

Bisphosphonate alternative regimens for the prevention of osteoporotic fragility fractures: BLAST-OFF, a mixed-methods study

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Scientific summary

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Scientific summary

Background

Alendronate (ALN) is recommended as the first-line osteoporosis treatment to prevent osteoporotic fractures; however, long-term adherence (both treatment compliance and persistence) is poor. Alternative bisphosphonates (BP) are available, which vary in frequency of use and/or route of administration and have been shown to improve long-term adherence compared to ALN. However, the most clinically effective and cost-effective alternative regimen remains unclear. Furthermore, clinicians should optimise dosing regimens on the basis of the patient's understanding, preference and characteristics. What is the most cost-effective BP in clinical trials may not be the most cost-effective or acceptable to patients in everyday clinical practice.

Objectives

1. Explore patient, clinician and stakeholder views, experiences and preferences of ALN compared to alternative BP.
2. Update and refine the 2016 systematic review and cost-effectiveness analysis of BP and estimate the value of further research into the relative benefits.
3. Undertake stakeholder/consensus engagement to identify important research questions and further rank research priorities.

Methods

The study was conducted in two stages, stages 1A and 1B in parallel, followed by stage 2:

- Stage 1A: we elicited patient and clinician experiences of different BP regimens to understand their preferences and those of other stakeholders compared to ALN. This was undertaken by performing a systematic review and framework synthesis of qualitative studies around clinician and patient views, followed by semistructured qualitative interviews with multidisciplinary stakeholders.
- Stage 1B: we updated and expanded the existing Health Technology Assessment systematic review and clinical and cost-effective health economic model (2016), incorporating a more comprehensive review of treatment efficacy, safety, side effects, compliance and long-term persistence. The model takes a NHS and Personal Social Services perspective, with future costs and quality-adjusted life-years (QALYs) discounted at 3.5% per annum. Costs are reported in pound sterling based on 2021 prices.
- Stage 2: using an approach based on the James Lind methodology for identification and prioritisation of research questions, we identified questions that needed to be answered about the effectiveness and acceptability of BP. Findings from stages 1A and 1B, together with multidisciplinary meetings, identified areas of uncertainty. These questions were then ranked in a multidisciplinary, nationally representative stakeholder event, conducted online over MS Teams.

Results

We identified, through a systematic review of previous studies on patient and clinician experiences of BP treatment, how patients and healthcare professionals make sense (coherence) of BP by balancing perceptions of need against concerns, how uncertainty prevails about BP-perceived effectiveness and a number of individual and service factors that have potential to increase self-efficacy in recommending

and adhering to BP. The qualitative interview study examining experiences of alternate BP regimens found that intravenous (IV) BP zoledronate (ZOL) treatment was generally more acceptable to patients. Such IV regimens were perceived to be more straightforward to engage in, although a portion of patients taking ALN were satisfied with their current treatment.

The systematic review and network meta-analysis of previous studies of effectiveness found that IV ZOL was the most effective BP compared to ALN, risedronate and oral ibandronate for reducing the risk of fragility fractures. Adherence was higher in IV ZOL users. It was found that clinical decision-making could be facilitated by considering adherence patterns in BP users who were at increased risk of fracture. However, the higher hospital administration costs for IV ZOL meant that the incremental cost-effectiveness ratios for IV ZOL compared to ALN were greater than £30,000 per QALY across all risk categories. This was despite the fact that IV ZOL was predicted to result in fewer fractures than ALN, due to its higher treatment persistence and a longer offset period.

The prioritisation exercise highlighted a need for further research to tackle the issues relating to patient factors influencing treatment selection and effectiveness, including in younger adults, how to optimise long-term care and support patient and clinician decision-making and the clinical and cost-effectiveness of giving IV ZOL in alternate settings to hospital care.

Conclusions

We have identified the factors that influence how patients and clinicians make sense of BP, described the experience of BP taking in terms of burden and identified factors that both facilitate and hinder confidence in taking and prescribing and monitoring BP. IV ZOL treatment was generally more acceptable to patients. IV ZOL was found to be the most effective BP and with greater adherence; however, the cost-effectiveness of IV ZOL relative to ALN was limited by the high hospital administration costs. Further research is needed to support people to make decisions influencing treatment selection and effectiveness and establish how to optimise long-term care. In addition, research is needed to explore the clinical and cost-effectiveness of IV ZOL delivered in alternate settings, such as in the community, compared to ALN treatment.

Patient and public involvement

We have worked closely with the Royal Osteoporosis Society (ROS) and the Nottingham ROS (NotROS) Support Group, who together have influenced the design of this application, choice of study outcomes and were involved throughout the study.

Trial registration

This trial is registered as ISRCTN10491361.

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