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CLINICAL APPLICATION OF ROCHE BONE MARKERS

New challenges for the health care industry

The estimated national direct expenditures (hospitals and nursing homes) for osteoporotic hip fractures were $18 billion dollars in 2002, and the cost is rising. One in two women and one in four men over age 50 will have an osteoporosis-related fracture in her/his remaining lifetime. In the United States, 10 million individuals are estimated to already have the disease and almost 34 million more are estimated to have low bone mass, placing them at increased risk for osteoporosis. Of the 10 million Americans estimated to have osteoporosis, eight million are women and two million are men (*1*).

Osteoporosis is responsible for more than 1.5 million fractures annually, including:

- 300,000 hip fractures,
- 700,000 vertebral fractures,
- 250,000 wrist fractures, and
- 300,000 fractures at other sites (*1*).

Women with a hip fracture are at a four-fold greater risk of a second one, and the risk factors are similar to those for the first hip fracture. Osteoporotic fractures lower a patient's quality of life.

Osteoporosis

Osteoporosis is often called a "silent disease" because bone loss occurs without symptoms. People may not know that they have osteoporosis until their bones become so weak that a sudden strain, bump or fall causes a fracture or the collapse of a vertebra . The main cause of osteoporosis is lack of estrogen in post menopausal women, and low levels of testosterone in men. Other factors however include family history of the disease, malabsorption, long term immobility, heavy drinking and smoking.

Bone Mineral Density Measurements

The current method of elucidating the status of bone is the measurement of bone mineral density (BMD), and this will remain as the primary diagnostic indicator of bone structure and status at any one point in time. A measurable increase in bone mineral density however, can only be determined by these methods over a prolonged period of time. BMD determinations carried out two years after the initiation of therapy can show whether or not a patient is responding; i.e., whether there is a significant increase in BMD at the lumbar spine. Regardless of the treatment selected, BMD measurement is generally not suitable for determining a patient's response to therapy after only one year.

Poor Treatment Response

There are a variety of reasons for poor treatment response. Non-compliance (patients take medication irregularly or not at all) is probably the most common cause, however, others include poor absorption of bisphosphonates. Furthermore, for patients treated with Risedronate, it has been shown that a reduction in fracture risk does not always correlate to a corresponding BMD increase, whereas Bone Marker measurements showed better correlations.

The most common series of drugs used for antiresorptive therapy are the bisphosphonates. They have a strong affinity for bone

apatite, and this is the basis of their use in the treatment of osteoporosis. The biggest problem currently associated with treatment by bisphosphonates is adherence. Bisphosphonates must be taken in the morning and on an empty stomach; the patient is required to sit upright for one hour before they can continue with their daily routine. Currently, approximately 50% of patients discontinue their treatment within one year. This makes it difficult to separate non-responders from non-compliant individuals. By using bone markers to gain a baseline level and then measuring again at three months, one can encourage the patient to continue compliance or discuss the reasons for failure (2-5).

New Bone Markers at Three Months

Recently, assays for markers of bone formation, turnover, and resorption have improved significantly in quality. This is due to their measurement in serum rather than the traditional urine matrix, and this has led to their increased use as a means of therapy monitoring and adherence testing. The following assays are available from **Roche Diagnostics**:

- The turnover marker Elecsys N-MID Osteocalcin is an immunoassay for the quantitative determination of osteocalcin. Osteocalcin, the most important non-collagen protein in the bone matrix, is a bone-specific, calcium-binding protein which is dependent on vitamin K (*6*).

- The resorption marker C-terminal collagen degradation product (ß-CrossLaps) which as its name suggests is a breakdown product of type I collagen (*6*).

Together these markers give a direct indication of the status of the bone remodelling cycle and can demonstrate treatment response at three months rather than the two years required for a significant change in bone mineral density. For the initial assessment before treatment selection, both Roche markers can be measured for disease management.

What Happens to Bone Markers Under Therapy?

A 35% or greater reduction in bone marker levels after three months indicates therapeutic success with antiresorptive treatment. A non-responder would suggest secondary causes of osteoporosis, inadequate treatment, or a non-compliant individual. However, if there is an initial reduction in response to treatment followed by a rise in bone markers, this is either caused by a fracture or more likely the onset of poor compliance. Given that 50% of sufferers are non-compliant at some point in their treatment bone markers offer an extremely cost effective means of patient management.

Better Treatments and More Compliance.

The goal of osteoporosis therapy is to prevent fractures and their consequences, as well as to maintain mobility and quality of life. There are two different strategies for treatment: antiresorptive therapy, which aims to prevent further loss of bone mass, and stimulation of bone formation (Parathormone-based treatment), which aims to increase the building of new bone. By using bone markers to gain a baseline level and then measuring again at three months, one can encourage the patient to continue compliance or discuss the reasons for failure. If necessary, treatment changes can be made at this point, saving twenty-one months of wasted or inappropriate therapy

For further information, references and availability of bone marker assays please contact Jim Harris @ 1-317-521-7060.

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3.Roux C, *et al*. *Joint Bone Spine* 2005; 72:26-31.
4.Christgau *et al.*, *Bone* 2000; 26:505-511.
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6.Roche Diagnostics package inserts 02/06