Strontium ranelate (Protelos) for osteoarthritis

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The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Strontium ranelate (Protelos) for osteoarthritis

Target group
- Osteoarthritis (OA): patients who require disease modifying therapy – add-on therapy.

Technology description
Strontium ranelate (Protelos) is an osteoprotegerin stimulant that has a dual effect on bone metabolism. It simultaneously increases bone formation and reduces bone resorption by inhibiting osteoclast formation and activity, resulting in a rebalance of bone turnover in favour of bone formation. It also improves bone biomechanical properties, increasing bone strength. Strontium ranelate is administered as an oral suspension for the treatment of OA at 2g once daily. Strontium ranelate is licensed for the treatment of postmenopausal osteoporosis in the EU. It is also in phase III trials for osteoporosis in men.

Common adverse events (AEs) associated with strontium ranelate when used to treat postmenopausal osteoporosis are nausea and diarrhoea, while the most serious AEs (SAEs) are venous thromboembolism and severe hypersensitivity syndromes, such as rash with eosinophilia and systemic symptoms.

Innovation and/or advantages
If licensed, strontium ranelate could provide an additional treatment option for patients with OA.

Developer
Servier Laboratories Ltd.

Availability, launch or marketing dates, and licensing plans
In phase III clinical trials.

NHS or Government priority area
This topic is relevant to The Musculoskeletal Services Framework (2006) and The National Service Framework for Older People (2001).

Relevant guidance
- NICE clinical guideline. The care and management of osteoarthritis. 2008¹.
- NHS Clinical Knowledge Summaries. Osteoarthritis. 2008⁵.
Clinical need and burden of disease

OA is a lead cause of pain and disability in the UK and is one of the most common musculoskeletal disorders. The disease causes progressive degeneration of articular cartilage and subsequent joint space narrowing. The most commonly affected joints include the knee, hip, spine and small joints of the hands. Prevalence is difficult to determine because the clinical syndrome (joint pain and stiffness) does not always correspond with the structural changes of OA visible at X-ray.

OA is thought to affect approximately 8 million people in the UK, of whom 1 million seek medical treatment. It is more common in women than men, and the prevalence has been shown to increase with age. An estimated 20% of adults aged 45-64 years and 35% of women aged 75 years and over report knee pain attributable to OA – knee pain causes disability in about 25% of adults aged 50 and over. Similarly, the hand and hip are common sites of OA associated pain, with 31% of adults over the age of 45 reporting hand pain and 12% of adults over 65 reporting hip pain.

In 2009-10 there were 221,199 finished consultant episodes for OA (ICD M15-M19) in England, of which 60% were in females. In 2009, 93% of primary hip and 97% of primary knee replacement operations were due to OA. In England and Wales, approximately 17 million prescriptions were dispensed for non-steroidal anti-inflammatory drugs (NSAIDs) in 2009, at a cost of almost £96 million.

Existing comparators and treatments

Guidelines for OA care recommend a holistic approach, taking into account the global needs of an individual.

Current management options for OA include:

- Patient education and self management interventions (e.g. use of suitable footwear).
- Thermotherapy.
- Acupuncture.
- 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, tap turners, and walking sticks).
- Pharmacological interventions for pain relief:
  - Acetaminophen (paracetamol).
  - Topical 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

<table>
<thead>
<tr>
<th>Trial</th>
<th>ISRCTN33207390, CL3-12911-028; strontium ranelate vs placebo; phase III.</th>
<th>ISRCTN92624244, CL3-12911-022; strontium ranelate vs placebo; phase III.</th>
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</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Servier Laboratories Ltd.</td>
<td>Servier Laboratories Ltd.</td>
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<tr>
<td>Status</td>
<td>Completed but unpublished.</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>‘Trial registry’\textsuperscript{12}.</td>
<td>‘Trial registry’\textsuperscript{13}.</td>
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<tr>
<td>Location</td>
<td>Belgium.</td>
<td>China, Korea, Taiwan.</td>
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<tr>
<td>Design</td>
<td>Randomised, placebo-controlled.</td>
<td>Randomised, placebo-controlled.</td>
</tr>
<tr>
<td>Participants and schedule</td>
<td>n=140; adults ≥50 years; primary knee OA. Randomised to strontium ranelate 1g or 2g daily; or placebo.</td>
<td>n=450 (planned); adults ≥50 years; primary knee OA. Randomised to strontium ranelate 1g or 2g daily, or placebo.</td>
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<tr>
<td>Follow-up</td>
<td>Active treatment period 2 yrs.</td>
<td>Active treatment period 3 yrs.</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>Changes in the algofunctional behaviour of the target knee.</td>
<td>Radiographic assessment of knee OA.</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td>Algofunctional assessment; radiographic assessment of knee OA; physical examination.</td>
<td>Algofunctional assessment; physical examination; safety.</td>
</tr>
</tbody>
</table>

Estimated cost and cost impact

The cost of strontium ranelate has not yet been determined for this indication. However, strontium ranelate (Protelos) for the treatment of osteoporosis costs £25.60 for 28 x 2g containing sachets\textsuperscript{13}.

Claimed or potential impact – speculative

Patients

☐ Reduced mortality or increased length of survival – delete as appropriate
☐ Reduction in associated morbidity or improved quality of life for patients and/or carers
☐ Quicker, earlier or more accurate diagnosis or identification of disease
☐ None identified
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Services

- Increased use
- Service organisation
- Staff requirements
- Decreased use
- Other:
  - None identified

Costs

- Increased unit cost compared to alternative
  - New costs: new add-on treatment option.
- Increased costs: more patients coming for treatment
- Increased costs: capital investment needed
- Savings:
  - None identified

Other issues

- Clinical uncertainty or other research question identified:
  - Expert opinion suggests more symptom and structural modifying data is needed on treatments that claim to affect bone structure.
  - None identified

References
