3)	−4.1 (0.2)
ASQoL CfB,†† [MI] mean (SE)	−5.3 (0.4)	−5.9 (0.4)	−5.6 (0.4)	−5.7 (0.3)
SF-36 PCS CfB,†† [MI] mean (SE)	11.4 (0.9)	12.2 (0.9)	12.3 (0.9)	12.0 (0.6)

Randomised set. *Primary endpoint; †Secondary endpoint in BE MOBILE 1; ††Secondary endpoint in BE MOBILE 2. Missing data were imputed using NRI for binary endpoints and MI (based on the missing at random assumption) for all continuous endpoints, for which a reference-based MI approach was applied for the Week 16 timepoint (based on data from the placebo group). [a]n=109; [b]n=118; [c]n=94; [d]n=184; [e]Patients received maximum of one TNFi; [f]n=17; [g]n=10; [h]n=37.

Table 3 Safety overview

n (%) [EAIR]	BE MOBILE 1 (nr-axSpA) BKZ 160 mg Q4W Total[a] N=244	BE MOBILE 2 (r-axSpA) BKZ 160 mg Q4W Total[a] N=330
Any TEAE	183 (75.0) [202.1]	249 (75.5) [200.8]
Severe TEAEs	8 (3.3) [3.9]	14 (4.2) [4.9]
Study discontinuation due to TEAEs	6 (2.5) [2.9]	15 (4.5) [5.2]
Drug-related TEAEs	81 (33.2) [51.3]	135 (40.9) [67.1]
Serious TEAEs[b]	9 (3.7) [4.4]	20 (6.1) [7.1]
Deaths	0	0
Most frequently reported TEAEs[c]		
Nasopharyngitis	30 (12.3) [15.7]	30 (9.1) [11.0]
Upper respiratory tract infection	23 (9.4) [11.9]	21 (6.4) [7.5]
Oral candidiasis	18 (7.4) [9.0]	20 (6.1) [7.2]
Any fungal infections	37 (15.2) [19.6]	40 (12.1) [14.9]
Adjudicated IBD[d]	2 (0.8) [1.0]	3 (0.9) [1.0]
Crohn's disease	1 (0.4) [0.5]	2 (0.6) [0.7]
Ulcerative colitis	1 (0.4) [0.5]	1 (0.3) [0.3]
Uveitis[e,f]	3 (1.2) [1.5]	7 (2.1) [2.4]
Adjudicated SIB	1 (0.4) [0.5]	1 (0.3) [0.3]
Psoriatic conditions[g]	5 (2.0) [2.4]	6 (1.8) [2.1]

Safety set. MedDRA (Version 19.0). [a]Includes patients who switched from PBO to BKZ (events after switch only); [b]Includes TEAEs that were fatal; life threatening; requiring in-patient hospitalisation or prolongation of existing hospitalisation; resulting in persistent or significant disability or incapacity; or any other medically important serious event; [c]TEAEs >5% in patients receiving BKZ are reported by preferred term; [d]At baseline, 4/244 (1.6%) patients with nr-axSpA and 4/330 (1.2%) patients with r-axSpA had a medical history of IBD; [e]At baseline, 39/244 (16.0%) patients with nr-axSpA and 56/330 (17.0%) patients with r-axSpA had a medical history of uveitis; [f]Includes the preferred terms autoimmune uveitis, uveitis, iridocyclitis and iritis; [g]Includes the preferred terms psoriasis and pustular psoriasis.

ASAS20/40: Assessment of SpondyloArthritis international Society 20/40 response; **ASAS 5/6:** ASAS 5/6 response; **ASAS PR:** ASAS partial remission; **ASDAS-CRP:** Ankylosing Spondylitis Disease Activity Score C-reactive protein; **ASDAS-MI:** ASDAS major improvement; **ASQoL:** Ankylosing Spondylitis Quality of Life; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BASFI:** Bath Ankylosing Spondylitis Functional Index; **BASMI:** Bath Ankylosing Spondylitis Metrology Index; **BKZ:** bimekizumab; **CfB:** change from baseline; **CRP:** C-reactive protein; **CV:** coefficient of variation; **EAIR:** exposure adjusted incidence rate; **HLA-B27:** human leukocyte antigen B27; **hs-CRP:** high sensitivity-C-reactive protein; **IR:** inadequate responders; **MASES:** Maastricht Ankylosing Spondylitis Enthesitis Score; **MI:** multiple imputation; **MRI:** magnetic resonance imaging; **nr-axSpA:** non-radiographic axial spondyloarthritis; **NRI:** non-responder imputation; **OC:** observed case; **PBO:** placebo; **Q4W:** every four weeks; **r-axSpA:** radiographic axial spondyloarthritis; **SE:** standard error; **SF-36 PCS:** Short Form-36 Physical Component Summary; **SIB:** suicidal ideation behaviour; **SIJ:** Sacroiliac Joints; **SPARCC:** Spondyloarthritis Research Consortium of Canada; **TNFi:** tumour necrosis factor inhibitor; **ULN:** upper limit of normal.

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References: [1]Van der Heijde D, *et al.* Ann Rheum Dis 2023;0:1–12. **Author Disclosures:** **JFM:** Consultant and/or investigator for AbbVie, Amgen, Biogen, Bristol Myers Squibb, Dermavant, Eli Lilly, Janssen, LEO Pharma, Pfizer, Novartis, Regeneron, Sanofi, Sun Pharma and UCB Pharma. **XB:** Speaker for AbbVie, Bristol Myers Squibb, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer and UCB Pharma; paid instructor for AbbVie, Bristol Myers Squibb, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer and UCB Pharma; consultant for AbbVie, Bristol Myers Squibb, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer and UCB Pharma. **DT:** Honoraria for participation on advisory boards, as a speaker and consultant for AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly, Galapagos, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Samsung, Sanofi Genzyme and UCB Pharma; research grants received from LEO Pharma and Novartis. **DP:** Speaker for AbbVie, Bristol Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer and UCB Pharma; consultant for AbbVie, Biocad, Eli Lilly, Gilead, GSK, MSD, MoonLake Immunotherapeutics, Novartis, Pfizer, Samsung Bioepis and UCB Pharma; grant/research support from AbbVie, Eli Lilly, MSD, Novartis and Pfizer. **FVdB:** Consultant for AbbVie, Amgen, Eli Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer and UCB Pharma; speakers bureau fees AbbVie, Bristol Myers Squibb, Celgene, Janssen, Merck, Novartis, Pfizer and UCB Pharma. **DvdH:** Consulting fees from AbbVie, Bayer, Bristol Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Lilly, Novartis, MoonLake Immunotherapeutics, Pfizer, Takeda and UCB Pharma; director of Imaging Rheumatology BV. **AD:** Speaker for Janssen, Novartis, and Pfizer; consultant for AbbVie, Amgen, Aurinia, Bristol Myers Squibb, Eli Lilly, GSK, Janssen, MoonLake Immunotherapeutics, Novartis, Pfizer and UCB Pharma; grant/research support from AbbVie, Bristol Myers Squibb, Eli Lilly, GSK, Novartis, Pfizer and UCB Pharma. **MO:** Employee and stockholder of UCB Pharma. **UM, CF, AME, TV, JSS, AM:** Employees of UCB Pharma. **HX:** Speaker for AbbVie, Janssen, Novartis, Pfizer and UCB Pharma; consultant for AbbVie, Beigene, BioMap, IASO, Pfizer and UCB Pharma; clinical investigator for Peking-Tsinghua Center for Life Sciences. **Acknowledgements:** Substantial contributions to study conception/design or acquisition/analysis/interpretation of data: **JFM, XB, DT, DP, FvdB, DvdH, AD, MO, UM, CF, AME, TV, JSS, AM, HX;** drafting of the publication or revising it critically for important intellectual content: **JFM, XB, DT, DP, FvdB, DvdH, AD, MO, UM, CF, AME, TV, JSS, AM, HX;** final approval of the publication: **JFM, XB, DT, DP, FvdB, DvdH, AD, MO, UM, CF, AME, TV, JSS, AM, HX**. We would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to these studies. The authors acknowledge Celia Menckeberg, PhD, UCB Pharma, for publication coordination, Alexandra Quinn-Savory, MPH, Costello Medical, London, UK for medical writing and editorial assistance and the Creative team, Costello Medical, UK for graphic design assistance. These studies were funded by UCB Pharma. All costs associated with development of this presentation were funded by UCB Pharma.

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