OP0019

## BIMEKIZUMAB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: 24-WEEK EFFICACY & SAFETY FROM BE MOBILE 2, A PHASE 3, MULTICENTRE, RANDOMISED, PLACEBO-CONTROLLED STUDY

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**Background:** Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. In a phase 2b study, BKZ showed rapid and sustained efficacy and was well tolerated up to 156 weeks (wks) in patients (pts) with active ankylosing spondylitis (AS).[1,2]

**Objectives:** To assess efficacy and safety of BKZ vs placebo (PBO) in pts with active AS up to Wk 24 in the ongoing pivotal phase 3 study, BE MOBILE 2.

**Methods:** BE MOBILE 2 (NCT03928743) comprises a 16-wk double-blind, PBO-controlled period and 36-wk maintenance period. Pts were aged ≥18 yrs, met modified New York criteria and had active AS (BASDAI ≥4, spinal pain ≥4) at BL. Pts were randomised 2:1, BKZ 160 mg Q4W:PBO. From Wk 16, all pts received BKZ 160 mg Q4W. Primary and secondary efficacy endpoints were assessed at Wk 16.

**Results:** Of 332 randomised pts (BKZ: 221; PBO: 111), 322 (97.0%) completed Wk 16 and 313 (94.3%) Wk 24. BL characteristics were comparable between groups: mean age 40.4 yrs, symptom duration 13.5 yrs; 72.3% pts male, 85.5% HLA-B27+, 16.3% TNFi-experienced. At Wk 16, the primary (ASAS40: 44.8% BKZ vs 22.5% PBO; p<0.001) and all ranked secondary endpoints were met (Table 1). Responses with BKZ were rapid, including in PBO pts who switched to BKZ at Wk 16, and increased to Wk 24 (Figure 1; Table 1). Substantial reductions of hs-CRP by Wk 2 and MRI SIJ and spine inflammation by Wk 16 were achieved with BKZ vs PBO (Table 1). At Wk 24, ≥50% pts had achieved ASDAS <2.1 (Figure 1).

Over 16 wks, 120/221 (54.3%) BKZ pts had ≥1 TEAE vs 48/111 (43.2%) PBO; three most frequent on BKZ were nasopharyngitis (BKZ: 7.7%; PBO: 3.6%), headache (4.1%; 4.5%) and oral candidiasis (4.1%; 0%). No systemic candidiasis was observed. Up to 16 wks, incidence of SAEs was low (1.8%; 0.9%); no MACE or deaths were reported; 2 (0.9%) IBD cases occurred in pts on BKZ.

**Conclusion:** Dual inhibition of IL-17A and IL-17F with BKZ in pts with active AS resulted in rapid, clinically relevant improvements in efficacy outcomes vs PBO. No new safety signals were observed.[1,2]

**REFERENCES:**

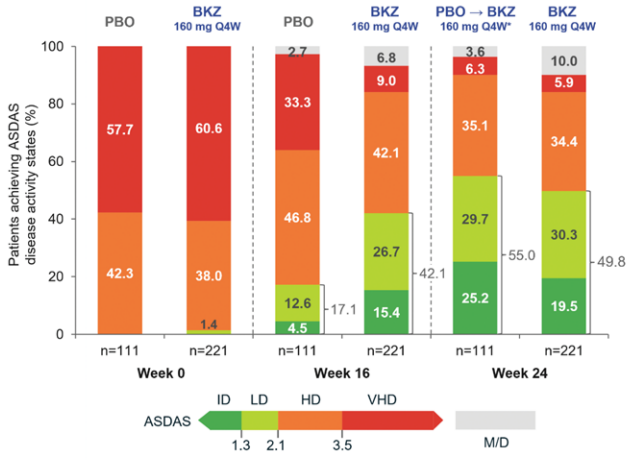
[1] van der Heijde D. Ann Rheum Dis 2020;79:595–604; **2.** Gensler L. Arthritis Rheumatol 2021;73(suppl 10):0491.

**Table 1. Efficacy at Wks 16 and 24**

| | | BL | | Wk 16 | | | Wk 24 | |
|---|---|---|---|---|---|---|---|---|
| | | PBO N=111 | BKZ 160 mg Q4W N=221 | PBO N=111 | BKZ 160 mg Q4W N=221 | p value | PBO→BKZ 160 mg Q4W N=111 | BKZ 160 mg Q4W N=221 |
| **Ranked endpoints in hierarchical order** | **ASAS40*** [NRI] n (%) | - | - | 25 (22.5) | 99 (44.8) | <0.001 | 63 (56.8) | 119 (53.8) |
| | **ASAS40 in TNFi-naïve†** [NRI] n (%) | - | - | 22 (23.4)[a] | 84 (45.7)[b] | <0.001 | 56 (59.6)[a] | 100 (54.3)[b] |
| | **ASAS20†** [NRI] n (%) | - | - | 48 (43.2) | 146 (66.1) | <0.001 | 85 (76.6) | 159 (71.9) |
| | **BASDAI CfB†** [MI] mean (SE) | 6.5 (0.1) | 6.5 (0.1) | –1.9 (0.2) | –2.9 (0.1) | <0.001 | –3.3 (0.2) | –3.3 (0.1) |
| | **ASAS PR†** [NRI] n (%) | - | - | 8 (7.2) | 53 (24.0) | <0.001 | 28 (25.2) | 56 (25.3) |
| | **ASDAS-MI†** [NRI] n (%) | - | - | 6 (5.4) | 57 (25.8) | <0.001 | 43 (38.7) | 67 (30.3) |
| | **ASAS 5/6†** [NRI] n (%) | - | - | 16 (14.4) | 94 (42.5) | <0.001 | 57 (51.4) | 107 (48.4) |
| | **BASFI CfB†** [MI] mean (SE) | 5.2 (0.2) | 5.3 (0.2) | –1.1 (0.2) | –2.2 (0.1) | <0.001 | –2.2 (0.2) | –2.4 (0.2) |
| | **Nocturnal spinal pain CfB†** [MI] mean (SE) | 6.8 (0.2) | 6.6 (0.1) | –1.9 (0.2) | –3.3 (0.2) | <0.001 | –3.7 (0.3) | –3.8 (0.2) |
| | **ASQoL CfB†** [MI] mean (SE) | 8.5 (0.4) | 9.0 (0.3) | –3.2 (0.3) | –4.9 (0.3) | <0.001 | –4.9 (0.4) | –5.4 (0.3) |
| | **SF-36 PCS CfB†** [MI] mean (SE) | 34.6 (0.8) | 34.4 (0.6) | 5.9 (0.8) | 9.3 (0.6) | <0.001 | 10.6 (0.8) | 10.8 (0.6) |
| | **BASMI CfB†** [MI] mean (SE) | 3.8 (0.2) | 3.9 (0.1) | –0.2 (0.1) | –0.5 (0.1) | 0.005 | –0.5 (0.1) | –0.6 (0.1) |
| **Other endpoints[n]** | **Enthesitis-free state†[c]** [NRI] n (%) | - | - | 22 (32.8)[d] | 68 (51.5)[e] | - | 33 (49.3)[d] | 70 (53.0)[e] |
| | **ASAS40 in TNFi-experienced** [NRI] n (%) | - | - | 3 (17.6)[f] | 15 (40.5)[g] | - | - | - |
| | **ASDAS-CRP CfB** [MI] mean (SE) | 3.7 (0.1) | 3.7 (0.1) | –0.7 (0.1) | –1.4 (0.1) | - | –1.7 (0.1) | –1.6 (0.1) |
| | **hs-CRP (mg/L)** [MI] geometric mean (median) | 6.7 (6.3) | 6.5 (8.2) | 6.0 (6.3) | 2.4 (2.4) | - | 1.9 (2.2) | 2.1 (2.3) |
| | **MRI spine Berlin CfB[h]** [OC] mean (SD) | 3.3 (4.9)[i] | 3.8 (5.3)[j] | 0.0 (1.4)[k] | –2.3 (3.9)[l] | - | - | - |
| | **SPARCC MRI SIJ score CfB[h]** [OC] mean (SD) | 5.8 (7.7)[i] | 7.4 (10.7)[m] | 1.1 (6.9)[k] | –5.6 (9.9)[l] | - | - | - |

Randomised set. *Primary endpoint; †Secondary endpoint; [a]n=94; [b]n=184; [c]MASES=0 in pts with BL MASES >0; [d]n=67; [e]n=132; [f]n=17; [g]n=37; [h]In pts in MRI sub-study; [i]n=45; [j]n=82; [k]n=43; [l]n=79; [m]n=83; [n]Nominal p values not shown.

**Figure.** ASDAS states over time




Randomised set. Data reported as observed case. *At Wk 16, pts on PBO switched to BKZ.

**Abbreviations:** AS: ankylosing spondylitis; ASAS20/40: Assessment of SpondyloArthritis international Society 20/40% 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; BL: baseline; CfB: change from baseline; HD: high disease; HLA-B27: human leukocyte antigen B27; hs-CRP: high sensitivity-CRP; IBD: inflammatory bowel disease; ID: inactive disease; IL: interleukin; LD: low disease; MACE: Major Adverse Cardiovascular Event; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; M/D: missing data; MI: multiple imputation; MRI: magnetic resonance imaging; n: number; NRI: non-responder imputation; OC: observed case; PBO: placebo; Pts: patients; Q4W: every four weeks; SAEs: serious adverse events; SD: standard deviation; SE: standard error; SPARRC: Spondyloarthritis Research Consortium of Canada; SIJ: Sacroiliac Joints; SF-36 PCS: Short Form-36 Physical Component Summary; TNFi: tumour necrosis factor inhibitor; VHD: very high disease; Wks: weeks; yr: year.

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OP0020

## SEX DIFFERENCES IN EFFECTIVENESS OF FIRST-LINE TUMOR NECROSIS FACTOR INHIBITORS IN AXIAL SPONDYLOARTHRITIS; RESULTS FROM FIFTEEN COUNTRIES IN THE EUROSPA RESEARCH COLLABORATION NETWORK

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**Background:** Evidence reveals sex differences in physiology, disease presentation and response to treatment in axial spondyloarthritis (axSpA). Pooled data from four randomized controlled trials demonstrated reduced treatment efficacy of a tumor necrosis factor inhibitor (TNFi) in females compared to males with ankylosing spondylitis[1]. However, real-life evidence confirming these data in large cohorts is scarce. We sought to validate prior studies using data from a large multinational cohort based on real-life clinical practice.

**Objectives:** To investigate sex differences in treatment response and drug retention rates in clinical practice among patients with axSpA, treated with their first TNFi.

**Methods:** Data from biologic-naïve axSpA patients initiating a TNFi in the EuroSpA registries were pooled. In the primary analysis, propensity-score weighting was applied to assess the causal effect of sex on clinically important improvement (CII) according to ASDAS-CRP at 6 months. A generalized linear regression model was used to estimate the causal risk difference (RD) and relative risk (RR) of sex on CII. Possible covariates influencing the outcome were determined a priori and selected based on availability in the database (<20% missing). The final covariates included in the model were country, age and TNFi start year. In the secondary analysis, drug retention was assessed over 24 months of follow-up by Kaplan-Meier curves and log-rank test.

**Results:** In total, 6,451 axSpA patients with available data on ASDAS-CRP at baseline and 6 months were assessed for treatment response. Baseline characteristics are shown in the Table 1. In the adjusted analysis, the probability for females to have CII was 15% (RR, 0.85; 95% confidence interval [CI], 0.82 to