Alendronate Beats Risedronate in Increasing BMD

BY DOUG BRUNK
San Diego Bureau

San Diego — Postmenopausal women with low bone density who received once-weekly alendronate 70 mg had significantly greater increases in bone mineral density and reductions in markers of bone turnover over a 2-year period, compared with those who received once-weekly risedronate 35 mg, results from a randomized, double-blind trial demonstrated.

In addition, there were no differences between the two treatment groups in terms of upper-gastrointestinal adverse events or overall safety and tolerability, Dr. Anne E. de Papp reported during a poster session at the annual meeting of the International Society for Clinical Densitometry.

"There has always been a perception that risedronate is better tolerated," Dr. de Papp, senior medical director of clinical development for Merck & Co., said in an interview. "This is nice evidence that at least in a clinical trial setting, there is no difference [between risedronate and alendronate] in upper GI tolerability."

However, she quickly cautioned that this head-to-head study only compared surrogate end points for bone fracture risk, not the actual rate of clinical fractures. "To do a head-to-head fracture trial between two agents that are active therapies for osteoporosis would require huge numbers of patients for many years," she said. "I think when you're comparing two drugs that work by the same mechanism of action, it's reasonable to compare them using surrogate markers of efficacy.

In addition, there were no differences between the two treatment groups in terms of GI adverse events.

DR. de PAPP

"We saw greater gains in BMD and greater reductions in [markers of] bone turnover [with alendronate treatment], but the contention is, what does that mean in terms of fracture outcomes? We don't know, but … there is evidence to support that drugs causing greater gains in BMD and greater reductions in bone turnover are associated with greater fracture reduction."

In the study, led by Dr. Sydney Bonnick of the Denton, Tex.–based Clinical Research Center of North Texas, researchers performed a 1-year extension of the original 1-year, randomized, double-blind Fosamax Actonel Comparison Trial (J. Bone Miner. Res. 2005;20:141-51).

Of the 833 patients, 419 received once-weekly risedronate 35 mg and 414 received once-weekly alendronate 70 mg. Their mean age was 64 years, and all had low bone density. This was defined as greater than or equal to 2.0 standard deviations below young normal mean bone mass in at least one of four sites: total hip, hip trochanter, femoral neck, or lumbar spine (L1-L4).

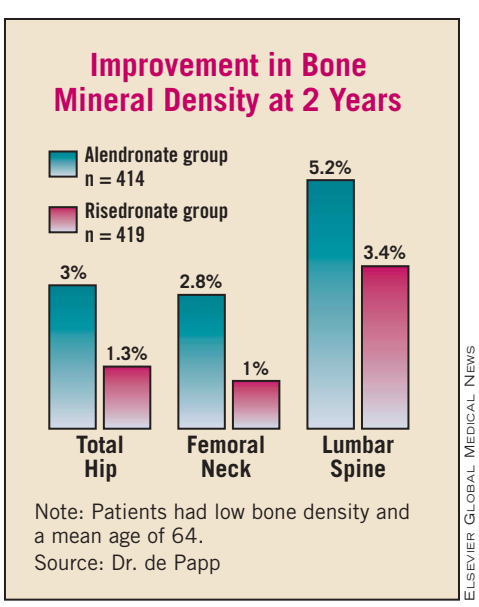
All patients underwent a DXA and lab analyses of biochemical markers at baseline and at 2 years.

Patients in the alendronate group had significantly greater increases in bone mineral density (BMD) at 2 years, compared with their counterparts in the risedronate group at the following sites: hip trochanter (4.6% vs. 2.5%), total hip (3.0% vs. 1.3%), femoral neck (2.8% vs. 1.0%), and lumbar spine (5.2% vs. 3.4%).

Significantly greater reductions of serum bone-specific alkaline phosphatase and other bone markers were seen in the alendronate group, compared with the risedronate group.

No significant differences between the two treatment groups were seen in terms of overall safety and tolerability, including gastrointestinal adverse events.

Merck & Co. funded the study. ■



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Childhood Fracture History Tied To Low BMD, Osteoporosis Later

BY KERRI WACHTER
Senior Writer

Nashville, Tenn. — A history of fracture in childhood and adolescence may be a marker for osteoporosis later in life, suggest study findings presented at the annual meeting of the American Society for Bone and Mineral Research.

Girls with fractures have lower gains in bone mineral density (BMD) and lower bone mineral mass at pubertal maturity, especially at sites containing predominantly trabecular bone, said Dr. Serge L. Ferrari, professor of medicine at the Service of Bone Diseases at the Geneva University Hospital.

Girls with fractures had less BMD gain throughout puberty at the ultradistal radius and lumbar spine, compared with those with no fracture history.

The researchers followed 125 girls from prepuberty to pubertal maturity, assessing BMD using dual x-ray absorptiometry at both fractured and nonfractured sites including the ultradistal radius, proximal radius, femur trochanter, lumbar spine, femur neck, and femur diaphysis. Questionnaires were used to assess calcium intake, and both children and parents were interviewed to monitor for any accidents, falls, or fractures.

During an average of 8.5 years follow-up, 59 fractures occurred in 42 girls, 48% of the fractures involved the forearm and/or the wrist.

Before puberty and at the age of peak height velocity, BMD values at the proximal radius tended to be lower in girls with fractures. At pubertal maturity, BMD in girls with fractures was significantly lower at the ultradistal radius, femur trochanter, and lumbar spine. BMD at the femur neck and femur diaphysis were not significantly different between the two groups at pubertal maturity.

Girls with fractures also had significantly less BMD gain throughout puberty at the lumbar spine (–8%) and ultradistal radius (–12%), compared with those without a history of fracture. This trend almost reached significance at the femur trochanter and the proximal radius.

Using Cox proportional hazard models, the researchers identified four factors that were significantly associated with decreased hazard ratios for fractures: radial diaphysis BMD at baseline and BMD gain (over puberty) at the ultradistal radius, lumbar spine, or femur trochanter.

BMD measurements at all sites were highly correlated between baseline and pubertal maturity. There were also within-trait correlations between mature daughters and their mothers, yielding heritability estimates of 80%-90% for the hip, spine, and proximal radius. This suggests a strong genetic component for BMD.

Fractures are common in childhood and adolescence, with one in three girls and one in two boys having a traumatic fracture as they grow. Three-quarters of these fractures are in the upper limbs.

Studies have suggested there is underlying fragility involved in traumatic fractures of childhood and adolescence. The peak incidence of traumatic fractures coincides with the age of peak height velocity, the age at which longitudinal growth is fastest. And the age of peak height velocity precedes the age of peak bone mass velocity, when most bone mass is acquired, by about 1 year. The hypothesis follows that bone fragility at peak height velocity results from a transient deficit in bone mineral accrual relative to bone size. ■

Triad Components Found in Female High School Athletes

A significant proportion of female high school athletes meet the criteria for one of three health disorders that comprise the female athlete triad syndrome, according to a cross-sectional study.

Jeanne F. Nichols, Ph.D., of San Diego State University, and her colleagues reported that of 170 female athletes aged 13-18 years, 18% demonstrated disordered eating, 24% menstrual irregularity, and 22% low bone mass. Although only 10 girls (6%) qualified as having two triad components and 2 (1%) had the full triad, the investigators stated that "a substantial number of these young athletes may be at increased risk for developing the full triad over time" (Arch. Pediatr. Adolesc. Med. 2006;160:137-42).

The researchers also identified several interrelationships among the triad components.

Girls whose menstrual cycles occurred at intervals longer than 35 days or who missed their period for more than 3 months within the previous year reported significantly more dietary restraint, scored significantly higher on an eating disorder questionnaire, and experienced menarche more than 6 months later than girls with normal menstrual cycles.

Similarly, girls with low and very low bone mineral density scores experienced menarche more than 7 and 12 months later, respectively, than girls with normal bone density. These findings were observed despite similar values for chronological age, body weight, and the percentage of body fat between the groups being compared.

Few studies to date have concurrently assessed the prevalence of all three triad components in female athletes, and no studies have tested for the triad among high school athletes. Most reports on triad components focus on collegiate or elite athletes.

"We believe that screening for disordered eating and menstrual irregularity is potentially more important for high school than for college athletes as a first step in preventing comorbidities associated with the triad, particularly because adolescence is a critical period for optimizing bone mineral accrual," noted the investigators.

Adolescents with pathogenic eating patterns may be at risk for serious health problems in the short and long term, such as nutrient deficiencies, cardiac disturbances, and osteoporosis, Dr. Nichols and her associates said. Also, teens with persistent menstrual dysfunction are at risk of premature osteoporosis.

—Kara A. Nyberg