| **Study Reference** | **Participant Characteristics** | **Intervention; Duration** | **Discontinuations due to AE****Risk in Treatment Group; Risk in Control Group****(RR [95% CI])** | **Serious AEs****Risk in Treatment Group; Risk in Control Group****(RR [95% CI])** | **Gastrointestinal Adverse Eventsa****Risk in Treatment Group; Risk in Control Group****(RR [95% CI])** | **Other Adverse Events** | **Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Chapurlat et al, 2013284 | Women at least 1 year postmenopausal; mean age 63 years; mean T-score -1.4; unknown prior osteoporotic fractures | 150 mg ibandronate monthly; 2 years | Due to AEs (including fractures)4/71; 6/76 [0.71 (0.21 to 2.42)] | 15/71; 13/76[1.23 (0.63 to 2.41)] | NR | NR | Fair |
| McClung et al, 2004285 | Women at least 1 year postmenopausal; mean age 58 years; mean T-score 1.0; no prior osteoporotic fractures | 0.5, 1.0, 2.5 mg ibandronate daily; 2 years | Any withdrawals because of AEs: 5/161; 5/165; 7/163; 9/159[0.55 (0.19 to 1.60)][0.54 (0.18 to 1.56)][0.76 (0.29 to 1.99)]Percentage of all subjectswho withdrew from study medication because of an AE was numerically higher in the placebo group (9%, 5%,5%, and 7% in the placebo, 0.5-, 1-, and 2.5-mg groups,respectively), although the differences between placebo andibandronate groups did not reach significance. | Any Serious AEs6/161;13/165;5/163; 8/159[0.74 (0.26 to 2.09)][1.57 (0.67 to 3.68)][0.61 (0.20 to 1.82)]Any drug related serious AEs0/161; 0/165; 0/163; 0/159RR not calculable  | Dyspepsia16/161; 14/165; 15/163; 14/159[1.13 (0.57 to 2.23)[0.96 (0.47 to 1.96)][1.05 (0.52 to 2.09)]Gastroenteritis 9/161; 4/165; 5/163; 6/159[1.48 (0.54 to 4.07)][0.64 (0.18 to 2.23][0.81 (0.25 to 2.61)]Nausea6/161;1/165; 4/163; 3/159[1.98 (0.50 to 7.76)][0.32 (0.03 to 3.06)][1.30 (0.30 to 5.72)]GI Pain2/161; 0/165; 4/163; 4/159[0.49 (0.09 to 2.66)][0.11 (0.01 to 1.98)][0.98 (0.25 to 3.83)]GI disorder1/161; 2/165; 0/163; 3/159[0.33 (0.03 to 3.13)][0.64 (0.11 to 3.79)][0.14 (0.01 to 2.68)]Eructation1/161; 1/165; 1/163; 1/159[0.99 (0.06 to 15.65)][0.96 (0.06 to 15.28)][0.98 (0.06 to 15.47)] | NR | Fair |
| McClung et al, 2004285(continued) |    |    |    |    | Gastritis0/161; 1/165; 2/163; 1/159[0.33 (0.01 to 8.02)][0.96 (0.06 to 15.28)][1.95 (0.18 to 21.30)]Dysphagia2/161; 1/165; 1/163; 0/159[4.94 (0.24 to 102.06)][2.89 (0.12 to 70.46)][2.91 (0.12 to 71.32)]Vomiting2/161; 0/165; 1/163; 0/159[4.94 (0.24 to 102.06)]1mg vs. Placebo: RR not calculable[2.92 (0.12 to 71.32)]Esophagitis1/161; 0/165; 1/163; 1/159[0.99 (0.06 to 15.65)][0.32 (0.01 to 7.83)][0.98 (0.06 to 15.46)]GI carcinoma0/161; 0/165; 1/163; 0/159.5mg vs. Placebo: RR not calculable1mg vs. Placebo: RR not calculable[0.98 (0.02 to 49.17)]GI hemorrhage 0/161; 0/165; 0/163; 1/159[0.33 (0.01 to 8.02)][0.32 (0.01 to 7.83)][0.33 (0.01 to 7.92)]Hemorrhage gastritis1/161; 0/165; 0/163; 0/159[2.96 (0.12 to 72.20)] |    |  |
| McClung et al, 2004285(continued) |   |   |   |   | 1mg vs. Placebo: RR not calculable2.5mg vs. Placebo: RR not calculable0.96 (0.02 to 48.29)][0.98 (0.02 to 48.87)] |   |  |
| Ravn et al, 1996286 | Women at least 10 years postmenopausal; mean age 65 years; mean T-score -0.852; no prior osteoporotic fractures | 0.25,0.5, 1.0, 2.5, or 5.0 mg ibandronate daily; 1 year | 1/30;4/30;2/30;0/30;6/30; 2/30[0.50 (0.05 to 5.22)][2.00 (0.40 to 10.11)][1.00 (0.15 to 6.64)][0.20 (0.01 to 4.00)][3.00 (0.66 to 13.69)] | 1/30; 1/30; 0/30; 2/30;1/30; 3/30[0.33 (0.04 to 3.03)][0.33 (0.04 to 3.03)][0.14 (0.01 to 2.65)][0.67 (0.12 to 3.71)][0.33 (0.04 to 3.03)] | GI AEs12/30; 17/30; 8/30; 5/30; 17/30; 11/30[1.09 (0.57 to 2.07)][1.55 (0.88 to 2.72)][0.73 (0.34 to 1.55)][0.45 (0.18 to 1.15)][1.55 (0.88 to 2.72)]Diarrhea6/30; 5/30; 2/30; 2/30; 9/30; 2/30[3.00 (0.66 to 13.69)][2.50 (0.53 to 11.89)][1.00 (0.15 to 6.64)][1.00 (0.15 to 6.64)][4.50 (1.06 to 19.11)] | Infection1/26;0/22; 0/26;0/24; 0/18; 0/25[2.8889 (0.12 to 67.76)][1.13 (0.02 to 54.72)][0.96 (0.02 to 46.76)][1.04 (0.02 to 50.43)][1.37 (0.03 to 65.94)]Death0/26;0/22; 0/26;1/24; 0/18; 1/25[0.32 (0.01 to 7.53)] | Fair |
| Reginster, et al, 2005287 | Women at least 3 years postmenopausal; mean age 64 years; mean T-score -1.14; unknown prior fracture | 50, 50/100, 100,or 150 mg ibandronate monthly; 3 months | Any AE leading to withdrawal: 0/18; 0/18; 0/36;1/36; 2/36[0.39 (0.02 to 7.71)][0.39 (0.02 to 7.71)][0.20 (0.01 to 4.03)][0.50 (0.05 to 5.27)]Any drug-related AE leading to withdrawal: 0/18; 0/18; 0/36;1/36; 2/36[0.39 (0.02 to 7.71)[0.39 (0.02 to 7.71)[0.20 (0.01 to 4.03)][0.50 (0.05 to 5.27)] | 0/18; 0/18; 0/36; 0/36; 0/36RR not calculable | Upper GI AEs within 3 days of treatment: 0/18; 4/18; 8/36; 9/36; 6/36[0.15 (0.01 to 2.52)][1.33 (0.43 to 4.13)][1.33 (0.51 to 3.46)][1.50 (0.60 to 3.78)]Upper GI AEs anytime during treatment: 3/18; 11/18;15/36; 15/36; 12/36[0.50 (0.16 to 1.55)][1.83 (1.02 to 3.31)][1.25 (0.68 to 2.28)][1.25 (0.68 to 2.28)] | Deaths0/18; 0/18; 0/36; 0/36; 0/36[1.95 (0.04 to 94.37)][1.9474 (0.04 to 94.37)][1.00 (0.02 to 49.08)][1.00 (0.02 to 49.08)] | Fair |
| Riis et al, 2001288 | Women at least 5 years postmenopausal; mean age 67 years; on average spinal T-score was below -3.2; unknown prior fracture | Continuoustherapy with 2.5 mg of ibandronate daily orintermittent cyclical therapy with 20 mg of ibandronateevery other day for the first 24 days out of every 3 months,followed by a 9-week period without active drug; 2 years | NR | NR | No differences betweenContinuous treatment, intermittent treatment, and placeboDuring the first 12 months, the ibandronate treated groups showed a numerically higher incidence of diarrhea compared with the placebo groups. Incidence of diarrhea was lower during the second year | Deaths1/81; 0/78; 1/81[1.00 (0.06 to 15.72)][0.35 (0.01 to 8.37)] | Fair |
| Tanko et al 2003289 | Women 1-10 years postmenopausal; mean age 55 years; mean T-score for lumbar spine 1.03; no prior osteoporotic fractures | 5, 10,or 20 mg ibandronate weekly; 2 years | Withdrawals due to AEs related to treatment: 8 | 12% experienced a serious AE, but none were assessed as related to study drug (6 withdrew as a result of serious AE) | Gastrointestinal AEs6%; 5%; 3%; 3% | NR | Fair |
| Thiebaud et al 1997290 | Women at least 5 years postmenopausal; mean age 64 years; mean T-score 0.71 lumbar spine; no prior osteoporotic fractures | 0.25,0.5, 1.0, or 2.0 mg ibandronate every 3 months; 1 year | 7 withdrew because of AEs | 3 non-drug related Serious AEs | 6/24; 6/27; 7/26; 3/23; 4/26No differences between the groups emerged[1.63 (0.52 to 5.07][1.44 (0.46 to 4.54][1.75 (0.58 to 5.27][0.85 (0.21 to 3.40)] | NR | Fair |

**Abbreviations:** AE=adverse event; CI=confidence interval; GI=gastrointestinal; mg=milligram; NR=not reported; RR=risk ratio.