| **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 subjects  who 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 AEs  6/161;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 AEs  0/161; 0/165; 0/163; 0/159  RR not calculable | Dyspepsia  16/161; 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)]  Nausea  6/161;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 Pain  2/161; 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 disorder  1/161; 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)]  Eructation  1/161; 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) |  |  |  |  | Gastritis  0/161; 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)]  Dysphagia  2/161; 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)]  Vomiting  2/161; 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)]  Esophagitis  1/161; 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 carcinoma  0/161; 0/165; 1/163; 0/159  .5mg vs. Placebo: RR not calculable  1mg 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 gastritis  1/161; 0/165; 0/163; 0/159  [2.96 (0.12 to 72.20)] |  |  |
| McClung et al, 2004285  (continued) |  |  |  |  | 1mg vs. Placebo: RR not calculable  2.5mg vs. Placebo: RR not calculable  0.96 (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 AEs  12/30; 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)]  Diarrhea  6/30; 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)] | Infection  1/26;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)]  Death  0/26;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; 0/36  RR 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)] | Deaths  0/18; 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 between  Continuous treatment, intermittent treatment, and placebo  During 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 | Deaths  1/81; 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 AEs  6%; 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; 4/26  No 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.