

## Oral Abstract

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### ORI

### Zoledronate suppresses bone turnover for at least 2 years; a randomized, placebo-controlled trial

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**Background and Aim:** Intravenous zoledronate, administered annually at a dose of 5mg, decreases fracture risk by 35-70% in osteoporotic postmenopausal women and mortality by 28% after hip fracture. Because of these effects, and the convenience of annual administration, zoledronate is likely to become a first-line therapy for treatment of osteoporosis. However, the optimal inter-dose interval has not been established. We set out to determine the duration of action of a single 5mg intravenous dose of zoledronate.

**Methods:** 50 osteopenic postmenopausal women were randomized to receive either 5mg of intravenous zoledronate or placebo. The primary endpoints were markers of bone turnover (PINP and  $\beta$ CTX); secondary endpoints were BMD at lumbar spine (LS), total hip (TH) and total body (TB). The study duration is 3 years, but the results presented herein are from a pre-specified 2-year interim analysis.

**Results:** The table shows mean (95%CI) percentage between-groups differences in turnover markers and BMD over 12, 18 and 24 months (treatment effect, all  $P < 0.0001$  for each variable, zoledronate vs placebo).

Time (mo)	$\beta$ CTX	P1NP	Oc	LS BMD	TH BMD	TB BMD
12	-57 (-70,-44)	-39 (-53,-26)	-46 (-58,-35)	4.8 (3.1,6.5)	3.7 (1.9,5.5)	1.2 (0.3,2.0)
18	-52 (-68,-37)	-47 (-61,-33)	-46 (-57,-34)	7.0 (5.3,8.7)	3.8 (2.0,5.6)	1.9 (1.0,2.8)
24	-44 (-59,-29)	-41 (-55,-27)	-40 (-52,-29)	5.7 (4.0,7.4)	3.9 (2.2,5.7)	1.7 (0.8,2.5)

Albumin-adjusted serum calcium and serum phosphate were lower, and plasma PTH was higher, in the zoledronate group than the placebo group ( $P < 0.01$  for each variable). eGFR was not different between groups.

**Conclusions:** The skeletal effects of a single 5mg dose of intravenous zoledronate persist for at least 24 months. The stability of bone turnover markers and BMD between 12 and 24 months after a dose suggest that the administration of zoledronate at intervals up to 24 months is likely to be associated with anti-fracture efficacy.