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Horizon Scanning Research & Intelligence Centre

DMI-9523 (Ampion) for moderate to severe osteoarthritis of the knee

LAY SUMMARY

Osteoarthritis is the most common type of arthritis in the UK and leads to painful and stiff joints. Osteoarthritis can affect any joint, but commonly affects knee joints. Daily routine activities can become difficult for patients with osteoarthritis of the knee.

There is no cure for osteoarthritis of the knee but there are treatments which help to reduce the pain. In cases where treatment does not work, knee surgery may be offered.

Ampion is a new drug for the treatment of osteoarthritis of the knee given as an injection into the affected joint. Some studies have suggested that Ampion may help in reducing knee pain in patients who have osteoarthritis of the knee.

If Ampion is licensed for use in the UK, it could be a new treatment option for patients with osteoarthritis of the knee which may improve patient quality of life better than existing treatments.

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NIHR Horizon Scanning Research & Intelligence Centre,
University of Birmingham. Email: nihrhsc@contacts.bham.ac.uk
Web: www.hsric.nihr.ac.uk

NHS National Institute for Health Research

TARGET GROUP

- Osteoarthritis of the knee: moderate to severe.

TECHNOLOGY

DESCRIPTION

DMI-9523 (Ampion; DA DKP; DA-DKP; DM 0523; DMI9523) is a small-molecule, non-steroidal drug comprised of two amino acids derived from human albumin. It may reduce inflammation by reducing levels of pro-inflammatory cytokines and inhibiting transcription factors involved in inflammation, such as ATF2, cJUN and NFkB. In addition, the compound may inhibit the early activation of memory T-cells and affect upstream inflammatory processes, in part by decreasing vascular permeability.

DMI-9523 is intended for the treatment of moderate to severe osteoarthritis of the knee. In a phase III clinical trial, DMI-9523 was administered at 4ml via intra-articular injection three times in total over four weeks (injections two weeks apart)[1].

DMI-9523 does not currently have Marketing Authorisation in the EU for any indication. DMI-9523 is not currently in phase II or phase III clinical trials for any other indication.

INNOVATION and/or ADVANTAGES

If licensed, DMI-9523 will provide an additional treatment option for patients with moderate to severe osteoarthritis of the knee.

DEVELOPER

Ampio Pharmaceuticals.

AVAILABILITY, LAUNCH OR MARKETING

The results of phase III clinical trials have been reported.

PATIENT GROUP

BACKGROUND

Osteoarthritis is a degenerative joint disease that causes the joints to become painful and stiff. It is the most common type of arthritis in the UK[2]. It primarily involves the cartilage and surrounding tissues[3]. Its cause is unclear; however factors such as age and weight are factors that can influence the development of osteoarthritis[2]. Osteoarthritis of the knee describes a clinical syndrome of joint damage resulting in pain accompanied by varying degrees of functional limitation and reduced quality of life[4]. Osteoarthritis of the knee can make walking, standing and sitting extremely painful and drain people of energy[5]. Symptoms of osteoarthritis include joint tenderness, increased pain and stiffness after immobility, joints appearing slightly larger, grating or crackling sounds or sensations in the joints, limited range of movement in joints, weakness and muscle wasting (loss of muscle bulk)[6].

NHS or GOVERNMENT PRIORITY AREA

This topic is relevant to:

- The Musculoskeletal Services Framework (2006).
- The National Service Framework for Older People (2001).
- NHS England. 2013/14 NHS Standard Contract for specialised rheumatology services (Adult). A13/S/a.
- NHS England. 2013/14 NHS Standard Contract for specialised orthopaedics (Adult). D10/S/a.

CLINICAL NEED and BURDEN OF DISEASE

The knee is the most common site for osteoarthritis[5]. Over half of all people who have sought treatment for osteoarthritis have knee osteoarthritis. Osteoarthritis is the most prevalent joint disorder and cause of disability in the UK, and osteoarthritis of the knee is a leading cause of pain and disability[7]. In the UK approximately 8.5 million people have painful joints attributed to osteoarthritis[8]. It is estimated that 4.11 million people have osteoarthritis of the knee in England, with 1.37 million people affected by severe osteoarthritis of the knee[5]. Women are more likely than men to have sought treatment for knee osteoarthritis[5]. The number of people with osteoarthritis of the knee is estimated to increase to 5.4 million in 2020, and reach 6.4 million by 2035[5].

In 2014-15, there were 38,087 hospital admissions for osteoarthritis (ICD-10 M19) in England, resulting in 35,417 bed days and 38,875 finished consultant episodes[9]. 94,407 knee replacement operations were carried out in 2015 due to osteoarthritis[10].

The population likely to be eligible to receive DMI-9523 could not easily be estimated from available routine published sources.

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE Guidance

- NICE technology appraisal in development. Osteoarthritis – diacerein (ID332). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Osteoarthritis – naproxcinod (ID417). Expected date of issue to be confirmed.
- NICE interventional procedure guidance. Joint distraction for ankle osteoarthritis (IPG538). December 2015.
- NICE interventional procedure guidance. Joint distraction for knee osteoarthritis without alignment correction (IPG529). July 2015.
- NICE interventional procedure guidance. Implantation of a shock or load absorber for mild to moderate symptomatic medial knee osteoarthritis (IPG512). January 2015.
- NICE interventional procedure guidance. Platelet-rich plasma injections for osteoarthritis of the knee (IPG491). May 2014.
- NICE interventional procedure guidance. Individually magnetic resonance imaging-designed unicompartmental interpositional implant insertion for osteoarthritis of the knee (IPG317). September 2009.
- NICE interventional procedure guidance. Arthroscopic knee washout, with or without debridement, for the treatment of osteoarthritis (IPG230). August 2007.

- NICE clinical guidelines. Osteoarthritis: Care and management in adults (CG177). February 2014.
- NICE quality standard. Osteoarthritis (QS87). June 2015.

Other Guidance

- Osteoarthritis Research Society International (OARSI). OARSI recommendations for the management of hip and knee osteoarthritis, part III: changes in evidence following systematic cumulative update of research published through January 2009. 2009[11].
- The Royal Australian College of General Practitioners. Guideline for the non-surgical management of hip and knee osteoarthritis. 2009[12].
- Osteoarthritis Research Society International (OARSI). OARSI recommendations for the management of hip and knee osteoarthritis, part II: OARSI evidence-based, expert consensus guidelines. 2008[13].
- NHS Clinical Knowledge Summaries. Osteoarthritis. 2008[14].
- The British Pain Society. Recommended guidelines for pain management programmes for adults. 2007[15].

CURRENT TREATMENT OPTIONS

Guidelines for osteoarthritis care recommend a holistic approach, taking into account the global needs of an individual[8,16]. Current management options for osteoarthritis of the knee include:

- Patient education and self-management interventions (e.g. use of suitable footwear).
- Thermotherapy.
- Exercise and manual therapy.
- Weight loss for people who are obese or overweight.
- Electrotherapy (e.g. TENS).
- Aids and devices (e.g. braces, joint supports, insoles and walking sticks).
- Arthroscopic lavage and debridement - recommended for people with a clear history of mechanical locking.
- Pharmacological interventions for pain relief:
  - Acetaminophen (paracetamol).
  - Topical non-steroidal anti-inflammatory drugs (NSAID) or capsaicin.
  - Oral NSAIDs (e.g. ibuprofen, naproxen) or selective COX-2 inhibitors (e.g. celecoxib).
  - Opioids (e.g. codeine).
  - Intra-articular injections (e.g. corticosteroid injections, hyaluronan injections [not recommended by NICE]).
- Joint replacement surgery – recommended for people whose quality of life is substantially impacted by joint symptoms and who are refractory to non-surgical treatment.

EFFICACY and SAFETY

Trial	NCT02556710, AP-003-B; Ampion vs placebo; phase III.	NCT01839331, AP-003-A; Ampion vs placebo; phase III.
Sponsor	Ampio Pharmaceuticals Inc.	Ampio Pharmaceuticals Inc.
Status	Ongoing.	Published.
Source of information	Trial registry[17].	Publication[18], trial registry[19].
Location	USA.	USA.

Design	Randomised, placebo-controlled.	Randomised, placebo-controlled.
Participants	n=484 (planned); aged 40-85 years; clinical diagnosis and radiological evidence of symptomatic osteoarthritis of the knee >6 months; moderate to severe pain; no analgesia taken 24 hours before efficacy measure; no NSAID at screening visit and 72 hours prior to baseline visit and for the duration of the study.	n=329; aged 40-85 years; clinical diagnosis and radiological evidence of symptomatic osteoarthritis of the knee >6 months; moderate to severe pain. No analgesia taken 12 hours before efficacy measure; no known liver abnormality.
Schedule	Randomised to Ampion 4ml intra-articular injection or placebo 4ml intra-articular injection.	Randomised to Ampion 4ml or 10ml intra-articular injection, or placebo 4ml or 10 ml intra-articular injection.
Follow-up	Follow-up period 12 weeks,	Follow-up period 12 weeks,
Primary outcomes	Improvement on the Western Ontario and McMaster Universities Arthritis Index (WOMAC) index.	Improvement in knee pain.
Secondary outcomes	Safety.	Improvement in stiffness and function, defined by Measures in Rheumatology Clinical Trials and Osteoarthritis Research Society International (MERACT-OARSI) criteria.
Key results	-	Mean change in WOMAC scores at 12 weeks (standard error) for 4ml Ampion, 4ml placebo, 10ml Ampion, and 10ml placebo, respectively: -0.93 (0.08), -0.71 (0.08), -0.92 (0.09), -0.73 (0.11); for combined arms, Ampion -0.93 (0.06) and placebo -0.72 (0.07), p=0.004.
Adverse effects (AEs)	-	For combined Ampion and placebo groups, respectively: any AE, 41% and 47%; any treatment-related AE, 10% and 13%; any severe AE, 5% and 6%; any serious AE, 2% and 2%; any treatment-related serious AE, 0% and 0%. The most commonly occurring treatment-related AE was arthralgia (n=17) and injection site pain (n=7).
Expected reporting date	Study completion date reported as February 2016.	-

Trial	NCT02024529, AP-004-A; Ampion vs placebo; phase III.	NCT02242435, AO-008; Ampion vs placebo; phase III.
Sponsor	Ampio Pharmaceuticals Inc.	Ampio Pharmaceuticals Inc.
Status	Completed.	Completed.
Source of information	Trial registry[20].	Trial registry[1].
Location	USA.	USA.
Design	Randomised, placebo-controlled.	Randomised, placebo-controlled.
Participants	n=538; aged 35-85 years; clinical diagnosis and radiological evidence of symptomatic osteoarthritis of the knee; moderate to severe pain.	n=342; aged 40-85 years; clinical diagnosis and radiological evidence of symptomatic osteoarthritis of the knee >6 months; moderate to severe pain. No analgesia taken 24 hours before efficacy measure.

Schedule	Randomised to Ampion 4ml intra-articular injection or placebo 4ml intra-articular injection.	Randomised to Ampion 4ml intra-articular injection three times over 4 weeks, 2 weeks apart; or placebo 4ml intra-articular injection three times over 4 weeks, 2 weeks apart.
Follow-up	Follow-up period 20 weeks.	Follow-up period 20 weeks.
Primary outcome/s	Improvement on WOMAC pain sub-score; safety.	Improvement on WOMAC osteoarthritis index; efficacy and safety.
Secondary outcome/s	Not reported.	Not reported.
Key results	Not reported.	Not reported.
Adverse effects (AEs)	Not reported.	Not reported.
Expected reporting date	Previously reported as September 2014.	Previously reported as April 2015.

ESTIMATED COST and IMPACT

COST

The cost of DMI-9523 (Ampion) 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: *requires intra-articular administration*
- ☐ 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:
- ☑ None identified

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