

# Targets in osteoporosis treatment

## *Metas para o tratamento da osteoporose*

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Although guidelines for many chronic diseases recommend targets to pursue as an important aspect of their management, there is considerable disagreements between organizations concerning which targets should be chosen, as well as what would be the optimum value for a specific target (1-6). These disagreements have become more pronounced recently for diabetes and dyslipidemias (1-4). In 2012 the American Diabetes Association and the European Association for the Study of Diabetes published a position statement on the management of type 2 diabetes in which remarkable changes were observed in relation to the previous recommendations (1). This was mainly due to the advent of new therapies, but also because new knowledge has emerged on the long-term adverse effects of drug therapy, especially the risk of hypoglycemia with more intensive control and consequently an increased cardiovascular risk. This was followed by the announcement of the 2013 diabetes algorithm proposed by the American Association of Clinical Endocrinologists, which introduced more rigorous targets for blood glucose control for the newly-diagnosed type 2 patient and more aggressive therapies and targets for the pre-diabetes states (2). At the end of 2013, another notable change occurred with the release of the American College of Cardiology/American Heart Association hypercholesterolemia guidelines (3), more evidence-based than the previous NCEP (National Cholesterol Education Program) guidelines, using more robust data to calculate absolute risk based on multiple prospective cohort studies, calibrating the calculations on intervention studies on primary prevention of major cardiovascular events with statins and considering the long-term side effects and drug interaction, especially in the more vulnerable elderly patient. New targets were proposed based on percentage changes in LDL-C as a target for statin therapy, and not simply a low or very low absolute value for LDL-C as some continue to advocate (4). Guidelines for hypertriglyceridemia and hypertension have also resulted in disagreement on when to start drug therapy or which targets should be pursued during treatment, especially in populations such as individuals with type 2 diabetes and in the elderly (5-7).

Is it time to consider the same approach to osteoporosis treatment? As with other chronic conditions, the field of osteoporosis has been growing fast and new noninvasive methods for the evaluation of bone turnover and strength are now available. In this issue of the journal many aspects of these new tools will be discussed.

Biochemical markers of bone remodeling are now widely available and a review of recent data suggests that they can be used as a target related to the effects of osteoporosis drugs and the prediction of a decrease in fracture risk (8). Particularly worthy of mention in this connection are the reduction on serum beta-CTX (C-terminal telopeptide) during anti-resorptive therapy and the rise in serum PINP (Serum collagen type I N-terminal propeptide) and osteocalcin during anabolic therapy with teripa-

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ratide (8,9). Even strontium ranelate, which leads to slight changes in bone markers in postmenopausal women with osteoporosis who had never taken any bone medication, can induce significant changes in bone markers in women previously treated with bisphosphonates (9,10) and these changes may be associated with an improvement in bone mineral density (BMD).

Much more controversy exists in relation to target bone mineral density values during osteoporosis treatment. Some studies suggest (11) that even patients with a decline in BMD may still benefit from oral bisphosphonate therapy. These patients may exhibit a reduced risk for fracture than those on a placebo, despite having a suboptimal BMD response, although the risk reduction is more pronounced in those patients who have experienced an unequivocal increase in BMD. It may therefore be difficult to tell a patient on bisphosphonate treatment who has experienced a decline in BMD over time that she has really lost her protection against osteoporotic fractures.

As in other chronic diseases, the new knowledge on the adverse effects of long-term therapy has also been evaluated for osteoporosis, and this is particularly true for atypical femoral fractures, which may exhibit a sharp increase in incidence with the long-term use of bisphosphonates (12,13). Although rare, individually these fractures may have a great impact on health, owing to the patient's considerable disability (13). As yet insufficient data is available for denosumab, which can also cause atypical femoral fractures and needs to be used continuously as it has no residual effects on bone after therapy has been discontinued (14).

In view of the above, another new target proposed in the treatment of osteoporosis is to limit the duration of bisphosphonate use to 3-5 years (15) and consider a drug holiday for those compounds which have residual effects on bone, such as alendronate and zoledronic acid, or even decrease the dose of alendronate for the high-risk patient in whom more prolonged therapy is preferred (16).

Hopefully, other methods developed to evaluate bone quality, such as trabecular bone score (TBS) on vertebral BMD images and peripheral high-resolution quantitative computed tomography (HR-pQCT), will be widely available for clinical use in the near future (17,18). This will allow more precise targets to be recommended for osteoporosis therapy.

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