National Institute for Health Research

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Risankizumab (by subcutaneous injection) for active psoriatic arthritis after inadequate control or intolerance to conventional drugs

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LAY SUMMARY

Psoriatic Arthritis (PsA) is a type of arthritis mainly affecting the joints which develops in people who have psoriasis. PsA may cause pain, swelling and stiffness in the joints, most commonly the hands feet and back. The disease comes in 'flares', where symptoms get worse, followed by periods of 'remission' where symptoms ease. The cause of psoriatic arthritis is not known but it is thought that family history and having a previous infection or injury may increase the chances of developing it.

Risankizumab is a drug which is injected into the skin. It works in a unique way by blocking an important molecule in inflammation from a process which allows the body's immune cells (specifically T-cells) to activate other immune cells and release substances which cause inflammation (cytokines). Risankizumab is currently being trialled in a range of diseases involving the immune system including plaque psoriasis, psoriatic arthritis and Crohn's disease. If licensed, risankizumab will offer an additional treatment option for patients with active psoriatic arthritis which is not adequately controlled by the drugs offered in the existing treatment pathway.

TARGET GROUP

Psoriatic arthritis (active) – after inadequate response to NSAIDs, conventional synthetic DMARDs or anti-TNF drugs.

TECHNOLOGY

DESCRIPTION

Risankizumab (ABBV066) is an anti-IL23 antibody which binds to the p19 subunit of IL23, preventing receptor activation and thereby disrupting the IL23/Th17 axis. This may be important in the treatment of psoriatic arthritis as the processes of inflammation occurring in psoriatic arthritis is thought to be similar to that occurring in the skin during psoriasis which involves the release of cytokines, including IL23, in the lymph nodes by activated dendritic cells which then activate type 1 and type 17 T helper cells, which perpetuate a cycle of inflammation.[1, 4] Risankizumab is intended for the treatment of several inflammatory diseases, including psoriasis arthritis.

In the phase III trial risankizumab is administered by subcutaneously 90mg/ml.[2]

Risankizumab does not currently have Marketing Authorisation in the EU for any indication.

Risankizumab is currently in phase III trials for plaque psoriasis and Crohn's disease and in phase II for psoriatic arthritis.

INNOVATION and/or ADVANTAGES

If licensed, risankizumab will offer an additional treatment option for patients with active psoriatic arthritis which is not adequately controlled by the drugs offered in the existing treatment pathway (NSAIDs, conventional synthetic DMARDs and biological agents including TNFα inhibitors).

DEVELOPER

AbbVie and Boehringer Ingelheim Ltd

PATIENT GROUP

BACKGROUND

Psoriatic arthritis is a type of inflammatory arthritis which affects the joints and connective tissues associated with psoriasis of the skin or nails. Psoriatic arthritis is a progressive disorder ranging from mild synovitis to severe progressive erosive arthropathy. It may cause pain, swelling and stiffness of the joints, most commonly the hands, feet, knees, neck, spine and elbows. Like psoriasis, psoriatic arthritis follows a relapsing-remitting course of flares and remission and the severity of the symptoms and joints affected can vary between people and even between flares. A characteristic feature of psoriasis includes enthesitis (inflammation of the entheses – the place where tendons and ligament join to the bones).[3, 11]

The cause of psoriatic arthritis is not known although it is thought there is a genetic contribution as 40% people with psoriatic arthritis have a family member with psoriasis or arthritis. It has also been

suggested that psoriatic arthritis may be triggered by an infection or injury or environmental factors.[3, 4]

About a third of people with psoriatic arthritis will have a mild form of the disease which will remain stable over time. Others may have more severe symptoms requiring longer term treatment. The severity of the arthritis does not depend on the severity of the person's psoriasis and someone with mild psoriasis may have severe arthritis (and vice versa).[5] Having psoriatic arthritis can cause symptoms which affect quality of life such as fatigue, anaemia and mood changes.[3]

CLINICAL NEED and BURDEN OF DISEASE

The prevalence of psoriasis in the UK population is estimated at 2%-3% of which 5-7% of people will develop psoriatic arthritis. The prevalence of psoriatic arthritis in the UK is estimated at 0.1-0.3% (50,000 to 156,000 people) of the general population. At least 20% of people with psoriasis have severe psoriatic arthritis with progressive joint lesions. Around 60% of people with psoriatic arthritis will have psoriasis when diagnosed, 25% will be diagnosed with psoriatic arthritis before psoriasis and in 15%, psoriatic arthritis and psoriasis will occur simultaneously.[6]

According to 2016-2017 HES data, there were 25,813 people (11,652 males and 14,158 females) diagnosed with arthropathic psoriasis (ICD 10 L40.5) 4,051 admissions and 4,201 finished consultant episodes for arthropathic psoriasis (ICD 10 L40.5).[7]

The severity of psoriatic arthritis can range from mild to severe and despite improvement on conventional synthetic DMARD medication, up to 47% people will develop joint damage which is visible on radiograph by 2 years. People with psoriatic arthritis also have 60% higher risk of mortality and a 3 year decreased life expectancy compared to the general population.[8]

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE Technology appraisal guidance in development. Psoriatic arthritis (moderate to severe) – leflunomide (ID391). Expected publication date TBC.
- NICE Technology appraisal guidance in development. Tofacitinib for treating active psoriatic arthritis following disease-modifying anti-rheumatic drugs (ID1220). Expected publication date TBC.
- NICE Technology appraisal guidance in development. Abatacept for treating active psoriatic arthritis after DMARDs (ID993). Expected publication date 25 July 2018.
- NICE Technology appraisal guidance. Certolizumab pegol and Secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs (TA445). May 2017.
- NICE Technology appraisal guidance. Ustekinumab for treating active psoriatic arthritis (TA340). March 2017.
- NICE Technology appraisal guidance. Apremilast for treating active psoriatic arthritis (TA433). February 2017.
- NICE Technology appraisal guidance. Golimumab for the treatment of psoriatic arthritis (TA220). April 2011.

- NICE Technology appraisal guidance. Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (TA199). August 2010.

NHS ENGLAND and POLICY GUIDANCE

- NHS England. 2013/14 NHS Standard Contract Specialised Orthopaedics (Adults). D10/S/a
- NHS England. 2013/14 NHS Standard Contract Specialised Dermatology Services (All Ages). A12/S/a

OTHER GUIDANCE

- European League Against Rheumatism (EULAR). European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. 2015.
- British Society of Rheumatology (BSR). The 2012 BSR and BHPR guideline for the treatment of psoriatic arthritis with biologics. October 2013.
- Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of psoriasis and psoriatic arthritis in adults (121). October 2010.

CURRENT TREATMENT OPTIONS

As a type of spondyloarthritis (a family of inflammatory arthritic diseases), the treatment pathway for psoriatic arthritis follows the general treatment pathway for spondyloarthritis.[9, 10]

The main aim in the treatment of psoriatic arthritis is to relive symptoms, slow disease progression and improve quality of life.[11] Treatments include a mixture of drug therapies for arthritic symptoms, skin treatments and surgery:[10, 11, 12]

1. Drug Therapies:
    - Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) – (e.g. ibruprofen, diclofenac, naproxen) lowest effective dose for pain relief. If the maximum dose is ineffective after 2-4 weeks it is recommended to switch to a different NSAID. Should be prescribed with a proton pump inhibitor (e.g. omeprazole) to prevent side effects on GI tract.
    - Corticosteroids – injection or oral to rescue joint inflammation and pain.
    - Disease-modifying anti-rheumatic drugs (DMARDs) – used to prevent disease progression. Can be taken in combination with NSAIDs or several DMARDs can be use at once.
        - Leflunomide – first line
        - Sulfasalazine or methotrexate – second line
    - Biological Therapies – offered to those who have not responded to at least two different DMARDs, including:
        - TNFα inhibitors: adalimumab, Apremilast, certolizumab pegol, etanercept, golimumab, infliximab
        - IL-17 inhibitor: Secukinumab
        - IL-12/IL-23 inhibitor: ustekinumab – not NICE recommended
2. Skin Treatments:
    - Topical treatments:
        - Tar based ointments
        - Dithranol ointment
        - Steroidal creams and lotions

    - Vitamin D ointments: calcipotriol and tacalcitol
    - Vitamin A like gels: e.g. tazarotene
- Phototherapy
- Methotrexate tablets/injections

3. Surgery: Surgery is mostly unnecessary in people with psoriatic arthritis but may be needed to repair damaged tendons or joints (joint replacement surgery).

EFFICACY and SAFETY		
Trial	NCT02719171, EudraCT-2015-003625-34, 2015-003625-34, JapicCTI-163225, 1311.5; risankizumab vs placebo; phase II	NCT02986373; EudraCT-2016-003113-94; 2016-003113-94; risankizumab only; phase II extension
Sponsor	AbbVie and Boehringer Ingelheim	AbbVie
Status	published in abstract	ongoing – not recruiting
Source of Information	abstract[13], trial registry[14]	trial registry[2]
Location	8 EU countries (not incl UK), USA, Canada, Japan and Taiwan	6 EU countries (not incl UK), USA, Canada, Japan and Taiwan
Design	Randomised, placebo-controlled, double blinded, parallel assignment	Open label, uncontrolled
Participants	n=185; aged 18 years and older; psoriatic arthritis; inadequately controlled by standard doses of non-steroidal anti-inflammatory drugs (NSAIDs) administered for >4 weeks, disease modifying anti-rheumatic drugs (DMARDs) administered for >3 months or tumour necrosis factor (TNF) inhibitors	n=185 (planned); aged 18-99 years; completed all doses of the study drug and week 24 of study 1311.5
Schedule	Randomised to receive one of five study arms: 1. Risankizumab – high dose 2. Risankizumab – medium/high dose 3. Risankizumab – medium dose 4. Risankizumab – low dose 5. Placebo	All participants receive subcutaneous injection of 90mg/ml risankizumab
Follow-up	Not reported	Not reported
Primary Outcomes	American College of Rheumatology (ACR) 20 response at Week 16	Adverse Events at 52 wks
Secondary Outcomes	• Change in Tender Joint Count: baseline to wk 16 • Change in Swollen Joint Count: baseline to wk 16 • Change in Dactylitis Count: baseline to wk 16 • American College of Rheumatology (ACR) 50 response at wk 16	• American College of Rheumatology 20 Response (ACR20) at 52 wks • Change from Baseline in Modified Total Sharp Score (mTSS) at 48 wks

	• American College of Rheumatology (ACR) 70 response at wk 16 • Change in Health Assessment Questionnaire-Disability Index (HAQ-DI): baseline to wk 16 • Change in Short Form-36 Health Survey (SF-36): baseline to wk 16 • Change in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index: baseline to wk 16 • Change in modified Nail Psoriasis Severity Index (mNAPSI): baseline to wk 16 • Psoriasis Area and Severity Index (PASI) 90 response: baseline to wk 16	
Key Results	185 people were recruited into the study and 172 (93%) completed 16 wks treatment: n=42 in arm 1, n=42 in arm 2, n=39 in arm 3, n=20 in arm 4, n=84 in arm 1 +2 and n=42 in arm 5. The median age was 51 years and 43.2% (n=80) participants were female. At 16 weeks, the primary endpoint (ACR20) was 57.1, 61.9, 59.0, 65.0, 59.5 and 35.7 in arms 1, 2, 3, 4, 1+2 and 5 (placebo) respectively. Arms 1, 3 and 4 were significantly different in primary outcome compared to placebo by p= <0.05 and arms 2 and 1+2 were significant different compared to placebo by p=<0.01.	-
Adverse effects (AEs)	AEs were experienced by 64.3% (n=27), 52.4% (n=22), 69.2% (n=27), 60.0% (n=12) and 69.0% (n=29) of participants in arm 1, 2, 3, 4 and 5 respectively. Of these 19.0% (n=8), 16.7% (n=7), 17.9 (n=7), 20.0% (n=4) and 19.0% (n=8) were drug related AEs in arm 1, 2, 3, 4 and 5 respectively.	-
Expected reporting date	-	Primary outcome measure: 8 July 2018

ESTIMATED COST and IMPACT

COST

The cost of risankizumab is not yet known.

IMPACT – SPECULATIVE

IMPACT ON PATIENTS AND CARERS

☐ Reduced mortality/increased length of survival

☒ Reduced symptoms or disability

☐ Other

☐ No impact identified

IMPACT ON HEALTH and SOCIAL CARE SERVICES

☐ Increased use of existing services

☐ Decreased use of existing services

☐ Re-organisation of existing services

☐ Need for new services

☒ Other: facilities to administer regular subcutaneous injections

☐ None identified

IMPACT ON COSTS and OTHER RESOURCE USE

☐ Increased drug treatment costs

☐ Reduced drug treatment costs

☒ Other increase in costs: *additional staff training required, additional costs for subcutaneous administration in clinic*

☒ Other reduction in costs: *reduced need for interventional procedures*

☐ Other

☐ None identified

OTHER ISSUES

☐ Clinical uncertainty or other research question identified

☒ None identified

REFERENCES

[1] Campa M, Mansouri B, Warren R and Menter A. *A Review of Biologic Therapies Targeting IL-23 and IL-17 for Use in Moderate-to-Severe Plaque Psoriasis*. Dermatol Ther. (2016) Mar; 6(1): 1–12.

[2] ClinicalTrials.gov. *A Study to Investigate Safety With Risankizumab in Psoriatic Arthritis Subjects Who Have Completed Week 24 Visit of Study 1311.5*. Available from: https://clinicaltrials.gov/ct2/show/NCT02986373. [Accessed 13 November 2017]. Last Updated 13 October 2013.
[3] American College of Rheumatology. *Psoriatic Arthritis.* Available from: https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Psoriatic-Arthritis. [Accessed 14 November 2017].
[4] Arthritis UK. *What causes psoriatic arthritis?* Available from: https://www.arthritisresearchuk.org/arthritis-information/conditions/psoriatic-arthritis/causes.aspx. [Accessed 14 November 2017].
[5] Arthritis UK. *What is the outlook for psoriatic arthritis?* Available from: https://www.arthritisresearchuk.org/arthritis-information/conditions/psoriatic-arthritis/outlook.aspx. [Accessed 14 November 2017].
[6] NICE Health Technology Appraisal. *Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (review of TA104 and TA125) – Final scope.* May 2009. Available from: https://www.nice.org.uk/guidance/ta199/documents/psoriatic-arthritis-etanercept-infliximab-golimumab-and-adalimumab-review-final-scope2. [Accessed 14 November 2017].
[7] NHS Digital. *Hospital Admitted Patient Care Activity, 2016-17*. Available from: http://digital.nhs.uk/catalogue/PUB22378 [Accessed 23 October 2017]
[8] NICE. *Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (TA199).* August 2010. Available from: https://www.nice.org.uk/guidance/ta199/chapter/2-Clinical-need-and-practice. [Accessed 14 November 2017].
[9] American College of Rheumatology. *Spondyloarthritis.* Available from: https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Spondyloarthritis. [Accessed 14 November 2017].
[10] NICE Treatment Pathways. *Spondyloarthritis.* Available from: https://pathways.nice.org.uk/pathways/spondyloarthritis. [Accessed 14 November 2017].
[11] NHS Choices. *Psoriatic arthritis*. Available from: https://www.nhs.uk/conditions/psoriatic-arthritis/#treating-psoriatic-arthritis. [Accessed 14 November 2017].
[12] Arthritis UK. *What treatments are there for psoriatic arthritis?* Available from: https://www.arthritisresearchuk.org/arthritis-information/conditions/psoriatic-arthritis/treatments.aspx. [Accessed 14 November 2017].
[13] 2017 American College Of Rheumatology (ACR/ARHP) Annual Meeting November 03 - 08, 2017, San Diego, USA. *Efficacy and Safety Results from a Phase 2 Trial of Risankizumab, a Selective IL-23p19 Inhibitor, in Patients with Active Psoriatic Arthritis*. Available from: https://plan.core-apps.com/tristar_acr17/abstract/b0ea96524600b0e597fbd53f02e23792. [Accessed 13 November 2017].
[14] ClinicalTrials.gov. *BI 655066/ABBV-066/Risankizumab Compared to Placebo in Patients With Active Psoriatic Arthritis - NCT02719171.* Available from: https://clinicaltrials.gov/ct2/show/NCT02719171. [Accessed 13 November 2017]. Last Updated 8 September 2017.