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LETTER

Bisphosphonate drug holidays in postmenopausal osteoporosis: effect on clinical fracture risk. Response to comments by Bredemeier

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Dear Editor,

We thank Dr. Bredemeier for his interest and for his comments [1] about our article entitled "Bisphosphonate drug holidays in postmenopausal osteoporosis: effect on clinical fracture risk" [2], in which we demonstrated that the risk of new clinical fractures was 40% higher in women who had taken a BP "drug holiday" in a cohort of 166 postmenopausal osteoporosis.

Dr. Bredemeier argues that if the duration of follow-up in both groups is similar, the hazard ratio (HR) should provide values similar to those observed using relative risk (RR). As indicated in the paper and as is usual, we used Cox proportional hazards models to investigate the relationships between continuation or discontinuation of osteoporosis medication and the risk of new clinical fractures, controlling for confounding factors. There is a distinction between rate and proportion. The incidence (hazard) rate is the number of new cases of disease (clinical fractures in our study) per population at risk per unit time, whereas the cumulative incidence is the proportion of new cases that develop in a given time period. We calculated the incidence (hazard) rate, whereas Dr. Bredemeier calculated the relative risk using the cumulative incidence. Using the Cox regression allowed us to gain power/precision, and this is the most commonly used multivariable survival method, as we previously indicated.

Survival without any new clinical fractures was also analyzed by means of Kaplan-Meier curves and log-rank tests. Kaplan-Meier curves are another way to estimate survival but cannot evaluate covariates like Cox model. We acknowledge that incomplete observations would have been censored. When fracture-free survival curves were compared between the two groups (censoring incomplete observations), no statistical significant difference was found (log-rank $p = 0.4035$). The table below illustrates the complete and incomplete observations.

	Patients with drug holiday	Patients still on medication
Complete observations		
Fracture during follow-up, *n* (%)	5 (16.1)	16 (11.9)
No fracture at the end of follow-up (3 years), *n* (%)	14 (45.2)	92 (68.1)
Incomplete observations, *n* (%)	12 (38.7)	27 (20.0)
Total	31	135

References

1. Bredemeier M (2017) Comments on Mignot et al.: Bisphosphonate drug holidays in postmenopausal osteoporosis: effect on clinical fracture risk. Osteoporos Int. doi: https://doi.org/10.1007/s00198-017-4263-1
2. Mignot MA, Taisne N, Legroux I, Cortet B, Paccou J (2017) Bisphosphonate drug holidays in postmenopausal osteoporosis: effect on clinical fracture risk. Osteoporos Int 28(12):3431–3438. https://doi.org/10.1007/s00198-017-4215-9

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