National Institute for Health Research

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Risankizumab (by subcutaneous injection) for moderate to severe chronic plaque psoriasis

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LAY SUMMARY

Plaque psoriasis is a skin disease causing red, flaky and itchy patches of skin commonly appearing on the elbows, knees, scalp and lower back. Plaque psoriasis is an autoimmune disease, meaning that the immune cells which usually fight infection attack the body's own tissues instead, in this case the skin. The damage caused by the immune cells causes more skin cell to be made, making these patches of skin appear. People with plaque psoriasis can encounter many problems due to their illness including physical health-related problems, problems with mood and impacts on finances and socializing.

Risankizumab is a drug which is injected into the skin. It works in a unique way by blocking a specific process which allows the body's immune cells (specifically T-cells) from attacking and damaging the skin. Risankizumab is currently being trialled in a range of diseases involving the immune system including Crohn's disease, and psoriatic arthritis. If licensed, risankizumab will offer an additional treatment option for people with chronic moderate to severe plaque psoriasis.

TARGET GROUP

Plaque psoriasis (chronic, moderate to severe)

TECHNOLOGY

DESCRIPTION

Risankizumab (ABBV066) is an anti-IL23 antibody which binds to the p19 subunit of cytokine IL23, preventing receptor activation and thereby disrupting the IL23/Th17 axis.[1] The disruption of this pathway in plaque psoriasis may be important as it is thought that the pathogenesis of plaque psoriasis 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. These T helper and other immune cells release further cytokines, including IL17, which activate keratinocytes and initiate a cycle of inflammation.[2] Risankizumab is intended for the treatment of several inflammatory diseases, including plaque psoriasis.

In the phase III trial risankizumab is administered by subcutaneously at 90mg/ml.[9]

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 is in phase II trials for psoriatic arthritis.

INNOVATION and/or ADVANTAGES

If licensed, risankizumab will offer an additional treatment option for people with chronic moderate to severe plaque psoriasis. This drug has the potential to offer advantages over other current treatment options for this indication as it targets the IL23/Th17 axis thought to be important in the pathogenesis of plaque psoriasis.[3]

DEVELOPER

AbbVie and Boehringer Ingelheim Ltd.

PATIENT GROUP

BACKGROUND

Plaque psoriasis is the most common type of psoriasis, making up approximately 90% of cases.[3] The disease follows a relapsing-remitting course and is characterised by dry red skin lesions (called plaques) covered in silver scales which commonly appear on the elbows, knees, scalp and lower back. The plaques can be itchy and sore and in severe cases the skin may crack and bleed.[4]

Plaque psoriasis is thought to occur when skin cells are replaced more quickly than usual, resulting in the build-up of immature skin cells on the surface of the skin (causing the development of plaques). The cause of this overproduction of skin cells is thought to have an autoimmune origin when T-cells attack healthy skin cells instead of pathogens, causing the deep skin layers to produce new skin cells

more quickly than usual. This in turn further triggers the immune system to produce more T-cells and so perpetuates a cycle of inflammation.

What first triggers the inflammatory process is currently not known and is thought to be a complex mix of factors including: genetic susceptibility, skin injury, excessive alcohol consumption, smoking, stress, hormonal changes (e.g. puberty or menopause), certain medicines (e.g. lithium, antimalarial medicines, anti-inflammatory medicines, ACE inhibitors and beta blockers), throat inflections and other immune disorders.[5]

For most people, plaque psoriasis is managed in primary care but up to 60% people will require a specialist referral at some point.[3] For many people with plaque psoriasis there can be functional, psychological and social impacts resulting from reduced employment and income, problems related to treatments, psoriatic arthritis and the stigma attached to having a visible skin disease.[3]

CLINICAL NEED and BURDEN OF DISEASE

The prevalence of psoriasis in the UK is estimated at 1.3%-2.2% (up to 1.8 million people) of the population of which approximately 90% of cases are plaque psoriasis.[3 6]

According to the 2016-2017 HES data, there was 1,314 admissions, 3,189 bed days and 1,422 finished consultant episodes for plaque psoriasis in the UK.[7]

The impact of plaque psoriasis on quality of life can range from mild to severe and can carry with it a physical, emotional and social burden. Skin lesions can be unsightly, painful and itchy and between 1.3% and 34.7% of people with psoriasis will develop psoriatic arthritis which can lead to joint deformation and disability. People with psoriasis are also at increased risk of developing other comorbidities such as cardiovascular disease, inflammatory bowel disease (IBD) and depression. Subsequent impacts on employment and treatment expenses mean increased financial impacts.[8]

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE Technology appraisal guidance in development. Tildrakizumab for treating moderate to severe plaque psoriasis (ID1060). Expected publication date TBC.
- NICE Technology appraisal guidance in development. Guselkumab for treating moderate to severe plaque psoriasis (ID A10232). Expected publication date TBC.
- NICE Technology appraisal guidance in development. Certolizumab pegol for treating moderate to severe plaque psoriasis (ID1232). Expected publication date TBC.
- NICE Technology appraisal guidance in development. Brodalumab for treating moderate to severe plaque psoriasis (ID878). Expected publication date 30 May 2018.
- NICE Technology appraisal guidance. Dimethyl fumarate for treating moderate to severe plaque psoriasis (TA475). September 2017.
- NICE Technology appraisal guidance. Ixekizumab for treating moderate to severe plaque psoriasis (TA442). April 2017.
- NICE Technology appraisal guidance. Apremilast for treating moderate to severe plaque psoriasis (TA419). November 2016.

- NICE Technology appraisal guidance. Secukinumab for treating moderate to severe plaque psoriasis (TA350). July 2015.
- NICE Clinical guideline. Psoriasis: assessment and management (CG153). September 2017.
- NICE Quality standard. Psoriasis (QS40). August 2013.
- NICE Technology appraisal guidance. Ustekinumab for the treatment of adults with moderate to severe psoriasis. TA180. September 2009
- NICE Technology appraisal guidance. Adalimumab for the treatment of adults with moderate to severe psoriasis (TA146). June 2008

NHS ENGLAND and POLICY GUIDANCE

- NHS England. 2013/14 NHS Standard Contact for Specialised Dermatology Services (All ages). A12/S/a.

OTHER GUIDANCE

- National Psoriasis Foundation. *From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis.* 2017

CURRENT TREATMENT OPTIONS

Current treatment options for psoriasis can be categorised into three main groups, which are often used in combination: topical, phototherapy and systemic. Topical treatments are generally first line therapies, second line therapies include phototherapy and systemic non-biological therapies and third line therapies include systemic biological therapies.[3]

- Topical therapies – first line (also seconemicizumab d line in combination with phototherapy or systemic therapy)
    - Treatments for the trunk and limbs:
        - Initial treatment: Potent corticosteroid once daily plus vitamin D once daily for up to 4 weeks
        - Subsequent treatment: Vitamin D applied twice daily (8-12 weeks)
        - Subsequent treatment: potent corticosteroid twice daily for 4 weeks OR coal tar preparation applied once-twice daily OR calcipotriol monohydrate and betamethasone dispropionate once daily for 4 weeks.
    - Treatment of the scalp:
        - Initial treatment: potent corticosteroid applied once daily for 4 weeks.
        - Subsequent treatment: alternative formulation of corticosteroid (e.g. shampoo) and/or topical agents to remove adherent scale (e.g. agents containing salicylic acid, emollients and oils) before application of the corticosteroid.
        - Subsequent treatment: calcipotriol monohydrate and betamethasone dispropionate once daily for 4 weeks OR vitamin D once daily (only in those who can't use corticosteroids and with mild to moderate scalp psoriasis).
        - Subsequent treatment: very potent corticosteroid twice daily for two weeks (adults only) OR coal tar applied once or twice daily
    - Treatment of the face, flexures and genitals:

        - Short term mild-moderate potency corticosteroids applied twice daily for a maximum of 2 weeks
        - Subsequent treatment: Calcineurin Inhibitors applied twice daily for up to 4 weeks
- Phototherapy – second line therapy. Phototherapy should be used in combination with topical treatments in people with inadequate response to phototherapy alone and should not be used routinely as a maintenance treatment.
    - UVB Light Therapy – two to three times per week. For those with plaque psoriasis that can't be controlled with topical treatments
    - PUVA (local ultraviolet A irradiation)
- Systemic Therapy (non-biologic) – second line. These therapies should be offered to people whose disease is not controlled by topical treatments and has significant impact on physical, psychological or social wellbeing and extensive psoriasis (more than 10% of body surface) OR associated with functional impairment or high levels of distress OR phototherapy has been ineffective or cannot be used.
    - Methotrexate – first choice (switch to Ciclosporin if response is inadequate). Incremental dosing (starting with 5-10mg dose once per week and gradually increasing to 25mg per week for up to 3 months).
    - Ciclosporin – first choice for those who need short term disease control or who are considering conception (switch to Ciclosporin if response is inadequate). Incremental dosing (starting with 2.5-3mg/kg a day and escalate to 5mg/kg a day after four weeks if no response).
    - Acitretin – if methotrexate and Ciclosporin are inappropriate/have failed. Incremental doing to achieve a target dose of 25mg per day with dose escalation to a maximum of 50mg daily (when no other treatment options are available).
- Systemic Therapy (biologic) – Third line. Offered to people with severe plaque psoriasis which has not responded to non-biologic systemic therapies and phototherapy or in people who have contraindications to these treatments.
    - Adalimumab – initial dose of 80mg followed by 40mg given every other week starting one week after the initial dose. Continued therapy beyond 16 weeks should be carefully reconsidered in a patient not responding. Beyond 16 weeks, patients with inadequate response may benefit from an increase in dosing frequency to 40mg every week. If adequate response after the increase in dosing frequency, the dose may be subsequently be reduced to 40mg every other week.
    - Etanercept – administered up to 25mg twice weekly. Treatment should be discontinued in those who have not responded adequately at 12 weeks.
    - Infliximab – administered as an initial dose of 5mg/kg infusion over 2 hours, followed by an additional 5mg/kg infusion at 2 and 6 weeks after the initial dose then every 8 weeks after. Treatment should be discontinued in those who have not responded adequately at 10 weeks.
    - Ixekizumab – Administered by subcutaneous injection at an initial dose of 160mg followed by 80mg dose every 2 weeks until 12 weeks. Treatment should be discontinued in those who have not responded adequately at 12 weeks.
    - Secukinumab - Administered by subcutaneous injection at an initial dose of 300mg on week 0, 1, 2 and 3, followed by a monthly maintenance dose. Treatment should be discontinued in those who have not responded adequately at 12 weeks.
    - Ustekinumab – Administered subcutaneously at week 0, 4 and then every 12 weeks. The recommended dose is 45mg for those ≤100kg and 90mg for those >100kg.

Treatment should be discontinued in those who have not responded adequately at 16 weeks.

EFFICACY and SAFETY	
Trial	UltIMMA, ltMMa-1, NCT02684370, EudraCT-2014-005117-23; M16-008; JapicCTI-163246; adults > 18 years old; risankizumab vs ustekinumab vs placebo; phase III
Sponsor	AbbVie Inc.
Status	complete but unpublished
Source of Information	Trial registry[9]
Location	3 EU countries (not UK), USA, Canada, Australia, Japan and South Korea
Design	Randomised, placebo and active controlled, double blind, parallel assignment
Participants	n=500; aged >18 years; stable moderate to severe chronic plaque psoriasis with or without psoriatic arthritis; candidates for systemic therapy
Schedule	Randomised to one of 3 study arms: 1. Subcutaneous injection of 90mg Risankizumab 2. Subcutaneous injection of 80mg ustekinumab 3. Placebo
Follow-up	Not reported
Primary Outcomes	Achievement of >= 90% reduction from baseline Psoriasis Area and Severity Index (PASI) score (PASI 90) at Week 16 Achievement of a static Physician Global Assessment (sPGA) score of clear or almost clear at Week 16
Secondary Outcomes	Achievement of a Dermatology Life Quality Index (DLQI) score of 0 or 1 at Week 16 Achievement of >= 75% reduction from baseline Psoriasis Area and Severity Index (PASI) score (PASI 75) at Week 12 Achievement of a static Physician Global Assessment (sPGA) score of clear or almost clear at Week 12 Achievement of 100% reduction from baseline Psoriasis Area and Severity Index (PASI) score (PASI 100) at Week 16 and Week 52 Achievement of >= 90% reduction from baseline Psoriasis Area and Severity Index (PASI) score (PASI 90) at Week 52 Change from baseline in psoriasis symptoms evaluated using the total score on the Psoriasis Symptoms Scale (PSS) at week 16 Achievement of total score on the Psoriasis Symptoms Scale (PSS) of 0 at week 16
Key Results	Not reported
Adverse effects (AEs)	Not reported

Expected reporting date	Not reported

Trial	NCT02694523, EudraCT-2015-003623-65; adults > 18 years old; risankizumab vs adalimumab; phase III
Sponsor	AbbVie Inc.
Status	complete but unpublished
Source of Information	Trial registry[10]
Location	7 EU countries (not UK), USA, Canada, Mexico and Taiwan
Design	Randomised, active controlled, double blind, parallel assignment
Participants	n=605; aged >18 years; stable moderate to severe chronic plaque psoriasis with or without psoriatic arthritis; candidates for systemic therapy
Schedule	Randomised to one of 2 study arms: 1. Subcutaneous injection of 90mg/ml Risankizumab with matching adalimumab placebo 2. Subcutaneous injection of adalimumab with matching risankizumab placebo
Follow-up	Not reported
Primary Outcomes	Achievement of >=90% reduction from baseline Psoriasis Area and Severity Index (PASI) score (PASI 90) at Week 16 Achievement of a static Physician Global Assessment (sPGA) score of clear or almost clear at Week 16
Secondary Outcomes	Achievement of >=75% reduction from baseline PASI score (PASI 75) at Week 16 Achievement of 100% reduction from baseline PASI score (PASI 100) at Week 16 Achievement of >=90% reduction from baseline PASI score (PASI 90) at Week 44 for those patients who were re-randomized at Week 16 Achievement of an sPGA score of clear or almost clear (0 or 1) at Week 44 Achievement of sPGA score of clear (0) at Week 44
Key Results	Not reported
Adverse effects (AEs)	Not reported
Expected reporting date	Not reported

Trial	ultIMMA2, NCT02684357, EudraCT-2015-003622-13, 2015-003622-13; risankizumab plus placebo vs. ustekinumab plus placebo vs placebo, phase III
Sponsor	AbbVie Inc.
Status	published in abstract

Source of Information	Press release[11], trial registry[12]
Location	7 EU countries (not incl UK), USA, Canada, Mexico
Design	Randomised, placebo-controlled, active-controlled
Participants	n=500; aged 18 years and older; diagnosis of chronic plaque psoriasis (with or without psoriatic arthritis); moderate to severe; candidates for systemic therapy or phototherapy; candidate for treatment with ustekinumab
Schedule	Randomised to one of 3 treatment arms: 1. Risankizumab (90mg/ml subcutaneously) plus ustekinumab placebo 2. Ustekinumab (90mg/ml subcutaneously) plus risankizumab placebo 3. Risankizumab placebo plus ustekinumab placebo
Follow-up	Active treatment duration not stated. Follow up at 16 and 52 weeks.
Primary Outcomes	•Achievement of >= 90% reduction from baseline Psoriasis Area and Severity Index score (PASI 90) at Week 16 •Achievement of a static Physician Global Assessment (sPGA) score of clear or almost clear at Week 16
Secondary Outcomes	•Achievement of a Dermatology Life Quality Index (DLQI) score of 0 or 1 at Week 16 •Achievement of >= 75% reduction from baseline Psoriasis Area and Severity Index score (PASI 75) at Week 16 •Achievement of a static Physician Global Assessment (sPGA) score of clear or almost clear at Week 52 •Achievement of Psoriasis Area and Severity Index score 75% (PASI 75) at Week 52 •Achievement of >= 75% reduction from baseline Psoriasis Area and Severity Index score (PASI 75) at Week 12 •Achievement of a static Physician Global Assessment (sPGA) score of clear or almost clear at Week 12 •Achievement of 100% reduction from baseline Psoriasis Area and Severity Index score (PASI 100) at Week 16 •Achievement of >= 90% reduction from baseline Psoriasis Area and Severity Index score (PASI 90) at Week 52 •Achievement of 100% reduction from baseline Psoriasis Area and Severity Index score (PASI 100) at Week 52 •Change from baseline in psoriasis symptoms evaluated using the total score on the Psoriasis Symptom Diary (PSS) at week 16

	•Achievement of total score on the Psoriasis Symptom Diary (PSS) of 0 at week 16
Key Results	Risankizumab was significantly effective at producing 90% improvement in PAS90 and sPGA at week 16 compared to placebo (<0.001) and ustekinumab (0.001). It can therefore be inferred the drug met its primary endpoints. Risankizumab was also significantly effective at producing sPGA score of clear/almost clear at 16 weeks compared to ustekinumab (p<0.001) and placebo (<0.001). PASS 100 score was also significantly different between the risankizumab group at week 16 and at 1 year compared to ustekinumab (p<0.001 and p<0.001 respectively) and placebo (p<0.001 and p<0.001 respectively).[11]
Adverse effects (AEs)	Serious adverse events were experienced by n=2, n=3 and n=1 in the risankizumab, ustekinumab and placebo respectively at 16 weeks and by n=7, n=7 and n=0 in the risankizumab, ustekinumab and placebo respectively at 12 months. Once participant receiving risankizumab died from sudden cardiac arrest at 101 days after the last dose of the drug and a second subject in the risankizumab group died at 161 days after the last dose due to an unknown cause of death.[11]
Expected reporting date	-

Trial	IMMvent, NCT02694523, EudraCT-2015-003623-65, 2015-003623-65; Risankizumab plus placebo vs. Adalimumab plus placebo; phase III
Sponsor	AbbVie Inc.
Status	Published in abstract
Source of Information	Press Release[11], trial registry[13]
Location	7 EU counties (not incl UK), USA, Canada, Mexico, Taiwan
Design	Randomised, placebo-controlled, active-controlled
Participants	n=605; aged 18 years or older; diagnosis of chronic plaque psoriasis (with or without psoriatic arthritis) for at least 6 months; stable moderate to severe; candidate for systemic therapy or phototherapy, candidate for treatment with adalimumab
Schedule	Randomised (in 1:1 ratio) to once of 2 treatment arms: 1. Risankizumab (150mg by subcutaneous injection at baseline, 4 weeks and every 12 weeks after) plus adalimumab placebo 2. Adalimumab (80mg [initial dose] followed by 40mg per week by subcutaneous injection) plus risankizumab placebo Those randomised to the risankizumab group received this throughout the study and those randomised to the adalimumab group followed the treatment based on 16 week response (those with less than PASI 50 at week 16 switch to risankizumab, those with PASI 90 continued with adalimumab and those with between PASI 50 and PASI 90 response were re-randomised.
Follow-up	Active treatment for 44 weeks

Primary Outcomes	•Achievement of >=90% reduction from baseline Psoriasis Area and Severity Index (PASI) score (PASI 90) at Week 16 •Achievement of a static Physician Global Assessment (sPGA) score of clear or almost clear at Week 16
Secondary Outcomes	•Achievement of >=75% reduction from baseline PASI score (PASI 75) at Week 16 •Achievement of 100% reduction from baseline PASI score (PASI 100) at Week 16 •Achievement of >=90% reduction from baseline PASI score (PASI 90) at Week 44 for those patients who were re-randomized at Week 16 •Achievement of an sPGA score of clear or almost clear (0 or 1) at Week 44 •Achievement of sPGA score of clear (0) at Week 44
Key Results	Risankizumab was significantly effective in producing 90% of improvement PASI 90 and sPGA score of clear or almost clear (sPGA 0/1) at week 16 compared to adalimumab (p=<0.001 and p=<0.001 respectively). In the second phase of week 16 to week 44, subjects with a response of PASI 50 to less than PASI 90 to adalimumab at week 16 were re-randomized to either switch to risankizumab (n=53) or continue adalimumab (n=56).[11]
Adverse effects (AEs)	Serious adverse events were experienced by n=3, n=3 and n=0 in the risankizumab, ustekinumab and placebo respectively at 16 weeks and by n=6, n=4 and n=0 in the risankizumab, ustekinumab and placebo respectively at 44 months. In the adalimumab group, one participant was diagnosed with stage IV gallbladder cancer and died 3 weeks after diagnosis and another participant was diagnosed with gallstones and underwent gallbladder surgery after which the participant deteriorated and died post-surgery. In the risankizumab group one participant died of an acute myocardial infarction on day 73 of the study.[11]
Expected reporting date	-

Trial	IMMhance, NCT02672852, EudraCT-2014-005102-38, JapicCTI-163251, 2014-005102-38; risankizumab vs placebo; phase III
Sponsor	AbbVie Inc.
Status	Ongoing – not recruiting
Source of Information	Trial registry[14]
Location	4 EU countries (not incl UK), USA, Australia, Canada, Japan, Republic of Korea
Design	Randomised, placebo-controlled
Participants	n=500 (planned); aged 18 years or older; diagnosis of chronic plaque psoriasis (with or without psoriatic arthritis) for at least 6 months; stable moderate to severe chronic plaque psoriasis; candidate for systemic therapy or phototherapy.
Schedule	Randomised to one of two study arms: 1. Risankizumab (90mg/ml subcutaneous injection) 2. Placebo (by subcutaneous injection)

Follow-up	Active treatment duration of 88 weeks with a 16 week follow-up period.
Primary Outcomes	•Achievement of >= 90% reduction from baseline Psoriasis Area and Severity Index (PASI) score (PASI90) at week 16 [Time Frame: week 16] •Achievement of an static Physician Global Assessment (sPGA) score of clear or almost clear at week 16 [Time Frame: Week 16]
Secondary Outcomes	•Achievement of 100% reduction from baseline PASI score (PASI100) at week 16 •Achievement of PASI 90 at Week 52 •Achievement of PASI 100 at Week 52 •Achievement of a 75% reduction from baseline PASI score (PASI 75) at week 16 •Achievement of an sPGA score of clear(0) at Week 16 •Achievement of a Dermatology Life Quality Index (DLQI) score of 0 or 1 at Week 16 •Achievement of an sPGA score of clear (0) or almost clear (1) at Week 52 •Achievement of PASI 75 at Week 52
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Estimated study completion date 3 August 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: increased treatment options for patients

☐ 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

☒ None identified

IMPACT ON COSTS and OTHER RESOURCE USE

☐ Increased drug treatment costs

☐ Reduced drug treatment costs

☐ Other increase in costs

☐ Other reduction in costs

☒ Other: *uncertain unit cost compared to existing treatments*

☐ None identified

OTHER ISSUES

☒ Clinical uncertainty or other research question identified: *no published efficacy results as yet.*

☐ None identified

REFERENCES

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