NIHR | Innovation Observatory

HEALTH TECHNOLOGY BRIEFING SEPTEMBER 2021

Bimekizumab for non-radiographic axial spondyloarthritis

NIHRIO ID	27169	NICE ID	10422
Developer/Company	UCB Pharma Ltd	UKPS ID	652674

Licensing and market availability plans	Currently in phase III clinical development.

SUMMARY

Bimekizumab is in clinical development for the treatment of adults with non-radiographic axial spondyloarthritis (nr-axSpA). This condition affects patients predominantly in the spine and other areas of the body and is caused by inflammation. This inflammation can lead to back pain, fatigue and in serious cases, to severe disability as the bones of the spine fuse into a fixed position or joints become progressively damaged. It is characterised by an absence of radiographic sacroiliitis which is usually seen in patients with ankylosing spondylitis (AS). AS is also known as radiographic axial spondyloarthritis (r-axSpA). A proportion of patients with nr-axSpA will progress to AS. Some patients with nr-axSpA do not respond well to current treatment options, resulting in a clear unmet medical need.

Bimekizumab is a drug administered by subcutaneous injection that neutralises the function of certain proteins that regulate immune responses, interleukin (IL)-17A and IL- 17F cytokines. Neutralizing both IL-17A and IL-17F prevents them from interacting with their receptors (targets), which reduces skin and joint inflammation as well as pathological bone formation. If licensed, bimekizumab will provide an additional targeted treatment option for adults with nr-axSpA.

PROPOSED INDICATION

Adult patients with non-radiographic axial spondyloarthritis (nr-axSpA).[1]

TECHNOLOGY

DESCRIPTION

Bimekizumab (BKZ,UCB4940) is an investigational novel humanised monoclonal IgG1 antibody that potently and selectively neutralises both IL-17A and IL-17F, two key cytokines driving inflammatory processes. IL-17A and IL-17F have similar pro-inflammatory functions and independently cooperate with other inflammatory mediators to drive chronic inflammation and damage across multiple tissues.[2] Moreover, in preclinical models, both IL-17A and IL-17F have been shown to cooperate with tumour necrosis factor (TNF) to stimulate production of key proinflammatory cytokines and amplify tissue inflammation. When compared with IL-17A blockade alone, dual neutralisation of IL-17A and IL-17F resulted in lower levels of expression of linked genes and cytokines, as well as a greater suppression of disease-relevant immune cell migration.[3]

Bimekizumab is in clinical development for the treatment of adults with non-radiographic axial spondyloarthritis (nr-axSpA). In the phase III trial, NCT03928704, patients receive 160 mg bimekizumab every 4 weeks by subcutaneous injection.[1,4]

INNOVATION AND/OR ADVANTAGES

The current NICE recommended treatments for nr-axSpA include the use of secukinumab and ixekizumab, which target IL-17A, only if the patient has responded inadequately to conventional therapy (non-steroidal anti-inflammatories (NSAIDs) or TNF-αinhibitors).[5]

Bimekizumab targets both the IL17A and IL17F, which results in greater reduction of inflammation than inhibition of IL17A alone.[6]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Bimekizumab (Bimzelx) has a marketing authorisation for plaque psoriasis in both the UK and EU.[7]

The most common side effects with bimekizumab are upper respiratory tract infections (nose and throat infection), which may affect more than 1 in 10 people, and oral candidiasis (thrush, a fungal infection in the mouth or throat).[8]

Bimekizumab is in phase III clinical development for psoriatic arthritis, hidradenitis suppurativa and ankylosing spondylitis.[9]

PATIENT GROUP

DISEASE BACKGROUND

Axial spondyloarthritis (axSpA) is an arthritis caused by the inflammation of the spine and the sacroiliac (SI) joints. There are two forms of axSpA; the most studied form of axSpA is

radiographic axSpA also known as ankylosing spondylitis (AS), which according to the modified New York criteria is characterised by sacroiliitis on radiographs. The second form of axSpA is known as nr-axSpA which is characterised by a visible inflammation on magnetic resonance imaging (MRI) of the SI joints but an absence of radiographic sacroiliitis.[10]

The main clinical manifestations include back pain and progressive spinal rigidity as well as inflammation of the hips, shoulders, peripheral joints and fingers/toes and fatigue.[11,12] The cause of nr-axSpA is still unclear, but research has shown that a majority of people with nr-axSpA carry a particular gene known as the HLA-B27. Microbial infection can act as a triggering factor of the host innate immune system and AS development.[12,13] Research has shown that many people with nr-axSpA will progress to the radiographic form of axSpA after years of disease meanwhile, others suffer from the disease for decades, sometimes for the duration of their lifetime, without any evidence of radiographic damage.[14]

Nr-axSpA tends to present in the late teens to early twenties with an average age of onset of 24 years. About 95% of people are aged less than 45 years when their symptoms start – a time of life when most people are at an important stage of their lives, looking to forge social relationships, start families and build a career.[15]

CLINICAL NEED AND BURDEN OF DISEASE

Nr-axSpA is a type of axial spondyloarthritis where x-ray changes are not present but inflammation is visible on MRI or symptoms are manifested.[15] The proportion of patients with nr-axSpA and ankylosing spondylitis (radiographic axSpA) have been found to be similar (ratio of 1:1).[16] In line with previous NICE technology appraisals, the company estimates the UK patient population range to be between 238 and 500 per 100,000.[17,18]

Almost half of people with Nr-axSpA progress to the radiographic version of the disease over a period of 8 to 10 years. People with axial spondyloarthritis report that it profoundly affects their quality of life and day-to-day activities, such as work.[19]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

There is currently no cure for nr-axSpA but there are treatments available to help alleviate the symptoms patients experience. Treatment involves physiotherapy and exercise, painkillers including NSAIDs, biological treatments, corticosteroids and disease-modifying antirheumatic drugs (DMARDs).[13,20] Biological DMARDs, which includes TNF-alpha inhibitors, are typically used when the disease has not responded adequately to conventional therapy. Interleukin 17 inhibitors are also licenced by MHRA and approved by NICE for treating nr-axSpA.[19]

CURRENT TREATMENT OPTIONS

For patients with nr-axSpA, NICE recommends the following biologics:[20,21]

- Adalimumab, certolizumab pegol and etanercept are recommended options for treating severe nr-axSpA in patients who are intolerant of, or whose disease has responded inadequately to NSAIDs.
- Secukinumab and ixekizumab are recommended as options for treating active non-radiographic axial spondyloarthritis with objective signs of inflammation only if tumour necrosis factor (TNF)-alpha inhibitors are not suitable or do not control the condition well enough.

- Golimumab is recommended, within its marketing authorisation, as an option for treating severe non-radiographic axial spondyloarthritis in adults whose disease has responded inadequately to, or who cannot tolerate, nonsteroidal anti-inflammatory drugs.

PLACE OF TECHNOLOGY

If licensed, bimekizumab will provide an additional targeted treatment option for adults with nr-axSpA.

CLINICAL TRIAL INFORMATION

Trial	**BE MOBILE 1; NCT03928704**, 2017-003064-13; A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Bimekizumab in Subjects With Active Nonradiographic Axial Spondyloarthritis **Phase III** - Recruiting **Location(s):** 9 EU countries, UK, United States and other countries. **Primary completion date:** September 2021	**BE MOVING;** NCT04436640, 2019-004163-47; A Multicenter, Open-Label Extension Study to Assess the Long-Term Safety, Tolerability, and Efficacy of Bimekizumab in the Treatment of Study Participants With Active Axial Spondyloarthritis, Ankylosing Spondylitis, and Nonradiographic Axial Spondyloarthritis **Phase III** - Enrolling by invitation **Location(s):** 9 EU countries, UK, USA, Turkey and Japan **Primary completion date:** July 2024
Trial design	Randomised, parallel assignment, quadruple masked	Open label, single group assignment
Population	N = 240 (estimated), nonradiographic axial spondyloarthritis, aged 18 years and older .	N = 485, Study participant completed NCT03928704 or NCT03928743, aged 18 years and older
Intervention(s)	Subjects will receive bimekizumab at pre-specified time-points.	Subjects will receive bimekizumab at prespecified time-points.
Comparator(s)	Subjects randomised to this arm will receive placebo during the double-blind treatment period and receive bimekizumab during the maintenance period.	None.
Outcome(s)	Primary outcome; - Assessment of SpondyloArthritis International Society 40% response criteria (ASAS40) response at Week 16 [Time Frame: Week 16] See trial record for full list of other outcomes	Primary outcomes; - Percentage of participants with treatment-emergent adverse events (TEAEs) during the study [Time Frame: From Baseline (Day 1) until Safety Follow-Up (up to Week 128)] - Percentage of participants with serious adverse events (SAEs) during the study [Time Frame: From

		Baseline (Day 1) until Safety Follow-Up (up to Week 128)] - Percentage of participants with treatment-emergent adverse Events (TEAEs) leading to withdrawal from the study [Time Frame: From Baseline (Day 1) until Safety Follow-Up (up to Week 128)] See trial record for full list of other outcomes.
Results (efficacy)	-	-
Results (safety)	-	-

ESTIMATED COST

The cost of bimekizumab is not yet known.

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal. Secukinumab for treating non-radiographical axial spondyloarthritis (TA719) July 2021.
- NICE technology appraisal. Ixekizumab for treating axial spondyloarthritis (TA718). July 2021.
- NICE technology appraisal. Golimumab for treating non-radiographic axial spondyloarthritis (TA497). January 2018.
- NICE technology appraisal. TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis (TA383). February 2016.
- NICE guideline. Spondyloarthritis in over 16s: diagnosis and management (NG65). February 2017. Last updated June 2017.
- NICE quality standard. Spondyloarthritis (QS170). June 2018.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Specialised Rheumatology Services (Adult). A13/S/a.

OTHER GUIDANCE

- NICE Clinical Knowledge Summary. Ankylosing spondylitis. May 2018.[22]
- Assessment of Spondyloarthritis International Society – European League Against Rheumatism. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. 2017.[23]

ADDITIONAL INFORMATION

REFERENCES

1 ClinicalTrials.gov. *A study to evaluate the efficacy and safety of bimekizumab in subjects with active nonradiographic axial spondyloarthritis (BE MOBILE 1). Trial ID: NCT03928704*. 2019. Status: Recruiting. Available from: https://clinicaltrials.gov/ct2/show/NCT03928704 [Accessed 10 August 2021].

2 UCB. *UCB's key pipeline molecule bimekizumab demonstrated improved outcomes for ankylosing spondylitis patients.* 2019. Available from: https://www.ucb.com/stories-media/Press-Releases/article/UCB-s-Key-Pipeline-Molecule-Bimekizumab-Demonstrated-Improved-Outcomes-for-Ankylosing-Spondylitis-Patients [Accessed 10 August 2021].

3 Papp KA MJ, Gottlieb AB, Griffiths CEM, Cross N, Peterson L, Cioffi C, Blauvelt A. Dual neutralization of both interleukin 17A and interleukin 17F with bimekizumab in patients with psoriasis: Results from BE ABLE 1, a 12-week randomized, double-blinded, placebo-controlled phase 2b trial. *Journal of the American Academy of Dermatology,*. 2018 79(2). Available from: https://doi.org/10.1016/j.jaad.2018.03.037.

4 EU Clinical Trials Register. *A phase 3, multicenter, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of bimekizumab in subjects with active nonradiographic axial spondyloarthritis. Trial ID: 2017-003064-13*. 2019. Available from: https://www.clinicaltrialsregister.eu/ctr-search/search?query=2017-003064-13 [Accessed 10 August 2021].

5 NICE. *Spondyloarthritis in over 16s: diagnosis and management [NG65].* 2017. Available from: https://www.nice.org.uk/guidance/ng65/chapter/Recommendations#pharmacological-management-of-spondyloarthritis [Accessed 10 August 2021].

6 van der Heijde D, Gensler L, Deodhar A, Baraliakos X, Poddubnyy D, Farmer M, et al. Dual neutralisation of IL-17A and IL-17F with bimekizumab in patients with active ankylosing spondylitis (AS): 12 week results from a phase 2b randomised, double-blind, placebo-controlled, dose-ranging study. *Annals of Rheumatic Disease*. 2018;77. Available from: https://ard.bmj.com/content/annrheumdis/77/Suppl_2/70.1.full.pdf.

7 National Insititute for Health and Care Excellence (NICE). *Bimekizumab for treating moderate to severe plaque psoriasis.* 2021. Available from: https://www.nice.org.uk/guidance/TA723 [Accessed 10 August 2021].

8 European Medicines Agency. *Bimzelx.* 2021. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/bimzelx [Accessed 10 August 2021].

9 Clinicaltrials.gov. *Search for: Bimekizumab | Phase 2, 3.* 2021. Available from: https://clinicaltrials.gov/ct2/results?term=Bimekizumab&age_v=&gndr=&type=&rslt=&phase=1&phase=2&Search=Apply [Accessed 10 August 2021].

10 de Koning A, Schoones JW, van der Heijde D, van Gaalen FA. Pathophysiology of axial spondyloarthritis: consensus and controversies. *European journal of clinical investigation*. 2018;48(5):e12913. Available from: https://doi.org/10.1111/eci.12913.

11 NHS. *Symptoms-Ankylosing spondylitis.* 2019. Available from: https://www.nhs.uk/conditions/ankylosing-spondylitis/symptoms/ [Accessed 10 August 2021].

12 Zhu W, He X, Cheng K, Zhang L, Chen D, Wang X, et al. Ankylosing spondylitis: etiology, pathogenesis, and treatments. *Bone research*. 2019;7(1):1-16. Available from: https://www.nature.com/articles/s41413-019-0057-8.

13 NHS. *Causes-Ankylosing spondylitis.* 2019. Available from: https://www.nhs.uk/conditions/ankylosing-spondylitis/causes/ [Accessed 10 August 2021].

14 Slobodin G, Eshed I. Non-radiographic axial spondyloarthritis. *Isr Med Assoc J*. 2015;17(12):770-6. Available from: https://pubmed.ncbi.nlm.nih.gov/26897981/.

15 National Axial Spondyloarthritis Society. *Facts & Figures.* 2021. Available from: https://nass.co.uk/about-as/as-facts-and-figures/ [Accessed 10 September 2021].

16 Baraliakos X, Braun J. Non-radiographic axial spondyloarthritis and ankylosing spondylitis: what are the similarities and diffierences? *RMD Open*. 2015;1. Available from: https://doi.org/10.1136/rmdopen-2015-000053.
17 Braun J, Bollow M, Remlinger G, Eggens U, Rudwaleit M, Distler A, et al. Prevalence of spondylarthropathies in HLA-B27 positive and negative blood donors. *Arthritis & Rheumatism*. 1998;41(1):58-67. Available from: https://doi.org/10.1002/1529-0131(199801)41:1<58::AID-ART8>3.0.CO;2-G.
18 Dean LE, Jones GT, MacDonald AG, Downham C, Sturrock RD, Macfarlane GJ. Global prevalence of ankylosing spondylitis. *Rheumatology*. 2013;53(4):650-7. Available from: https://doi.org/10.1093/rheumatology/ket387.
19 National Insititute for Health and Care Excellence (NICE). *Final appraisal document – secukinumab for treating non-radiographic axial spondyloarthritis.* 2021. Available from: https://www.nice.org.uk/guidance/ta719/documents/final-appraisal-determination-document [Accessed 10 September 2021].
20 NICE Pathways. *Managing spondyloarthritis in adults.* 2021. Available from: https://pathways.nice.org.uk/pathways/spondyloarthritis#path=view%3A/pathways/spondyloarthritis/managing-spondyloarthritis-in-adults.xml [Accessed 10 September 2021].
21 NICE treatment summaries. *Spondyloarthritis.* Available from: https://bnf.nice.org.uk/treatment-summary/spondyloarthritis.html [Accessed 10 September 2021].
22 NICE Clinical Knowledge Summary. *Ankylosing spondylitis.* 2019. Available from: https://cks.nice.org.uk/ankylosing-spondylitis#!topicSummary [Accessed 10 September 2021].
23 Van der Heijde D, Ramiro S, Landewe R, Baraliakos X, Van den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Annals of the Rheumatic Diseases*. 2016;76:978 - 91. Available from: https://doi.org/10.1136/annrheumdis-2016-210770.

NB: This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.