Bimekizumab Treatment was Efficacious to 2 Years Regardless of Duration of axSpA Symptoms: Results from Two Phase 3 Studies

Sofia Ramiro,[1,2] Fabian Proft,[3] Raj Sengupta,[4] Astrid van Tubergen,[5] Anna Moltó,[6] Lianne S. Gensler,[7] Mitsumasa Kishimoto,[8] Vanessa Taieb,[9] Diana Voiniciuc,[10] Ute Massow,[11] Victoria Navarro-Compán[12]

[1]Leiden University Medical Center, Department of Rheumatology, Leiden, The Netherlands; [2]Zuyderland Medical Center, Heerlen,The Netherlands; [3]Charité – Universitätsmedizin Berlin, Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; [4]The Royal National Hospital for Rheumatic Diseases, Bath, UK; [5]Maastricht University Medical Center, Department of Medicine, Division of Rheumatology, Maastricht, The Netherlands; [6]Groupe Hospitalier Cochin, AP-HP, Paris, France; [7]University of California, San Francisco, Department of Medicine/Rheumatology, San Francisco, California, USA; [8]Kyorin University School of Medicine, Department of Nephrology and Rheumatology, Tokyo, Japan; [9]UCB, Colombes, France; [10]UCB, Slough, UK; [11]UCB, Monheim am Rhein, Germany; [12]La Paz University Hospital, IdiPaz, Department of Rheumatology, Madrid, Spain; [13]UCB, Madrid, Spain.

Presenting on behalf of the authors: Miguel Ángel Mendez[13]

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Objective

To evaluate the impact of shorter vs longer duration of symptoms (DoS on the 2-year efficacy of bimekizumab (BKZ) in the treatment of axial spondyloarthritis (axSpA).

Introduction

- Recently, early axSpA has been defined for research purposes as a DoS of ≤2 years by the Assessment of SpondyloArthritis international Society (ASAS).[1] Evidence evaluating whether treatment in early axSpA leads to better outcomes compared with established disease is scarce.
- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- BKZ has shown efficacy to Week 52 in patients with non-radiographic (nr-) and radiographic (r-)axSpA in the phase 3 trials BE MOBILE 1 and 2.[2,3] Here, we report BKZ efficacy in patients with early axSpA vs established disease, across the full disease spectrum of axSpA, to 2 years.

Methods

- In BE MOBILE 1 (nr-axSpA; NCT03928704) and BE MOBILE 2 (r-axSpA; NCT03928743), patients were randomised to subcutaneous BKZ 160 mg every 4 weeks (Q4W) or placebo (PBO); all received BKZ in Weeks 16–52.
  - At Week 52, patients could enter an ongoing open-label extension (NCT04436640) and continue BKZ treatment.
- We present a post hoc analysis of the following clinical efficacy outcomes to Week 104, in patients with DoS ≤2 or >2 years in BE MOBILE 1:
  - ASAS 40% improvement (ASAS40; non-responder imputation [NRI])
  - Axial Spondyloarthritis Disease Activity Score (ASDAS) <2.1 (multiple imputation [MI])
  - Mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) change from baseline (CfB; MI).
- We also report the above outcomes for patients with DoS ≤5 or >5 years in BE MOBILE 1 and 2 to optimise subgroup sample sizes (only 17 patients had DoS ≤2 years in BE MOBILE 2).
- In addition to the above outcomes, we report mean MRI Spondyloarthritis Research Consortium of Canada (SPARCC) sacroiliac joint (SIJ) inflammation score (observed case [OC]) for MRI sub-study patients with DoS ≤5/>5 years in BE MOBILE 1 (only 27 patients had DoS ≤5 years in the BE MOBILE 2 MRI sub-study).
- For all outcomes, continuous BKZ and PBO/BKZ switchers were pooled within each trial from Week 52.
- To compare treatment effect (BKZ vs PBO efficacy) between DoS subgroups, relative odds ratio (rOR; ASAS40, ASDAS <2.1) and relative differences (BASDAI CfB, MRI SPARCC SIJ) were calculated at Week 16, sample size permitting.
  - Trials were not powered for post hoc analyses; results should be interpreted as nominal.

Results

Clinical Efficacy Outcomes

- Better outcomes were seen with BKZ vs PBO at Week 16, regardless of DoS, across all efficacy measures (**Figure 1–2**). Outcomes were sustained or improved in all DoS subgroups to Week 104.
- At Week 16, numerically larger proportions of BKZ-treated patients with DoS ≤5/≤2 years achieved ASAS40 and ASDAS <2.1 vs patients with DoS >5/>2 years.
  - No statistically significant difference was detected in treatment effect with BKZ vs PBO at Week 16 between patients with DoS ≤5 vs >5 years (BE MOBILE 1 and 2) or between patients with DoS ≤2 vs >2 years (BE MOBILE 1)
  - At Week 104, numerically larger proportions of patients with DoS ≤5/≤2 years achieved ASAS40 and ASDAS <2.1 vs patients with DoS >5/>2 years (**Figure 1–2**).
- No statistically significant difference in treatment effect with BKZ vs PBO was detected at Week 16 in mean BASDAI CfB between patients with DoS ≤5 vs >5 years, or DoS ≤2 vs >2 years in BE MOBILE 1, but a larger improvement was found in BASDAI in patients with DoS ≤5 vs >5 years in BE MOBILE 2 (**Figure 1–2**).
  - At Week 104, there were numerically larger reductions (i.e., improvements) from baseline in mean BASDAI for patients with DoS ≤5/≤2 years vs patients with DoS >5/>2 years (**Figure 1–2**).

MRI Inflammation

- Baseline MRI SPARCC SIJ scores indicated more inflammation in patients with DoS ≤5 vs >5 years in BE MOBILE 1 (**Figure 3**).
- BKZ treatment led to reduction in mean MRI SPARCC SIJ scores to Week 16.
  - No statistically significant difference in treatment effect was detected with BKZ vs PBO between patients with DoS ≤5 vs >5 years at Week 16 (**Figure 3**)
  - Mean MRI SPARCC SIJ scores remained low to Week 104 and indicated resolution of inflammation, regardless of DoS.

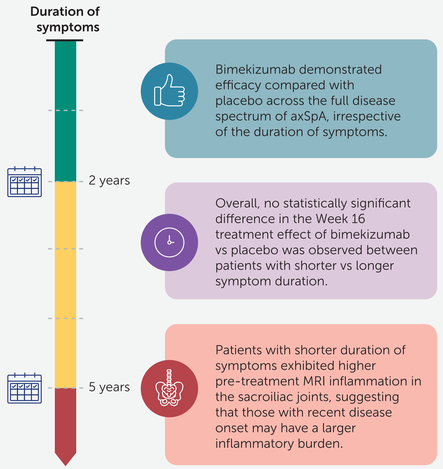
Conclusions

Overall, no statistically significant differences in the Week 16 treatment effect of bimekizumab compared to placebo were found between patients with shorter vs longer DoS. However, bimekizumab treatment demonstrated sustained efficacy through 2 years, irrespective of DoS, highlighting its therapeutic potential for both early and established axSpA.

Summary

Recently, **early axSpA** has been defined for research purposes as a duration of symptoms of ≤2 years.[1]

We assessed the long-term efficacy of bimekizumab in patients with **shorter vs longer** duration of symptoms of axSpA (≤2 vs >2 years and ≤5 vs >5 years) **over 2 years**.

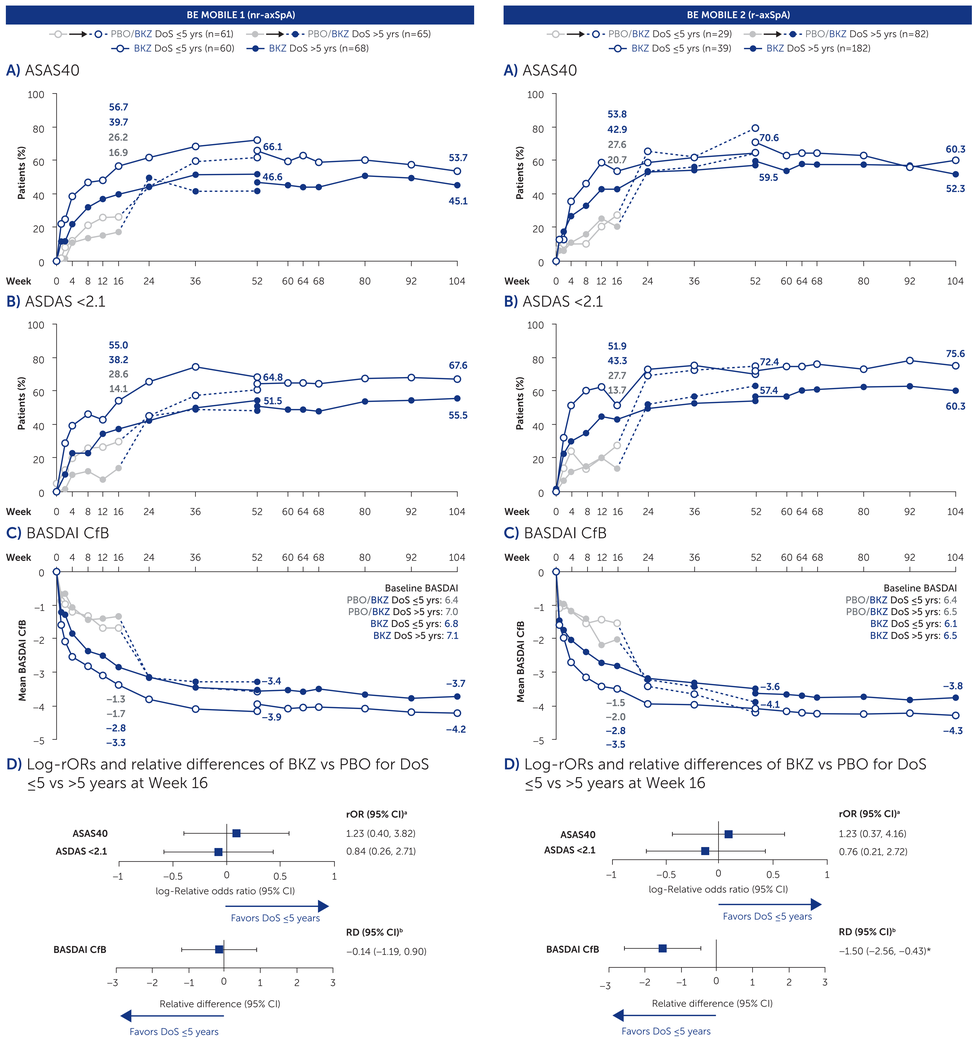


Bimekizumab demonstrated efficacy compared with placebo across the full disease spectrum of axSpA, irrespective of the duration of symptoms.

Overall, no statistically significant difference in the Week 16 treatment effect of bimekizumab vs placebo was observed between patients with shorter vs longer symptom duration.

Patients with shorter duration of symptoms exhibited higher pre-treatment MRI inflammation in the sacroiliac joints, suggesting that those with recent disease onset may have a larger inflammatory burden.

Figure 1 ASAS40 (NRI), ASDAS <2.1 (MI) and mean BASDAI CfB (MI) stratified by DoS ≤5 and >5 years in BE MOBILE 1 and 2



Randomised set. BKZ-randomised patients received BKZ 160 mg Q4W to Week 16; all patients received BKZ from Week 16–52. n refers to the number of patients in their respective subgroups at baseline. Beyond Week 52, all data are pooled across BKZ- and PBO–randomised patients. **[a]** Odds ratios for the comparison of BKZ vs PBO were calculated using logistic regression. For patients with nr-axSpA, factors for logistic regression included treatment, MRI/CRP classification, region, DoS, and treatment × DoS. For patients with r-axSpA, factors for logistic regression included treatment, prior TNF inhibitor exposure, region, DoS, and treatment × DoS. The relative odds ratio is the odds ratio of the comparison of BKZ vs PBO with shorter vs longer DoS. This value, and its associated 95% CIs and p value are extracted from the interaction effect of treatment and DoS from the logistic regression; **[b]** Relative differences in least-square means and 95% CIs for the comparison of BKZ vs PBO were calculated using ANCOVA. For patients with nr-axSpA, factors for ANCOVA included treatment, MRI/CRP classification, region, baseline BASDAI value, DoS, and treatment × DoS. For patients with r-axSpA, factors included treatment, prior TNF inhibitor exposure, region, baseline BASDAI value, DoS, and treatment × DoS. *Larger improvements in BASDAI achieved in patients with DoS ≤5 vs >5 years (nominal p <0.05).

Figure 2 ASAS40 (NRI), ASDAS <2.1 (MI) and mean BASDAI CfB (MI) stratified by DoS ≤2 and >2 years in BE MOBILE 1

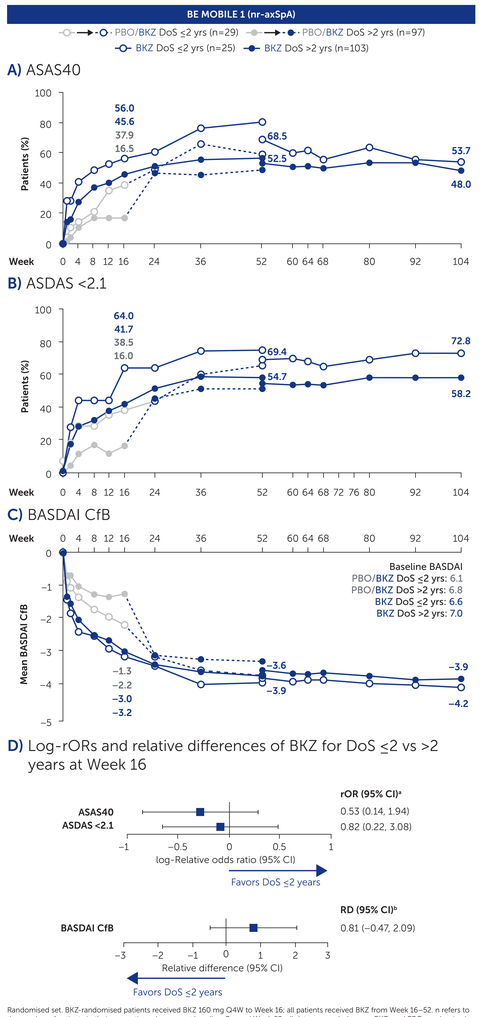


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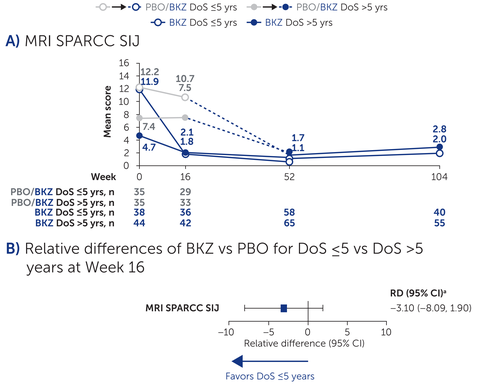
Figure 3 MRI inflammation stratified by DoS ≤5 and >5 years in BE MOBILE 1 (OC)



Randomised set. Only study participants enrolled in the MRI sub-studies are included. Beyond Week 52, all data, including n numbers, are pooled across BKZ- and PBO-randomised patients. **[a]** Relative differences in least-square means and 95% CIs for the comparison of BKZ vs PBO were calculated using ANCOVA, including factors for treatment, MRI/CRP classification, baseline MRI SPARCC SIJ value, DoS, and treatment × DoS.

ANCOVA: analysis of covariance; **ASAS:** Assessment of SpondyloArthritis international Society; **ASAS40:** ASAS 40% improvement; **ASDAS:** Axial Spondyloarthritis Disease Activity Score; **axSpA:** axial spondyloarthritis; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BKZ:** bimekizumab; **CfB:** change from baseline; **CI:** confidence interval; **CRP:** C-reactive protein; **DoS:** duration of symptoms; **IL:** interleukin; **MI:** multiple imputation; **MRI:** magnetic resonance imaging; **nr-axSpA:** non-radiographic axSpA; **NRI:** non-responder imputation; **OC:** observed case; **PBO:** placebo; **Q4W:** every 4 weeks; **r-axSpA:** radiographic axSpA; **RD:** relative difference; **rOR:** relative odds ratio; **SIJ:** sacroiliac joint; **SPARCC:** Spondyloarthritis Research Consortium of Canada; **TNF:** tumor necrosis factor; **yrs:** years.

References: [1]Navarro-Compán V. Ann Rheum Dis 2023;10.1136/ard-2023-224232; [2]van der Heijde D. Ann Rheum Dis 2023;82:515–26; [3]Baraliakos X. Ann Rheum Dis 2024;83:199–213. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **SR**, **FP**, **RS**, **AvT**, **AM**, **LSG**, **MK**, **VT**, **DV**, **UM**, **VNC**. Drafting of the publication, or reviewing it critically for important intellectual content: **SR**, **FP**, **RS**, **AvT**, **AM**, **LSG**, **MK**, **VT**, **DV**, **UM**, **VNC**. Final approval of the publication: **SR**, **FP**, **RS**, **AvT**, **AM**, **LSG**, **MK**, **VT**, **DV**, **UM**, **VNC**. **Author Disclosures: SR:** Consultant for AbbVie, Eli Lilly and Company, Galapagos/Alfasigma, Janssen, Novartis, Pfizer, Sanofi and UCB; grants from AbbVie, Galapagos/Alfasigma, MSD, Novartis, Pfizer and UCB. **FP:** Speaker and consultant for AbbVie, Amgen, BMS, Celgene, Galapagos, Hexal, Janssen, Medscape, MSD, Novartis, Pfizer, Roche and UCB; grant/research support from Eli Lilly and Company, Novartis and UCB. **RS:** Speaker for AbbVie, Biogen, Celgene, Eli Lilly and Company, MSD, Novartis and UCB; research grants from AbbVie, Celgene and UCB. **AvT:** Speaker for Pfizer; consultant for Novartis, Pfizer and UCB; grant/research support from MSD, Novartis, Pfizer and UCB. **AM:** Consultant for AbbVie, MSD, Pfizer and UCB; grant/research support from AbbVie, MSD, Pfizer and UCB. **LSG:** Grants from UCB paid to institution; consulting fees from Acelyrin, Eli Lilly and Company, Janssen, Novartis, Pfizer and UCB. **MK:** Speakers' bureau: AbbVie, Amgen, Asahi-Kasei Pharma, Ayumi Pharma, BMS, Chugai, Daiichi Sankyo, Eisai, Gilead, Eli Lilly and Company, Janssen, Novartis, Tanabe-Mitsubishi and UCB; consultant: AbbVie, Amgen, Asahi-Kasei Pharma, Ayumi Pharma, BMS, Chugai, Gilead, Eli Lilly and Company, Janssen, Novartis, Takeda, Tanabe-Mitsubishi and UCB. **DV:** Contractor for UCB and employee of Veramed. **UM**, **MAM:** Employees of UCB. **VNC:** Speaker for AbbVie, Eli Lilly and Company, Fresenius Kabi, Janssen, MSD, Novartis, Pfizer and UCB; consultant for AbbVie, Alfasigma, Eli Lilly and Company, Galapagos, MoonLake Immunotherapeutics, MSD, Novartis, Pfizer and UCB; grant/research support from AbbVie and Novartis. **Acknowledgements:** 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, Breda, The Netherlands for publication coordination, Isabel Raynaud, MBBS IBSc, Costello Medical, Cambridge, UK, for medical writing and editorial assistance, Charlotte Frall, BSc, Costello Medical, Bristol, UK for editorial assistance and the Costello Medical Creative team for graphic design support. These studies were funded by UCB. All costs associated with development of this presentation were funded by UCB.