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Invited Plenary Abstract
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New Treatments for Postmenopausal Osteoporosis

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Bisphosphonates are, by far, the most commonly used antiresorptive treatments. In addition to alendronate, risedronate and ibandronate, zoledronate given by yearly injection is likely to be available in a near future. There is room, however, for new antiresorptive therapies. Selective estrogen receptor modulators have the potential to provide beneficial effects on other target organs than bone, and large phase III trials are ongoing with lasofoxifene, bazedoxifene and arzoxifene. Denosumab is a monoclonal antibody blocking RANK-ligand and subcutaneous injections have been shown to induce a profound and sustained suppression of bone turnover over 6 months. A fracture trial in postmenopausal osteoporosis is ongoing, but the drug has also a potential role in the management of malignant bone diseases and rhumatoid arthritis.

The fact that cathepsin K is the major osteoclast-derived enzyme responsible for the degradation of type I collagen in bone has led to the ongoing development of specific inhibitors of that enzyme (currently under phase II trials). Finally, there is growing interest in the development of selective antiresorptive agents that would inhibit bone resorption without subsequent inhibition of bone formation, in contrast to other antiresorptive therapy. The development of these "uncoupling" agents, such as chloride channel-7 inhibitors, is based on several recent experimental observations.

The development of anabolic agents specific for bone tissue is a challenge. Non-injectable parathyroid hormone fragments/analogs are likely to be available soon. An alternative strategy is to inhibit the calcium sensing receptor with a specific and short-acting antagonist. Another alternative is to develop parathyroid hormone analogs, with the goal to dissociate the anabolic and resorptive effects, based on interesting preclinical studies. Finally, the recent discovery of the role of sclerostin on the BMP/Wnt pathway and on the expression of osteocytes has led to the development of antisclerostin monoclonal antibodies, that have the potential in animal models to induce a marked stimulation of bone formation.

In conclusion, although currently available treatments are able to reduce the risk of vertebral, and to some extent non vertebral fractures, there is room for improvement. The availability of new agents, especially those stimulating bone formation, alone or in sequential combination with antiresorptives, will improve significantly our management of postmenopausal osteoporosis.