Table S1. Sensitivity analyses: results on primary outcome of change in joint space width (JSW) from baseline versus placebo.

Change in JSW expressed as means (SD). E (SE)=estimate of the treatment-placebo difference (standard error). CI=confidence interval.

[a]The mixed model for repeated measurements (MMRM) compared treatment groups for change in JSW over time in the intention-to-treat (ITT) set, using a covariance pattern model with an unstructured matrix, to yield between-group differences at 3 years using adjusted group means (baseline, gender, and centre as covariates).

[b]The multiple imputation method used Markov chain Monte Carlo data augmentation to impute all missing data. 100 complete data sets were generated and analysed in the ITT set using an MMRM and the results were combined for the inference.

[c]The pattern mixture model studied the impact of mechanisms associated with missing data. Patients were partitioned into groups according to missing data patterns (time of drop-out). For each data pattern, treatment groups were compared with placebo using an MMRM and estimates were averaged.

[d]The impact of patients with no post-baseline value was assessed using a sensitivity analysis in the randomised set by substituting missing JSN values in all groups with the mean value in the placebo group, and then using the same general linear model as in the main analysis.

[e]The treatment-placebo difference in primary endpoint was analysed in the per protocol set (all ITT patients without major protocol violations) using the same general linear model.

	Strontium ranelate 1 g/day	Strontium ranelate 2 g/day	Placebo
Intention to treat population (N=1371)	**n=445**	**n=454**	**n=472**
Change in JSW from baseline to end (mm)	–0.23 (0.56)	–0.27 (0.63)	–0.37 (0.59)
Main analysis (Lyon, France)			
• Difference from placebo (mm) E (SE), (95% CI)	0.14 (0.04), (0.05 to 0.23) p<0.001	0.10 (0.04), (0.02 to 0.19) p=0.018	
Mixed model for repeated measurements[a]			
• Difference from placebo (mm) E (SE), (95% CI)	0.14 (0.05), (0.04 to 0.24) p=0.004	0.10 (0.05), (0.00 to 0.20) p=0.043	
Multiple imputation[b]			
• Difference from placebo (mm) E (SE), (95% CI)	0.14 (0.05), (0.04 to 0.24) p=0.003	0.10 (0.05), (0.00 to 0.20) p=0.044	
Pattern mixture model[c]			
• Difference from placebo (mm) E (SE), (95% CI)	0.13 (0.04), (0.05 to 0.22) p=0.001	0.11 (0.04), (0.03 to 0.20) p=0.008	
Randomized set (N=1683)			
Sensitivity analysis[d]			
• Difference from placebo (mm) E (SE), (95% CI)	0.11 (0.03), (0.04 to 0.18) p=0.001	0.08 (0.03), (0.01 to 0.15) p=0.027	
Second reading (N=1371; Liege, Belgium)	**n=445**	**n=454**	**n=472**
Change in JSW from baseline to end (mm)	–0.19 (0.61)	–0.23 (0.69)	–0.34 (0.62)
• Difference from placebo (mm) E (SE), (95% CI)	0.15 (0.04), (0.07 to 0.23) p<0.001	0.12 (0.04), (0.04 to 0.20) p=0.004	
Per protocol set (N=865)[e]	**n=277**	**n=290**	**n=298**
Change in JSW from baseline to end (mm)	–0.24 (0.55)	–0.28 (0.63)	–0.40 (0.61)
• Difference from placebo (mm) E (SE), (95% CI)	0.16 (0.05), (0.05 to 0.27) p=0.003	0.13 (0.05), (0.02 to 0.24) p=0.015	