## STUDY NAME:

Denosumab or Zoledronic Acid in Postmenopausal Women With Osteoporosis Previously Treated With Oral Bisphosphonates

## IDENTIFIERS:

- PMCID: PMC4971333
- PMID: 27270237

## WHO SPONSORED THIS STUDY?

Alexion, Lilly, Amgen, Novartis, NBHA, Pfizer, the University of Alabama, Boehringer Ingelheim, Merck, Merck Serono, Radius, Eli Lilly, Sanofi, AbbVie, Bristol-Myers Squibb, Merck Sharp and Dohme, Rottapharm, Teva, Roche, GlaxoSmithKline, Servier, Theramex, Danone, Organon, Therabel, Chiltern, Galapagos, IBSA-Genévrier, Merckle, Teijin, Analis, Nycomed, Novo Nordisk, Ebewe Pharma, Zodiac, and Will-Pharma

## WHY WAS THIS STUDY CONDUCTED?

The objective of the study was to compare the effect of transitioning from oral bisphosphonates to denosumab or ZOL on bone mineral density and bone turnover.

## WHAT PEOPLE WERE INCLUDED IN THIS STUDY

This trial was run in the following countries: Belgium, Denmark, Poland, Spain, Canada, the United States, and Australia in which a total of 643 postmenopausal women aged 55 years or older with osteoporosis previously treated with oral bisphosphonates were enrolled.
Of 1297 women screened, 643 people were enrolled in the study.

<table>
<tr><td>Total enrolled</td><td colspan="4">N = 643</td></tr>
<tr><td>Enrolled</td><td rowspan="7">ZOL</td><td>N = 322</td><td rowspan="7">denosumab</td><td>N = 321</td></tr>
<tr><td>Consent withdrawn</td><td>n = 5</td><td>n = 3</td></tr>
<tr><td>Lost to follow-up</td><td>n = 2</td><td>n = 3</td></tr>
<tr><td>Other</td><td>n = 2</td><td>n = 2</td></tr>
<tr><td>Death</td><td>n = 1</td><td>n = 0</td></tr>
<tr><td>Completed</td><td>n = 312</td><td>n = 313</td></tr>
<tr><td>Total completed</td><td colspan="3">n = 625</td></tr>
</table>

Figure 1. Disposition of participants

## WHICH MEDICINES WERE STUDIED?

Denosumab and ZOL were the trial medicines. This was a 12-month international multicenter, randomized, double-blind, double-dummy, active-controlled, parallel-group study.

## WHAT WERE THE SIDE EFFECTS?

Serious and common side effects are listed below.

- Overall, 199 participants in each treatment group reported side effects during the study (62.2% in each). 25 participants (7.8%) in the denosumab group and 29 participants (9.1%) in the ZOL group reported serious side effects.
- There was one death during the study. A 79-year-old woman in the ZOL group died because of sepsis, anemia, and multiple organ failure after a fall, complicated by *Clostridium difficile diarrhea*. This death was not considered related to treatment by the investigator.
- No osteonecrosis of the jaw was reported.
- Two fractures were reported as consistent with atypical femoral fractures with denosumab and one with ZOL.
- Atypical femoral fracture might be related to the use of prior long-term bisphosphonate.

## WHAT WERE THE OVERALL RESULTS OF THE STUDY?

In terms of BMD changes, the denosumab group had significantly greater BMD changes from baseline at month 12 compared with the ZOL group at month 12 at the lumbar spine (primary outcome; 3.2% vs 1.1%; $P < .0001$), total hip (secondary outcome; 1.9% vs 0.6%; $P < .0001$), femoral neck (1.2% vs −0.1%; $P < .0001$), and one-third radius (0.6% vs 0.0%; $P < .05$).

In terms of bone turnover, the denosumab group had a greater median decrease from baseline compared with the ZOL group for serum C-telopeptide of type 1 collagen at all time points after day 10 and for serum procollagen type 1 N-terminal propeptide at month 1 and at all time points after month 3 (all $P < .05$).

The denosumab group had significantly greater median percentage changes from baseline in serum intact PTH at months 3 and 9 compared with the ZOL group (all $P < .05$).

## WHERE CAN I FIND MORE INFORMATION ABOUT THIS STUDY?

To learn more about this study, you can find more detailed information on these websites:

- https://pubmed.ncbi.nlm.nih.gov/27270237/
- https://academic.oup.com/jcem/article/101/8/3163/2835048?login=false