Risk Of Femur Fractures From Osteoporosis Drugs Fosamax, Boniva, Actonel, And Reclast Related To Number Of Years Used

Using These Bisphosphonates More Than Three (3) To Five (5) Years May Not Only Increase Side Effect Risk But There May Be No Benefit To Most Patients

(Posted by Tom Lamb at www.DrugInjuryWatch.com on May 22, 2012; see http://bit.ly/KR6Hem)

In May 2012 there were medical journal articles in *The New England Journal of Medicine* (*NEJM*) and the *Archives of Internal Medicine* which, together, may cause millions of women to stop using the popular osteoporosis drugs Fosamax (or alendronate, its generic equivalent), Boniva, Actonel, and Reclast due to these two primary findings:

First: There is an increased risk of atypical fractures (low-stress) of the femur in women who have used these bisphosphonate osteoporosis drugs for more than five (5) years; and,

Second: For perhaps 60% to 70% of women currently using Fosamax, Boniva, Actonel, Reclast, and other bisphosphonates there is little to no benefit when these osteoporosis medications are used for more than three (3) to five (5) years.

We will start with the *NEJM* articles that presented the findings of an FDA review of these bisphosphonate drugs prescribed for osteoporosis and, sometimes, osteopenia (moderate to low bone density that is not low enough to be called osteoporosis) which call into question the fracture-prevention benefits of long-term bisphosphonate use:

1. The May 9, 2012 *NEJM* Perspective article from the FDA is "Bisphosphonates for Osteoporosis — Where Do We Go from Here?" (free access).
2. In the same edition of that medical journal is an accompanying article by Dennis M. Black, Ph.D., Douglas C. Bauer, M.D., Ann V. Schwartz, Ph.D., M.P.H., Steven R. Cummings, M.D., and Clifford J. Rosen, M.D., "Continuing Bisphosphonate Treatment for Osteoporosis — For Whom and for How Long?" (free access).

For those who do not want to read through the actual *NEJM* articles, we get this summary of the findings from a May 9, 2012 piece, "New Cautions About Long-Term Use of Bone Drugs", by *New York Times* reporter Tara Parker-Pope:

> Although the concerns about the long-term safety of bone drugs are not new, the F.D.A. performed its own systematic review of the effectiveness of bisphosphonates after years of use. The agency's analysis, which found little if any benefit from the drugs after three to five years of use, may prompt doctors around the country to rethink how they prescribe them....
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> The F.D.A. report offered little specific guidance about long-term use, saying that the decision to continue or stop treatment should be based on an individual assessment of risks, benefits and preferences discussed between a patient and her doctor. The agency did say that women at low risk for fracture or with a bone density near normal may be good candidates to stop therapy after three to five years, but older patients at higher fracture risk and bone density "in the osteoporotic range" may benefit from continued therapy....
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> The recommendations are based on findings from two industry-sponsored studies led by the University of California, San Francisco, that focused on long-term use of the drugs. A study of Fosamax, which is sold generically as alendronate, continued for 10 years, and a study of Reclast, an injectable form of the drug zoledronic acid, continued for six years. According to the F.D.A. analysis, both studies showed significant reductions in fracture risks during the first three to four years of use but little or no benefit with longer use.

Next, we take up the the two *Archives of Internal Medicine* articles concerning the Swiss study which found that bisphosphonate therapy, *i.e.*, use of Fosamax, Boniva, Actonel, or Reclast, appears to be associated with an increased risk of atypical fractures of the femur, and may be driven by the duration of treatment, that were published online May 21, 2012.

- "Increasing occurrence of atypical femoral fractures associated with bisphosphonate use"; and,
- "Atypical femoral fracture risk in patients treated with bisphosphonates".

For the take-away from these two medical journal articles we draw upon this *MedPage Today* report, "Bone Drug Link to Uncommon Breaks Confirmed":

> ... Meier's group identified patients admitted to their level I trauma center with a fracture of the subtrochanteric femoral shaft area between 1999 and 2010 and divided them into two groups.
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> One arm consisted of patients with atypical fractures, defined as "a transverse or short oblique fracture line originating at the lateral femoral cortex between the lesser trochanter and the distal metaphysis."
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> Another arm was made up of patients with common or classic fractures that were in the same location as atypical fractures, but with spiral, wedge, segmental, or complex irregular appearance.
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> They also established a control group of people who did not have a history of femoral fracture....
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> After adjustment for potential risk factors, including vitamin D status, corticosteroids, proton pump inhibitor use, sex, and age, the authors found that any bisphosphonate use was associated with an [odds ratio (OR)] of 69.1 (95% CI 22.8-200.5) for an atypical fracture versus a classic fracture.
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> When categorized by duration of treatment compared with no treatment, the OR for an atypical fracture compared with a classic fracture was:

OR 35.1 for less than 2 years of treatment

OR 46.9 for 2 to 5 years

OR 117.1 for 5 to 9 years

OR 175.7 for more than 9 years

> When comparing the atypical-fracture group with the control group, the authors reported that bisphosphonate treatment was associated with an OR of 35.2 (95% CI 15.9-155.9, P<0.001).

No doubt these two sets of medical journal articles published by the *NEJM* and the *Archives of Internal Medicine* in May 2012 will serve to generate further studies about the efficacy and safety of Fosamax, Boniva, Actonel, Reclast, and other bisphosphonate drugs.
