Supplementary Table S1. Listing of patients with serious adverse events possibly related to allocated treatment at 72 weeks

| Symptom | Treatment | Age (y) | Prior bisphosphonates | Registration date | Onset date | Severity | Treatment for adverse events | Outcome | Causality |
|---|---|---|---|---|---|---|---|---|---|
| Nausea | Teriparatide | 86 | Not used | 2016/9/12 | 2017/11/21 | Gr3 | With | Resolved | Possible |
| Pancreatic carcinoma | Teriparatide | 88 | Not used | 2016/3/24 | 2017/6/5 | Gr5 | With | Death | Possible |
| Gastric ulcer | Alendronate | 79 | Used | 2016/10/4 | 2016/11/1 | Gr3 | With | Resolved | Possible |
| Herpes zoster | Alendronate | 81 | Not used | 2016/1/12 | 2017/1/12 | Gr3 | Without | Resolved | Possible |
| Cardiac failure acute | Alendronate | 82 | Not used | 2016/8/4 | 2017/12/11 | Gr5 | With | Death | Possible |
| Death (cause unknown) | Alendronate | 84 | Not used | 2016/7/29 | 2016/10/22 | Gr5 | Without | Death | Possible |

Supplementary Table S2. Baseline characteristics of postmenopausal women with severe osteoporosis with and without radiographs at 72 weeks

| | With radiographs (N=624) | | Without radiographs (N=359) | |
| --- | --- | --- | --- | --- |
| | Mean | SD | Mean | SD |
| Age (y) | 81.3 | 4.4 | 81.7 | 4.9 |
| Age at menopause (y) | 49.4 | 4.5 | 49.4 | 4.2 |
| Time from menopause (y) | 32.0 | 6.3 | 32.3 | 6.8 |
| Count of prevalent vertebral fractures | 1.8 | 2.0 | 1.5 | 1.8 |
| 0 | 29.6% | | 36.8% | |
| 1 | 27.2% | | 26.5% | |
| 2 | 16.5% | | 15.0% | |
| 3 | 9.9% | | 10.6% | |
| 4 | 5.9% | | 4.7% | |
| 5 or more | 10.7% | | 6.4% | |
| Maximum grade of prevalent vertebral fractures | | | | |
| Grade 1 | 9.5% | | 9.2% | |
| Grade 2 | 17.9% | | 14.8% | |
| Grade 3 | 42.9% | | 39.3% | |
| History of proximal femoral fractures | 14.3% | | 13.1% | |
| Prior treatment | 55.4% | | 51.5% | |
| Prior bisphosphonates | 30.3% | | 29.2% | |
| Comorbidities | | | | |
| Hypertension | 39.7% | | 34.0% | |
| Diabetes | 8.7% | | 8.6% | |
| Dyslipidemia | 17.3% | | 12.0% | |
| Rheumatoid arthritis | 0.8% | | 0.8% | |
| Osteoarthritis | 0.2% | | 0.0% | |
| Others | 29.5% | | 24.0% | |
| BMD at L2-L4 (T-score) | -2.3 | 1.4 | -2.3 | 1.5 |

Supplementary Table S3. Senstivitity analysis for the robustness of the primary analysis

| | Teriparatide | | | | Alendronate | | | | Rate ratio | 95% CI | | p |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Count | Persons | Person-years | Annual incidence rate | Count | Persons | Person-years | Annual incidence rate | | | | |
| Sensitivity analysis | | | | | | | | | | | | |
| Without covariate adjustment | 56 | 45 | 419.9 | 0.1249 | 96 | 73 | 553.6 | 0.1662 | 0.74 | 0.57 | 0.95 | 0.02 |
| Per-protocol population | 55 | 44 | 416.8 | 0.1320 | 94 | 71 | 539.1 | 0.1744 | 0.75 | 0.57 | 0.98 | 0.04 |
| Excluding adherence<70% | 23 | 17 | 197.3 | 0.1166 | 70 | 51 | 417.7 | 0.1676 | 0.72 | 0.55 | 0.95 | <0.01 |

*GEE-Poisson regression adjusted for age, counts and maximum grade of prevalent vertebral fractures,
  history of proximal femoral fractures and BMD as covariates and individual and institute as cluster
†Teriparatide and alendronate groups after excluding adherence<70% consisted of 142 and 302 patients, respectively

Supplementary Table 4. Comparison of BMD of lumbar, total hip, femoral neck and forearm between teriparatide and alendronate arms at 72 weeks

| | | Teriparatide (N=489) | | | | | | Alendronate (N=496) | | | | | | Difference | p for difference |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Median | IQR | n | p | Mean | SD | Median | IQR | n | p | | |
| **L2-L4** | | | | | | | | | | | | | | | |
| 0 weeks | T-score | -2.30 | 1.42 | -2.45 | 1.80 | 267 | | -2.39 | 1.42 | -2.64 | 1.87 | 266 | | | |
| 24 weeks | T-score | -2.06 | 1.42 | -2.25 | 1.93 | 192 | | -2.17 | 1.40 | -2.42 | 1.70 | 228 | | 0.11 | 0.30 |
| | Change from 0 week | 0.20 | 0.45 | 0.12 | 0.39 | 187 | <0.01 | 0.18 | 0.43 | 0.12 | 0.38 | 224 | <0.01 | 0.03 | |
| | % change from 0 week | 5.9% | 0.56 | 4.1% | 0.17 | 187 | | 5.5% | 1.38 | 4.6% | 0.15 | 224 | | 0.4% | |
| 48 weeks | T-score | -2.04 | 1.36 | -2.13 | 1.88 | 165 | | -2.10 | 1.42 | -2.33 | 1.87 | 220 | | 0.06 | 0.32 |
| | Change from 0 week | 0.28 | 0.58 | 0.25 | 0.45 | 159 | <0.01 | 0.26 | 0.54 | 0.18 | 0.38 | 216 | <0.01 | 0.02 | |
| | % change from 0 week | 10.7% | 0.67 | 8.9% | 0.21 | 159 | | 9.7% | 1.33 | 6.4% | 0.17 | 216 | | 1.0% | |
| 72 weeks | T-score | -1.96 | 1.41 | -2.09 | 1.78 | 151 | | -2.05 | 1.43 | -2.22 | 1.84 | 208 | | 0.09 | 0.34 |
| | Change from 0 week | 0.34 | 0.55 | 0.29 | 0.49 | 146 | <0.01 | 0.33 | 0.58 | 0.24 | 0.50 | 203 | <0.01 | 0.01 | |
| | % change from 0 week | 32.1% | 3.06 | 9.9% | 0.24 | 146 | | 13.8% | 1.54 | 9.1% | 0.23 | 203 | | 18.3% | |
| **Total hip** | | | | | | | | | | | | | | | |
| 0 weeks | T-score | -2.81 | 1.09 | -2.69 | 1.29 | 166 | | -2.85 | 1.07 | -2.72 | 1.52 | 161 | | | |
| 24 weeks | T-score | -2.77 | 1.08 | -2.67 | 1.35 | 139 | | -2.78 | 1.14 | -2.67 | 1.53 | 164 | | 0.01 | 0.98 |
| | Change from 0 week | 0.05 | 0.43 | 0.03 | 0.23 | 120 | 0.06 | -0.03 | 0.30 | -0.02 | 0.27 | 143 | 0.37 | 0.08 | |
| | % change from 0 week | 1.0% | 0.13 | 1.1% | 0.10 | 120 | | -1.0% | 0.12 | -0.7% | 0.10 | 143 | | 1.9% | |
| 48 weeks | T-score | -2.68 | 0.97 | -2.55 | 1.17 | 129 | | -2.70 | 1.05 | -2.62 | 1.50 | 160 | | 0.02 | 0.62 |
| | Change from 0 week | 0.06 | 0.28 | 0.04 | 0.25 | 108 | 0.03 | 0.04 | 0.27 | 0.00 | 0.32 | 134 | 0.13 | 0.02 | |
| | % change from 0 week | 1.0% | 0.15 | 1.5% | 0.10 | 108 | | 3.6% | 0.32 | 0.5% | 0.12 | 134 | | -2.7% | |
| 72 weeks | T-score | -2.71 | 1.11 | -2.66 | 1.13 | 118 | | -2.70 | 1.10 | -2.65 | 1.49 | 149 | | -0.01 | 0.43 |
| | Change from 0 week | 0.02 | 0.29 | 0.06 | 0.28 | 102 | 0.25 | 0.04 | 0.33 | 0.04 | 0.34 | 127 | 0.09 | -0.02 | |
| | % change from 0 week | 1.0% | 0.11 | 2.0% | 0.13 | 102 | | 6.4% | 0.51 | 1.2% | 0.15 | 127 | | -5.4% | |
| **Femoral neck** | | | | | | | | | | | | | | | |
| 0 weeks | T-score | -3.23 | 1.07 | -3.29 | 1.32 | 251 | | -3.21 | 1.05 | -3.28 | 1.35 | 231 | | | |
| 24 weeks | T-score | -3.26 | 1.08 | -3.25 | 1.44 | 188 | | -3.16 | 1.03 | -3.25 | 1.25 | 202 | | -0.10 | 0.74 |
| | Change from 0 week | -0.01 | 0.49 | 0.01 | 0.36 | 184 | 0.65 | -0.02 | 0.42 | 0.01 | 0.41 | 194 | 0.67 | 0.01 | |
| | % change from 0 week | -1.8% | 0.52 | 0.5% | 0.11 | 184 | | -3.1% | 0.38 | 0.3% | 0.13 | 194 | | 1.2% | |
| 48 weeks | T-score | -3.22 | 1.05 | -3.28 | 1.38 | 162 | | -3.13 | 1.06 | -3.19 | 1.28 | 196 | | -0.09 | 0.76 |
| | Change from 0 week | 0.01 | 0.56 | 0.03 | 0.40 | 158 | 0.99 | -0.01 | 0.53 | 0.02 | 0.39 | 191 | 0.97 | 0.01 | |
| | % change from 0 week | 2.1% | 0.28 | 1.0% | 0.12 | 158 | | -1.6% | 0.41 | 1.0% | 0.13 | 191 | | 3.6% | |
| 72 weeks | T-score | -3.23 | 1.06 | -3.28 | 1.29 | 151 | | -3.12 | 1.09 | -3.19 | 1.28 | 181 | | -0.11 | 0.63 |
| | Change from 0 week | 0.02 | 0.51 | 0.03 | 0.41 | 147 | 1.00 | 0.02 | 0.52 | 0.04 | 0.39 | 174 | 0.63 | 0.01 | |
| | % change from 0 week | -0.8% | 0.17 | 0.8% | 0.12 | 147 | | -0.9% | 0.43 | 1.4% | 0.15 | 174 | | 0.1% | |
| **Forearm** | | | | | | | | | | | | | | | |
| 0 weeks | T-score | -4.93 | 1.35 | -4.96 | 1.79 | 103 | | -5.09 | 1.51 | -5.00 | 1.84 | 112 | | | |
| 24 weeks | T-score | -4.73 | 1.37 | -4.72 | 1.95 | 70 | | -5.08 | 1.48 | -5.03 | 1.71 | 94 | | 0.35 | 0.09 |
| | Change from 0 week | 0.22 | 0.70 | 0.10 | 0.34 | 70 | 0.01 | 0.05 | 0.58 | 0.00 | 0.40 | 94 | 0.44 | 0.16 | |
| | % change from 0 week | 3.9% | 0.11 | 2.0% | 0.07 | 70 | | 0.3% | 0.09 | 0.0% | 0.07 | 94 | | 3.6% | |
| 48 weeks | T-score | -4.86 | 1.33 | -5.03 | 1.67 | 58 | | -4.92 | 1.28 | -4.94 | 1.54 | 88 | | 0.06 | 0.47 |
| | Change from 0 week | 0.15 | 0.73 | 0.02 | 0.38 | 58 | 0.05 | 0.20 | 0.84 | 0.09 | 0.35 | 88 | 0.01 | -0.05 | |
| | % change from 0 week | 2.0% | 0.12 | 0.5% | 0.08 | 58 | | 2.5% | 0.11 | 1.7% | 0.08 | 88 | | -0.5% | |
| 72 weeks | T-score | -4.81 | 1.26 | -4.86 | 1.74 | 56 | | -4.93 | 1.28 | -4.93 | 1.46 | 83 | | 0.12 | 0.48 |
| | Change from 0 week | 0.15 | 0.72 | 0.01 | 0.31 | 56 | 0.06 | 0.20 | 0.87 | 0.04 | 0.40 | 83 | 0.01 | -0.05 | |
| | % change from 0 week | 1.3% | 0.13 | 0.2% | 0.06 | 56 | | 2.8% | 0.13 | 0.7% | 0.08 | 83 | | -1.4% | |

*IQR: interquartile range