The median duration of exposure was 6.0 [IQR: 3.3; 10.1] months for VTE, and 12.0 [IQR: 4.8; 15.3] months for ATE. The IRR for VTE and ATE were increased during exposure, and during the 30 days following exposure (Table 1). The IRR for VTE was only increased during exposure and in the early post-exposure phase contrary to the IRR for ATE that was also increased in the pre-exposure 7-Day period. Analysis conducted on survival patients confirmed results.

Conclusion: The present study found an increased risk of VTE and ATE for baricitinib and tofacitinib. The risk persists in the month following the discontinuation of treatment but disappears after day 30 post-exposure.

Table 1.

	N	Patient-years	IRR	95%CI
Venous thromboembolic events				
Non-exposure (reference)	8	3975.0	1	-
Pre-exposure to JAK-i	1	135.2	4.7	0.6-38.0
Exposure to JAK-i	27	2090.5	9.8	4.1-23.3
Post-exposure 1-30 d	5	369.0	6.2	1.9-19.9
Post-exposure 31-60 d	1	139.0	1.5	0.2-12.6
Arterial thromboembolic events				
Non-exposure (reference)	7	4076.8	1	-
Pre-exposure to JAK-i	3	344.1	11.5	2.8-46.8
Exposure to JAK-i	32	6363.8	7.4	2.9-18.7
Post-exposure 1-30 d	8	659.2	11.5	3.8-34.6
Post-exposure 31-60 d	2	132.2	4.3	0.8-22.0

Disclosure of Interests: Amandine Gouverneur: None declared, Jérôme Avouac Consultant of: JA has/had consultancy relationship and/or has received research funding in the area of potential treatments for rheumatoid arthritis from (last three years): Abbvie, Galapagos, Pfizer, Bristol Myers Squibb, Sanofi, Nordic Pharma, Chugai and MSD., Grant/research support from: JA has/had consultancy relationship and/or has received research funding in the area of potential treatments for rheumatoid arthritis from (last three years): Abbvie, Galapagos, Pfizer, Bristol Myers Squibb, Sanofi, Nordic Pharma, Chugai and MSD., Clément Prati: None declared, Jean-Luc Cracowski: None declared, Thierry Schaeverbeke Consultant of: TS consultancy and/or research fundings: Abbvie, Lilly, Pfizer, Galapagos, Novartis, BMS, Medac, NordicPharma, Biogen, Mylan, Janssen., Grant/research support from: TS consultancy and/or research fundings: Abbvie, Lilly, Pfizer, Galapagos, Novartis, BMS, Medac, NordicPharma, Biogen, Mylan, Janssen., Antoine Pariente Grant/research support from: AP reports acting as an independant expert towards the French Medicines Agency (Agence Nationale de Securité du Médicament et des Produits de Santé, ANSM) and the European Medicines Agency (EMA). AP coordinates the DRUGS Systematised Assessment in real-liFe EnviRonment (DRUGS-SAFER) programme funded by the Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM)., Marie-Elise Truchetet Consultant of: has/had consultancy relationship and/or has received research funding in the area of potential treatments for rheumatoid arthritis and spondyloarthritis and their complications from (last three years): Abbvie, Galapagos, Lilly, Medac, Novartis, Pfizer, and Roche., Grant/research support from: has/had consultancy relationship and/or has received research funding in the area of potential treatments for rheumatoid arthritis and spondyloarthritis and their complications from (last three years): Abbvie, Galapagos, Lilly, Medac, Novartis, Pfizer, and Roche.

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Spondyloarthritis - treatment

POS0226

BIMEKIZUMAB LONG-TERM SAFETY AND EFFICACY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: 3-YEAR RESULTS FROM A PHASE 2B STUDY

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Background: Bimekizumab (BKZ), a monoclonal antibody that selectively inhibits interleukin (IL)-17A and IL-17F, has demonstrated clinical efficacy and safety in patients with ankylosing spondylitis (AS) treated over a period up to 96 weeks.[1,2]

Objectives: To report 3-year interim safety and efficacy of BKZ in patients with active AS from a phase 2b dose-ranging study (BE AGILE; NCT02963506) and its ongoing open-label extension (OLE; NCT03355573).

Methods: BE AGILE study design has been described previously.[1] Patients treated with BKZ 160 mg or 320 mg every 4 weeks (Q4W) at Week 48 in BE AGILE were eligible for OLE entry. All OLE patients received BKZ 160 mg Q4W. Treatment-emergent adverse events (TEAEs) are reported for the BE AGILE safety set (patients who received ≥1 dose of BKZ on study entry) for total exposure to BKZ across BE AGILE and the OLE. Efficacy outcomes are reported for the OLE full analysis set (patients who entered the OLE and had ≥1 dose of BKZ and ≥1 valid efficacy variable measurement in the OLE), and include: ASAS40, ASAS20, ASAS PR, ASDAS, ASDAS-CII, ASDAS-MI, ASDAS-ID (<1.3) and ASDAS <2.1. Data are reported as imputed (multiple imputation [MI] based on the missing at random assumption, or non-responder imputation [NRI]) and as observed case (OC).

Results: 262/303 (86%) patients randomised at BE AGILE study baseline completed Week 48 on BKZ 160 mg or 320 mg. At Week 48, 255/262 (97%) patients entered the OLE (full analysis set: 254); 219 patients had an efficacy assessment at Week 156. Over the 156 weeks, the exposure-adjusted incidence rate (EAIR) per 100 patient-years (PY) of TEAEs was 143.5, with an EAIR of 5.8 for serious TEAEs, 1.3 for serious infections, and 3.8 for *Candida* infections (Table 1). All *Candida* infections were mild or moderate; none were systemic or led to study discontinuation. Over 156 weeks, the EAIR of inflammatory bowel disease (1.2), anterior uveitis (0.8), and injection site reactions (0.5) remained low. Efficacy demonstrated at Week 48 in BE AGILE was maintained or improved up to Week 156 (Figure 1). Mean ASDAS improved from 3.9 at BE AGILE baseline to 2.0 and 1.8 at Weeks 48 and 156 respectively (by MI). At Week 156 in the NRI analyses, ASAS40 and ASAS PR were achieved by 62.6% (OC: 72.6%) and 32.7% (OC: 37.9%) patients respectively. ASDAS-ID and ASDAS <2.1 responder rates (NRI) were maintained or continued to increase from Week 48, and by Week 156, responses were achieved by 28.0% (OC: 33.0%) and 57.1% (OC: 67.4%) patients respectively. ASDAS-MI responder rates (NRI) continued to increase from 44.9% at Week 48 to 46.5% at Week 156 (OC: 52.9%).

Conclusion: The safety profile of BKZ in patients with AS was in line with previous observations.[1,2] Patients treated with BKZ demonstrated sustained and consistent efficacy over 156 weeks.

REFERENCES:

[1] van der Heijde D. Ann Rheum Dis 2020;79:595–604; **2.** Baraliakos X. Arthritis Rheumatol 2020;72 (suppl 10).

Table 1. Safety for total exposure to BKZ across BE AGILE and the OLE

	BE AGILE Weeks 0–48			BE AGILE + OLE Weeks 0–156
n (%) [EAIR/100 PY]	BKZ 160 mg (n=149; 114.2 PY)	BKZ 320 mg (n=150; 119.6 PY)	All BKZ (N=303; 261.3 PY)	All BKZ (N=303; 781.0 PY)
Any TEAE	103 (69.1) [168.7]	122 (81.3) [221.1]	235 (77.6) [186.2]	280 (92.4) [143.5]
Serious TEAEs	5 (3.4) [4.4]	6 (4.0) [5.1]	13 (4.3) [5.1]	43 (14.2) [5.8]
Key TEAEs of special monitoring				
Serious infections	3 (2.0) [2.7]	1 (0.7) [0.8]	4 (1.3) [1.5]	10 (3.3) [1.3]
Candida infections	10 (6.7) [9.1]	9 (6.0) [7.9]	19 (6.3) [7.5]	28 (9.2) [3.8]
Inflammatory bowel disease	1 (0.7) [0.9]	2 (1.3) [1.7]	4 (1.3) [1.5]	9 (3.0) [1.2]
Anterior uveitis	1 (0.7) [0.9]	1 (0.7) [0.8]	2 (0.7) [0.8]	6 (2.0) [0.8]
Study discontinuations due to TEAEs	7 (4.7)	10 (6.7)	20 (6.6)	38 (12.5)
Drug-related TEAEs	48 (32.2)	54 (36.0)	110 (36.3)	149 (49.2)
Deaths	1 (0.7)	0	1 (0.3)	2 (0.7)

TEAEs are reported for the BE AGILE safety set for total exposure to BKZ across BE AGILE and the OLE. There was one death in BE AGILE (cardiac arrest) and one in the OLE (road traffic accident); neither was considered treatment-related.

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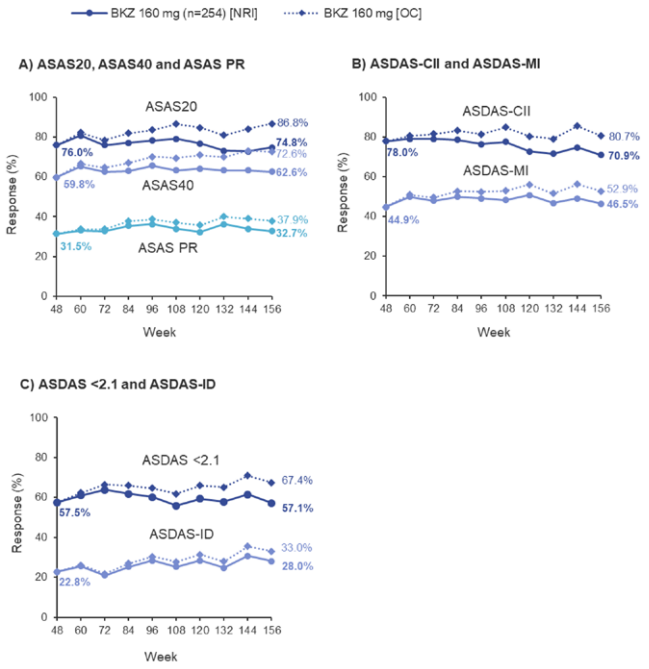
Figure. Efficacy responses from Week 48 to Week 156 (NRI and OC)



Full analysis set (N=254). Patients received BKZ 160 mg or 320 mg during the BE AGILE dose-ranging study. Missing data were imputed using NRI. ASAS: Assessment of SpondyloArthritis international Society; ASAS20/40: ASAS 20%/40% response; ASAS PR: ASAS partial remission; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-CII: ASDAS clinically important improvement (≥1.1 decrease from baseline ASDAS score); ASDAS-ID: ASDAS inactive disease (ASDAS<1.3); ASDAS-MI: ASDAS major improvement (≥2.0 decrease from baseline ASDAS score or achievement of lowest possible ASDAS score [0.6]); BKZ: bimekizumab; NRI: non-responder imputation; OC: observed case; OLE: open-label extension.

Disclosure of Interests: Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma, Employee of: Director of Imaging Rheumatology, Atul Deodhar Speakers bureau: Janssen, Novartis, Pfizer, Consultant of: AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, Gilead, GSK, Janssen, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB Pharma, Lianne S. Gensler Consultant of: AbbVie, Eli Lilly, Gilead, GSK, Novartis, Pfizer, UCB Pharma, Grant/research support from: Pfizer, Denis Poddubnyy Speakers bureau: AbbVie, BMS, Eli Lilly, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Biocad, Eli Lilly, Gilead, GSK, MSD, Novartis, Pfizer, Samsung Bioepis, UCB Pharma, Grant/research support from: AbbVie, MSD, Novartis, Pfizer, Alan Kivitz Shareholder of: Pfizer, Novartis, Speakers bureau: Amgen, Eli Lilly, Pfizer, Novartis, Consultant of: Novartis, UCB Pharma, Maxime Dougados Consultant of: AbbVie, Eli Lilly, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Eli Lilly, Novartis, Pfizer, UCB Pharma, Natasha de Peyrecave Employee of: UCB Pharma, Marga Oortgiesen Employee of: UCB Pharma, Thomas Vaux Employee of: UCB Pharma, Carmen Fleurinck Employee of: UCB Pharma, Xenofon Baraliakos Speakers bureau: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma, Paid instructor for: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma

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POS0227 SHOULD ALL PATIENTS TRIAL SUBCUTANEOUS METHOTREXATE PRIOR TO COMMENCING BIOLOGIC THERAPY – A REAL WORLD STUDY

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Background: Methotrexate (MTX) is the bed rock of inflammatory arthritis management. However intolerance is a major limiting factor for drug optimisation and retention. There is data to suggest that subcutaneous (SC) MTX is tolerated better and is now being recommended in several guidelines including ACR's. It is less clear though whether this strategy is effective in those where oral preparation is inefficacious and its potential to avoid escalation to biologic therapy.

Objectives: Our aim was to analyse the reasons for switching to SC formulation in a real world setting, clinical outcomes achieved and proportion requiring biologic prescription.

Methods: We undertook a retrospective survey of all patients prescribed SC MTX in a large university teaching hospital between 1983 and Apr 2019. We had access to full patient records including details on co-morbidities, drugs and disease management. We analysed demographics, reasons for SC MTX initiation, clinical outcomes and impact on biologic prescription.

Results: 352 patients were identified during the study period. The mean age of the cohort was 54 yrs (3-87). 192 (70%) were women. 260 (74%) were Caucasian, 64 (18%) Asian, 21 (6%) Afro-Caribbean and remaining of other ethnicity. Two most common diagnoses were RA [n=243 (69%)] and pSpA [n=66 (18%)]. Average disease duration was 74 months (11-324) with mean of three comorbidities (0-11).

284 (80%) had switched from oral to SC MTX. 137 (49%) stopped oral MTX due to side effects. Mean duration of oral MTX prior to switching was 26 months (0.25-167). Follow up period for SC MTX ranged from two to 132 months (mean 29) until the data cut-off date of Apr 2019. 103 (29%) patients progressed to biologic therapy.

Amongst RA patients, DAS28 improved from mean 4.16 (0.63-8.06) to 2.83 (0.14-7.32) following the switch. pSpA cohort's mean TJC and SJC improved from mean seven (0-42) and two (0-26) to two (0-25) and one (0-6) respectively.

Conclusion: Our study confirms that SC MTX is an effective solution irrespective of whether oral MTX is inefficacious or intolerable. This applies to people with both RA and pSpA. In accordance with prior published data, our findings support the utility of SC MTX for those intolerant of enteral option. Additionally, it shows that even in instances where oral MTX was ineffective, a switch to SC formulation achieved low disease activity despite multi-morbidity, long disease course and protracted oral MTX exposure. This intervention also prevented over two-thirds of patients progressing to biologic therapy with significant financial savings. SC MTX therefore remains a durable strategy with excellent disease outcomes and confers substantial economic benefits to healthcare.

Disclosure of Interests: None declared

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POS0228 BASELINE CHARACTERISTICS AND TREATMENT RESPONSE TO IXEKIZUMAB CATEGORISED BY SEX IN RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLARTHRITIS PATIENTS THROUGH 52 WEEKS: DATA FROM 3 PHASE III, RANDOMIZED, CONTROLLED TRIALS

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease of the axial skeleton comprising two subtypes within the same spectrum: radiographic (r-axSpA) and non-radiographic (nr-axSpA). Previous studies have shown that clinical presentation and treatment response of males and females may differ[1] despite similar disease burden.[2] Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets interleukin-17A, has demonstrated superior efficacy to placebo in the treatment of patients with r-axSpA (COAST-V/W [bDMARD- naïve/TNFi-experienced]) and nr-axSpA (COAST-X [bDMARD-naïve]).[3]

Objectives: Assess baseline characteristics and treatment response to IXE categorised by sex in patients with r-axSpA and nr-axSpA for up to 52 weeks.

Methods: Patients fulfilled the ASAS classification criteria for r-axSpA or nr-axSpA. Patients were randomized to receive 80 mg subcutaneous IXE every 2 weeks (Q2W) or 4 weeks (Q4W), or to placebo (PBO) [16 weeks COAST-V/W; 52 weeks COAST-X]. Baseline characteristics and treatment outcomes were assessed. Patients were categorised by sex, missing data was controlled for using non-responder imputation (NRI) and modified baseline observation carried forward (mBOCF) analysis was conducted on continuous efficacy variables.

Results: At baseline, females were older, with significantly higher pain and fatigue scores and peripheral joint symptoms (table 1). ASAS40 response rate with IXEQ4W was achieved in 39% of males with r-axSpA by week 16, and 44% by week 52. Females achieved 16.7% at week 16, and 33.3% at week 52. In nr-axSpA, 46% of IXEQ4W males achieved ASAS40 at week 16 and 30% at week 52. 23.9% of females achieved ASAS40 at week 16, increasing to 30.4% at week 52.

Conclusion: This analysis demonstrates that for the axSpA disease spectrum, females present with higher disease burden as reflected by higher scores in fatigue/tiredness, and spinal pain at night. Our findings indicate that males and females respond to IXE; however, females experience this benefit later in their treatment course, with a more prolonged attainment of peak response.