

Fig. E-1

Change in volumetric BMD and estimated strength at the spine at eighteen months according to prior bisphosphonate use. The whiskers indicate the 95% CI. NS = not significant.

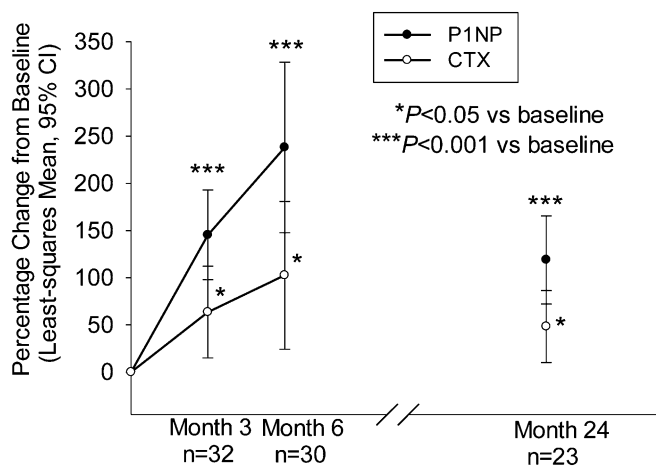


Fig E-2

Bone turnover markers over time. CTX = serum carboxyterminal cross-linking telopeptide of collagen type 1, and P1NP = serum procollagen type 1 N-terminal propeptide. The whiskers indicate the 95% CI.

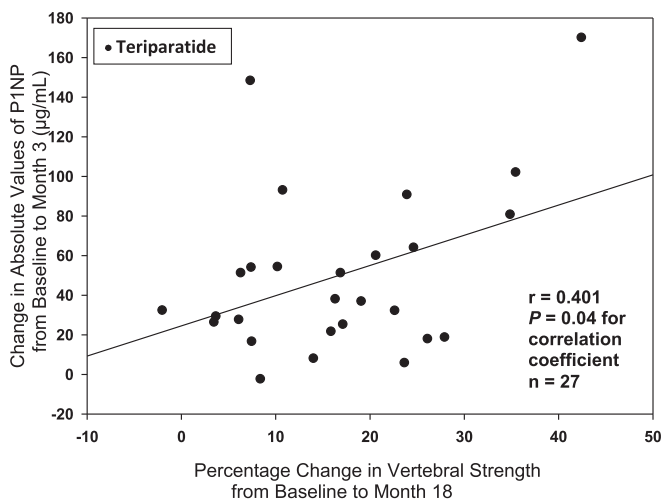


Fig. E-3

Correlation of absolute changes in P1NP (serum procollagen type 1 N-terminal propeptide) at month three and estimated vertebral strength at month eighteen.

**TABLE E-1 Percentage Change in Bone Compartments of Spine on QCT (FSA Population) \***

| Parameter              | Month-18 Completers, N = 28† | P Value | End Point, N = 30†‡    | P Value |
|------------------------|------------------------------|---------|------------------------|---------|
| Volumetric BMD         |                              |         |                        |         |
| Total                  | 10.05 (6.83 to 13.26)        | <0.001  | 9.89 (6.6 to 13.17)    | <0.001  |
| Peripheral             | 6.54 (4.13 to 8.95)          | <0.001  | 6.43 (3.93 to 8.92)    | <0.001  |
| Trabecular             | 12.61 (8.54 to 16.69)        | <0.001  | 12.38 (8.27 to 16.50)  | <0.001  |
| Estimated strength     |                              |         |                        |         |
| Total                  | 17.43 (12.09 to 22.76)       | <0.001  | 17.16 (11.70 to 22.63) | <0.001  |
| Peripheral             | 13.68 (9.52 to 17.84)        | <0.001  | 13.45 (9.24 to 17.65)  | <0.001  |
| Trabecular             | 21.15 (13.97 to 28.32)       | <0.001  | 21.05 (13.55 to 28.55) | <0.001  |
| Strength/density ratio | 6.56 (4.62 to 8.50)          | <0.001  | 6.45 (4.46 to 8.45)    | <0.001  |

\*QCT = quantitative CT, and FSA = full-set analysis. †The values are given as the least-squares mean percentage change from baseline, with the 95% CI in parentheses. ‡Includes data for those subjects who dropped out prior to month 18 and had a follow-up QCT scan at the time they discontinued.

**TABLE E-2 Percentage Change in Bone Compartments of Hip on QCT (FSA Population) \***

| Site                   | Month-18 Completers, N = 25† | P Value | End Point, N = 26†‡   | P Value |
|------------------------|------------------------------|---------|-----------------------|---------|
| Volumetric BMD         |                              |         |                       |         |
| Total                  | 2.22 (0.37 to 4.06)          | 0.021   | 2.26 (0.46 to 4.07)   | 0.017   |
| Peripheral             | −0.21 (−1.74 to 1.33)        | 0.783   | −0.17 (−1.67 to 1.33) | 0.815   |
| Trabecular             | 4.91 (2.26 to 7.56)          | <0.001  | 4.98 (2.39 to 7.57)   | <0.001  |
| Estimated strength     |                              |         |                       |         |
| Total                  | 2.54 (0.06 to 5.01)          | 0.045   | 2.60 (0.17 to 5.02)   | 0.037   |
| Peripheral             | 1.24 (−0.24 to 2.72)         | 0.096   | 1.24 (−0.20 to 2.68)  | 0.087   |
| Trabecular             | 1.33 (−0.52 to 3.18)         | 0.150   | 1.39 (−0.44 to 3.22)  | 0.129   |
| Strength/density ratio | 0.29 (−0.80 to 1.38)         | 0.581   | 0.31 (−0.75 to 1.37)  | 0.552   |

\*QCT = quantitative CT, and FSA = full-set analysis. †The values are given as the least-squares mean percentage change from baseline, with the 95% CI in parentheses. ‡Includes data for those subjects who dropped out prior to month 18 and had a follow-up QCT scan at the time they discontinued.

**TABLE E-3 Percentage Change in Areal BMD (FSA Population) \***

| Site                | Month-18 Completers, N = 28† | P Value | Month-24 Completers, N = 25† | P Value | End Point, N = 29†‡    | P Value |
|---------------------|------------------------------|---------|------------------------------|---------|------------------------|---------|
| Lumbar spine        | 7.22 (4.80 to 9.63)          | <0.001  | 8.70 (6.74 to 10.67)         | <0.001  | 8.18 (6.00 to 10.36)   | <0.001  |
| Femoral neck        | 2.79 (0.72 to 4.86)          | 0.011   | 2.76 (0.02 to 5.51)          | 0.049   | 2.61 (0.23 to 5.00)    | 0.033   |
| Total hip           | 0.29 (−1.26 to 1.84)         | 0.700   | 1.48 (−0.27 to 3.23)         | 0.092   | 1.03 (−0.58 to 2.64)   | 0.197   |
| 1/3 distal radius   | −2.07 (−3.65 to −0.49)       | 0.013   | −2.73 (−4.54 to −0.92)       | 0.005   | −2.73 (−4.39 to −1.08) | 0.002   |
| Ultra-distal radius | −1.89 (−4.22 to 0.44)        | 0.106   | 0.78 (−1.27 to 2.82)         | 0.436   | 0.09 (−2.08 to 2.25)   | 0.937   |

\*FSA = full-set analysis. †The values are given as the least-squares mean percentage change from baseline, with the 95% CI in parentheses. ‡Includes data for those subjects who dropped out prior to month 18 and had a follow-up DXA scan at the time they discontinued.

**TABLE E-4 Percentage Change in Bone Turnover Markers (BTMs) (FSA Population) \***

| BTM                      | Month 3, N = 32†            | P Value | Month 6, N = 30†             | P Value | Month 24, N = 23†           | P Value | End Point, N = 32†‡         | P Value |
|--------------------------|-----------------------------|---------|------------------------------|---------|-----------------------------|---------|-----------------------------|---------|
| P1NP ( $\mu\text{g/L}$ ) | 145.35<br>(97.67 to 193.03) | <0.001  | 238.04<br>(147.71 to 328.36) | <0.001  | 118.91<br>(72.25 to 165.57) | <0.001  | 110.52<br>(54.27 to 166.76) | <0.001  |
| CTX ( $\text{ng/mL}$ )   | 63.53<br>(15.06 to 112.01)  | 0.012   | 102.56<br>(24.25 to 180.87)  | 0.012   | 48.28<br>(10.15 to 86.42)   | 0.016   | 33.89<br>(-15.36 to 83.14)  | 0.169   |

\*FSA = full-set analysis, P1NP = serum procollagen type 1 N-terminal propeptide, and CTX = serum carboxyterminal cross-linking telopeptide of collagen type 1. †The values are given as the least-squares mean percentage change from baseline, with the 95% CI in parentheses. ‡Includes data for those subjects who dropped out prior to month 18 and had a follow-up BTM assessment at the time they discontinued.