| **Author, Year, Drug, Trial name** | **Adverse events reported** |
| --- | --- |
| Abrahamsen et al., 2010430  Alendronate (Fosamax) | Alendronate vs Untreated: Subtrochanteric or diaphyseal fractures: 1.0%(412/39,567) vs 0.4%(637/158,268) |
| Adachi et al., 2009361  Alendronate (Fosamax) | Alendronate monohydrate 10 mg/day vs Placebo: Any adverse event: 57.0%(166/291) vs 51.7%(76/147) Breast cancer: 0.7%(2/291) vs 0.0%(0/147) Death: 0.0%(0/291) vs 0.0%(0/147) Diverticulitis: 0.3%(1/291) vs 0.0%(0/147) Dyspepsia: 7.9%(23/291) vs 0.0%(0/147) Esophageal spasm: 0.3%(1/291) vs 0.0%(0/147) Non-serious upper GI bleed: 0.3%(1/291) vs 0.0%(0/147) Serious adverse event: 1.4%(4/291) vs 0.7%(1/147) Serious upper GI event: 20.3%(59/291) vs 12.9%(19/147) Upper GI event: 22.7%(66/291) vs 20.4%(30/147) Withdrawals: 18.6%(54/291) vs 11.6%(17/147) |
| Hagino et al., 2009487  Alendronate (Fosamax) | Alendronate 5 mg vs Minodronate 1 mg: Any adverse event: 84.4%(114/135) vs 88.8%(119/134) Abnormal lab data: 21.5%(29/135) vs 29.1%(39/134) Drug related GI AE: 9.6%(13/135) vs 14.2%(19/134) Gastrointestinal adverse event: 37.0%(50/135) vs 39.6%(53/134) Serious adverse event: 2.2%(3/135) vs 4.5%(6/134) Withdrawals: 10.4%(14/135) vs 8.2%(11/134) |
| Heckbert et al., 2008488  Alendronate (Fosamax) | Alendronate (current user) vs No alendronate: Atrial fibrillation: all: 47.4%(27/57) vs 42.1%(672/1,598) |
| Lems et al., 2006489  Alendronate (Fosamax) | Alendronate 5 mg/day + Calcium 1000 mg/day + Vitamin D 400 mg/day vs Placebo + Calcium 1000 mg/day + Vitamin D 400 mg/day: Any adverse event: 68.1%(64/94) vs 72.5%(50/69) Any serious adverse event: 12.8%(12/94) vs 17.4%(12/69) Cardiovascular disease: 4.3%(4/94) vs 8.7%(6/69) Dyspepsia: 18.1%(17/94) vs 14.5%(10/69) Gastroenteritis: 1.1%(1/94) vs 2.9%(2/69) Infection: 2.1%(2/94) vs 0.0%(0/69) Malignancy: 0.0%(0/94) vs 1.4%(1/69) New incident vertebral deformities: 9.6%(9/94) vs 2.9%(2/69) Other: 11.7%(11/94) vs 17.4%(12/69) Patients with upper GI effects: 17.0%(16/94) vs 17.4%(12/69) Stomatitis: 1.1%(1/94) vs 1.4%(1/69) Ulcer: 3.2%(3/94) vs 2.9%(2/69) Upper GI symptoms: 2.1%(2/94) vs 1.4%(1/69) Withdrawals: 16.0%(15/94) vs 24.6%(17/69) Withdrawals due to adverse events: 16.0%(15/94) vs 21.7%(15/69) |
| Papaioannou et al., 200855  Alendronate (Fosamax)  Trial: CFOS | Alendronate 70 mg/week + Calcium 1000 mg + Vitamin D 800 IU vs Placebo 70 mg/week + Calcium 1000 mg + Vitamin D 800 IU: Any adverse event: 55.6%(15/27) vs 65.5%(19/29) Any serious adverse event: 25.9%(7/27) vs 10.3%(3/29) Bronchial superinfection: 3.7%(1/27) vs 0.0%(0/29) Constipation: 3.7%(1/27) vs 3.4%(1/29) Difficulty swallowing: 3.7%(1/27) vs 0.0%(0/29) Esophagitis: 3.7%(1/27) vs 0.0%(0/29) Exacerbation of cystic fibrosis: 11.1%(3/27) vs 10.3%(3/29) GI upset: 3.7%(1/27) vs 0.0%(0/29) Hypoglycemic seizure: 3.7%(1/27) vs 0.0%(0/29) Intestinal obstruction: 3.7%(1/27) vs 3.4%(1/29) Nausea and/or vomiting: 11.1%(3/27) vs 13.8%(4/29) Reflux: 3.7%(1/27) vs 0.0%(0/29) Stomach pain/burn: 3.7%(1/27) vs 3.4%(1/29) Withdrawals: 14.8%(4/27) vs 17.2%(5/29) |
| Yan et al., 2009490  Alendronate (Fosamax) | Alendronate 70 mg/week + Calcium 500 mg/day + Vitamin D 200 IU/day vs Placebo week + Calcium 500 mg/day + Vitamin D 200 IU/day: Any adverse event: 43.2%(121/280) vs 36.8%(103/280) Abdominal distention: 2.5%(7/280) vs 0.7%(2/280) Abdominal pain: 6.8%(19/280) vs 4.6%(13/280) Acid regurgitation: 1.8%(5/280) vs 3.6%(10/280) Dyspepsia: 1.1%(3/280) vs 2.9%(8/280) Nausea: 4.3%(12/280) vs 2.9%(8/280) Upper GI event: 16.8%(47/280) vs 15.4%(43/280) Vomiting: 0.4%(1/280) vs 0.7%(2/280) |
| Bunch et al., 2009491  Bisphosphonates | Bisphosphonate (angiographic database) vs Bisphosphonate (health plan database) vs No bisphosphonate (angiographic database) vs No bisphosphonate (health plan database): Atrial Fibrillation: 10.2%(10/98) vs 2.9%(220/7,489) vs 10.1%(964/9,525) vs 2.6%(792/29,996) Death: 32.7%(32/98) vs 1.8%(134/7,489) vs 18.8%(1,791/9,525) vs 2.0%(606/29,996) Myocardial infarction: 10.2%(10/98) vs 0.9%(68/7,489) vs 7.8%(739/9,525) vs 1.1%(343/29,996) |
| Cardwell et al., 2010363  Bisphosphonates | Bisphosphonates vs Control: Esophageal cancer: 0.2%(79/41,826) vs 0.2%(72/41,826) Gastric cancer: 0.1%(37/41,826) vs 0.1%(43/41,826) |
| Cartsos et al., 2008492  Bisphosphonates | Intravenous bisphosphonate: Cancer Group vs Intravenous bisphosphonate: Osteoporosis group vs No bisphosphonate: Cancer Group vs No bisphosphonate: Osteoporosis group vs Oral bisphosphonate: Cancer Group vs Oral bisphosphonate: Osteoporosis group: Inflammatory necrosis of jaw: 0.5%(39/8,207) vs 0.5%(9/1,751) vs 0.1%(251/235,553) vs 0.1%(339/263,352) vs 0.1%(31/24,579) vs 0.1%(150/176,889) Surgery: Cancer Process: 0.1%(6/8,533) vs 0.0%(0/1,853) vs 0.1%(161/235,553) vs 0.0%(105/263,352) vs 0.0%(11/25,025) vs 0.0%(58/179,827) Surgery: Necrotic Process: 0.2%(20/8,533) vs 0.2%(4/1,853) vs 0.0%(81/235,553) vs 0.0%(73/263,352) vs 0.0%(7/25,025) vs 0.0%(43/179,827) |
| Green et al., 2010362  Bisphosphonates | Bisphosphonates vs Control: Colorectal cancer: 15.1%(276/1,831) vs 16.8%(10365/61,832) Esophageal cancer: 20.7%(90/435) vs 16.6%(2,864/17,240) Stomach cancer: 15.4%(49/319) vs 16.8%(1,969/11,706) |
| McHorney et al., 2007298  Bisphosphonates | Bisphosphonates: Non-adherence: 44.6%(453/1,015) Non-adherence due to adverse events: 6.6%(67/1,015) |
| Payer et al., 2009493  Bisphosphonates, None of the interventions | Bisphosphonates: GI and muscular AE: 33.0%(672/2,035) Gastrointestinal symptoms: 28.0%(570/2,035) Muscular side effects: 32.0%(651/2,035) Symptoms of Reflux: 37.0%(753/2,035) Withdrawals due to adverse events: 0.0%(0/2,035) |
| Eisman et al., 2008494  Ibandronate (Boniva)  Trial: DIVA | Intravenous ibandronate 2 mg every 2mo plus oral placebo + Calcium 500 mg + Vitamin D 400 IU vs Intravenous ibandronate 3 mg every 3mo plus oral placebo + Calcium 500 mg + Vitamin D 400 IU vs Intravenous placebo plus 2.5 mg daily oral ibandronate + Calcium 500 mg + Vitamin D 400 IU: Any adverse event: 88.6%(397/448) vs 85.3%(400/469) vs 87.7%(408/465) Anemia: 0.2%(1/448) vs 0.0%(0/469) vs 0.0%(0/465) Any serious adverse event: 16.3%(73/448) vs 13.2%(62/469) vs 14.4%(67/465) Death due to acute pancreatitis: 0.2%(1/448) vs 0.0%(0/469) vs 0.0%(0/465) Death due to gallbladder cancer: 0.0%(0/448) vs 0.0%(0/469) vs 0.2%(1/465) Death due to myocardial infarction: 0.2%(1/448) vs 0.4%(2/469) vs 0.0%(0/465) Death due to pulmonary edema: 0.0%(0/448) vs 0.0%(0/469) vs 0.2%(1/465) Death due to pulmonary embolism: 0.2%(1/448) vs 0.0%(0/469) vs 0.0%(0/465) Death due to ventricular arrhythmia and aortic dissection: 0.0%(0/448) vs 0.0%(0/469) vs 0.2%(1/465) Drug hypersensitivity: 0.0%(0/448) vs 0.2%(1/469) vs 0.0%(0/465) Esophageal ulcer: 0.0%(0/448) vs 0.2%(1/469) vs 0.0%(0/465) Gastric ulcer: 0.2%(1/448) vs 0.0%(0/469) vs 0.0%(0/465) Gastritis: 0.0%(0/448) vs 0.4%(2/469) vs 0.0%(0/465) Gastrointestinal ulcer: 0.2%(1/448) vs 0.0%(0/469) vs 0.0%(0/465) General flu-like symptoms: 1.6%(7/448) vs 4.5%(21/469) vs 18.9%(88/465) Increased hepatic enzyme: 0.2%(1/448) vs 0.0%(0/469) vs 0.0%(0/465) Influenza-like illness / acute-phase reaction: 5.6%(25/448) vs 4.9%(23/469) vs 1.5%(7/465) Melena: 0.0%(0/448) vs 0.2%(1/469) vs 0.0%(0/465) Myocardial infarction: 0.0%(0/448) vs 0.4%(2/469) vs 0.0%(0/465) Osteonecrosis of jaw: 0.0%(0/448) vs 0.0%(0/469) vs 0.0%(0/465) Polymyalgia rheumatica: 0.2%(1/448) vs 0.0%(0/469) vs 0.0%(0/465) Renal adverse event: 4.5%(20/448) vs 3.2%(15/469) vs 3.9%(18/465) Temporal arteritis: 0.0%(0/448) vs 0.2%(1/469) vs 0.0%(0/465) Withdrawals: 19.4%(87/448) vs 20.7%(97/469) vs 17.4%(81/465) |
| Lewiecki et al., 2010354  Ibandronate (Boniva)  Trial: BONE, MOBILE, DIVA | Ibandronate vs Placebo: Non-serious atrial fibrillation: 0.4%(29/6,830) vs 0.5%(10/1,924) Serious atrial fibrillation: 0.4%(28/6,830) vs 0.4%(8/1,924) |
| McClung et al., 2009495  Ibandronate (Boniva) | Ibandronate 150 mg monthly + Calcium 500 mg/day + Vitamin D 400 IU/day vs Placebo + 150 mg monthly + Calcium 500 mg/day + Vitamin D 400 IU/day: Any adverse event: 77.9%(60/77) vs 77.1%(64/83) Any serious adverse event: 3.9%(3/77) vs 1.2%(1/83) Arthralgia: 15.6%(12/77) vs 9.6%(8/83) Bacterial infection: 1.3%(1/77) vs 1.2%(1/83) Chest pain: 1.3%(1/77) vs 0.0%(0/83) Death: 0.0%(0/77) vs 0.0%(0/83) Dyspepsia: 5.2%(4/77) vs 4.8%(4/83) GI disorder: 31.2%(24/77) vs 24.1%(20/83) Gastroesophageal reflux disease: 5.2%(4/77) vs 3.6%(3/83) Influenza-like illness: 5.2%(4/77) vs 0.0%(0/83) Life-threatening adverse event: 0.0%(0/77) vs 0.0%(0/83) Myalgia: 6.5%(5/77) vs 2.4%(2/83) Nausea: 6.5%(5/77) vs 3.6%(3/83) |
| Orwoll et al., 2010411  Ibandronate (Boniva)  Trial: STRONG | Ibandronate vs Placebo: Any AE: 52.9%(46/87) vs 41.7%(20/48) Acute phase reaction: 3.4%(3/87) vs 4.2%(2/48) Any serious AE not leading to death: 6.9%(6/87) vs 8.3%(4/48) Arthralgia: 5.7%(5/87) vs 10.4%(5/48) Back pain: 4.6%(4/87) vs 6.3%(3/48) Constipation: 2.3%(2/87) vs 4.2%(2/48) Deaths: 1.1%(1/87) vs 4.2%(2/48) Drug-related AE: abdominal pain: 3.4%(3/87) vs 0.0%(0/48) Nasopharyngitis: 8.0%(7/87) vs 0.0%(0/48) Nausea: 4.6%(4/87) vs 0.0%(0/48) New morphometric vertebral fractures: 1.1%(1/87) vs 4.2%(2/48) Pain in extremity: 2.3%(2/87) vs 4.2%(2/48) Upper respiratory tract infection: 3.4%(3/87) vs 2.1%(1/48) Withdrawals: due to AE: 4.6%(4/87) vs 6.3%(3/48) |
| Stakkestad et al., 2008496  Ibandronate (Boniva)  Trial: MOBILE | Oral ibandronate 100 mg/month + Calcium 500-1500 mg/day + Vitamin D 400 IU vs Oral ibandronate 150 mg/month + Calcium 500-1500 mg/day + Vitamin D 400 IU: Any adverse event: 56.0%(201/359) vs 53.1%(191/360) Chest pain: 0.0%(0/359) vs 0.3%(1/360) Death from Pancreatic cancer: 0.0%(0/359) vs 0.3%(1/360) Serious AE: 7.8%(28/359) vs 7.5%(27/360) Serious upper GI event: 0.0%(0/359) vs 0.0%(0/360) Upper GI event: 4.5%(16/359) vs 6.9%(25/360) |
| Adami et al., 2005497  Risedronate (Actonel) | Risedronate 15 mg/day vs Risedronate 5 mg/day vs Placebo: Abdominal pain: 8.0%(49/609) vs 9.1%(57/628) vs 7.2%(45/622) Duodenal ulcer: 0.7%(4/609) vs 0.0%(0/628) vs 0.3%(2/622) Duodenitis: 0.5%(3/609) vs 0.6%(4/628) vs 0.2%(1/622) Dyspepsia: 5.1%(31/609) vs 6.2%(39/628) vs 5.8%(36/622) Dysphagia: 0.5%(3/609) vs 0.6%(4/628) vs 0.6%(4/622) Esophageal ulcer: 0.0%(0/609) vs 0.2%(1/628) vs 0.0%(0/622) Esophagitis: 0.8%(5/609) vs 0.5%(3/628) vs 0.6%(4/622) GI disorder: 2.8%(17/609) vs 3.8%(24/628) vs 3.5%(22/622) GI hemorrhage: 0.2%(1/609) vs 0.0%(0/628) vs 1.0%(6/622) Gastritis: 1.5%(9/609) vs 2.1%(13/628) vs 2.1%(13/622) Hematemesis: 0.0%(0/609) vs 0.6%(4/628) vs 0.0%(0/622) Melena: 0.2%(1/609) vs 0.0%(0/628) vs 0.2%(1/622) Peptic ulcer: 0.0%(0/609) vs 0.2%(1/628) vs 0.0%(0/622) Stomach ulcer: 0.7%(4/609) vs 0.3%(2/628) vs 0.3%(2/622) Substernal chest pain: 0.2%(1/609) vs 0.3%(2/628) vs 0.3%(2/622) |
| Barrera et al., 2005498  Risedronate (Actonel)  Trial: PEM | Risedronate 5mg/d or 30 mg/d: AEs: all: 3.1%(405/13,180) Allergy: 0.0%(2/13,180) Anemia: 0.0%(1/13,180) Conjunctivitis: 0.0%(3/13,180) Constipation: 1.2%(153/13,180) Deaths: cerebral vascular accident: 0.2%(28/13,180) Deaths: chronic obstructive pulmonary disease: 0.2%(30/13,180) Deaths: myocardial infarction: 0.3%(34/13,180) Diarrhea: 2.3%(305/13,180) Diplopia: 0.0%(1/13,180) Dry eye: 0.0%(6/13,180) Dry skin: 0.0%(1/13,180) Duodenitis: 0.0%(1/13,180) Dyspepsia: 6.5%(858/13,180) Edema: 1.4%(183/13,180) Episcleritis: 0.0%(1/13,180) Esophageal reflux: 0.0%(1/13,180) Facial edema: 0.0%(6/13,180) Fluid retention: 0.0%(1/13,180) GI unspecified: 1.6%(210/13,180) Hair loss: 0.0%(1/13,180) Headache/migraine: 1.6%(208/13,180) Hematemesis: 0.0%(3/13,180) Intolerance: 2.4%(315/13,180) Irritation of the eye: 0.0%(1/13,180) Jaundice: 0.0%(1/13,180) Malaise/lassitude: 1.6%(214/13,180) Melena: 0.0%(1/13,180) Menorrhagia: 0.0%(1/13,180) Mouth ulcer: 0.0%(4/13,180) Myalgia: 1.1%(140/13,180) Nausea/vomiting: reported in 2-6 month of treatment: 3.9%(515/13,180) Pain abdomen: 2.2%(295/13,180) Pain joint: 1.7%(223/13,180) Painful eye: 0.0%(1/13,180) |
| Barrera et al., 2005498  Continued | Risedronate 5mg/d or 30 mg/d: Palpitation: 0.0%(1/13,180) Paresthesia: 0.0%(1/13,180) Photosensitivity: 0.0%(2/13,180) Pruritus: 0.0%(4/13,180) Rash: 1.3%(166/13,180) Rectal hemorrhage: 0.0%(1/13,180) Respiratory tract infection higher: 1.8%(243/13,180) Respiratory tract infection lower: 3.1%(407/13,180) Skin irritation: 0.0%(1/13,180) Sore eye: 0.0%(5/13,180) Sore mouth: 0.0%(2/13,180) Stevens-Johnson syndrome: 0.0%(1/13,180) Swollen tongue: 0.0%(1/13,180) Ulceration of ileostomy site: 0.0%(1/13,180) Unspecified AE: 1.2%(155/13,180) Urticaria: 0.0%(3/13,180) Visual disturbance: 0.0%(1/13,180) Discontinued drug: all: 26.0%(3,423/13,180) |
| Boonen et al., 200974  Risedronate (Actonel) | Risedronate 35 mg/wk vs Placebo: AEs: any: 70.2%(134/191) vs 73.1%(68/93) AEs: serious: 15.2%(29/191) vs 16.1%(15/93) Arthralgia: 5.8%(11/191) vs 8.6%(8/93) Atrial fibrillation: 1.0%(2/191) vs 3.2%(3/93) Back pain: 6.8%(13/191) vs 2.2%(2/93) Benign prostatic hyperplasia: 4.7%(9/191) vs 3.2%(3/93) Chest pain: 0.0%(0/191) vs 2.2%(2/93) Constipation: 8.4%(16/191) vs 5.4%(5/93) Death due to lung neoplasm: 0.0%(0/191) vs 1.1%(1/93) Death due to pulmonary embolism: 0.0%(0/191) vs 1.1%(1/93) Death due to shock: 0.0%(0/191) vs 1.1%(1/93) Death due to small lung cancer: 0.5%(1/191) vs 0.0%(0/93) Death due to sudden cardiac event: 0.5%(1/191) vs 0.0%(0/93) Headache: mild: 4.7%(9/191) vs 0.0%(0/93) Headache: moderate: 0.5%(1/191) vs 0.0%(0/93) Influenza: 5.8%(11/191) vs 5.4%(5/93) Myocardial infarction: 1.0%(2/191) vs 3.2%(3/93) Nasopharyngitis: 5.8%(11/191) vs 5.4%(5/93) Pain in extremity: 4.7%(9/191) vs 3.2%(3/93) Pulmonary embolism: 1.0%(2/191) vs 1.1%(1/93) Sudden cardiac death: 0.5%(1/191) vs 0.0%(0/93) Upper GI AEs: dyspepsia: 3.1%(6/191) vs 4.3%(4/93) Withdrawals: due to AE: 3.7%(7/191) vs 9.7%(9/93) Withdrawals: total: 8.4%(16/191) vs 19.4%(18/93) |
| Delmas et al., 2007267  Risedronate (Actonel)  Trial: IMPACT | Risedronate No reinforcement vs Risedronate Reinforcement: Death: 0.3%(3/1,154) vs 0.1%(1/1,228) Withdrawals: Total: 13.2%(152/1,154) vs 12.1%(149/1,228) Withdrawals: due to AE: 8.9%(103/1,154) vs 7.4%(91/1,228) |
| Delmas et al., 200885  Risedronate (Actonel) | Risedronate 5mg vs Risedronate 75mg: Arthralgia: 9.5%(58/613) vs 10.4%(64/616) Back pain: 10.8%(66/613) vs 8.8%(54/616) Fever or influenza-like illness: 0.0%(0/613) vs 0.6%(4/616) Moderate to severe upper GI Treatment-emergent AE: 6.2%(38/613) vs 7.5%(46/616) Treatment-emergent AE: all: 81.2%(498/613) vs 84.7%(522/616) Treatment-emergent AE: possibly or probably related serious: 0.5%(3/613) vs 0.6%(4/616) Treatment-emergent AE: resulting in death: 0.5%(3/613) vs 0.3%(2/616) Treatment-emergent AE: serious: 4.7%(29/613) vs 7.5%(46/616) Upper GI Treatment-emergent AE: 21.2%(130/613) vs 22.2%(137/616) Withdrawals: total: 14.8%(91/613) vs 14.6%(90/616) |
| Delmas et al., 200886  Risedronate (Actonel) | Risedronate 150mg a month vs Risedronate 5mg/d: AEs: all: 79.2%(515/650) vs 78.5%(504/642) AE potentially associated with acute phase reaction: 1.4%(9/650) vs 0.2%(1/642) AEs: serious AE: 6.2%(40/650) vs 4.2%(27/642) Arthralgia: 5.5%(36/650) vs 7.3%(47/642) Atrial fibrillation: 0.6%(4/650) vs 0.5%(3/642) Constipation: 5.8%(38/650) vs 7.3%(47/642) Deaths: 0.0%(0/650) vs 0.5%(3/642) Diarrhea: 8.2%(53/650) vs 4.7%(30/642) Influenza: 8.9%(58/650) vs 4.2%(27/642) Osteonecrosis of the jaw: 0.0%(0/650) vs 0.0%(0/642) Selected musculoskeletal AE: 15.5%(101/650) vs 17.1%(110/642) Upper GI tract AE: 19.8%(129/650) vs 17.1%(110/642) Upper abdominal pain: 8.2%(53/650) vs 6.1%(39/642) Withdrawals: due to AE: 8.6%(56/650) vs 9.5%(61/642) |
| Li et al., 2005499  Risedronate (Actonel) | Placebo + CaltrateD 600 mg vs Risedronate Sodium 5 mg + Caltrate D 600 mg: Withdrawals: 13.3%(4/30) vs 6.7%(2/30) Withdrawals due to adverse events: 3.3%(1/30) vs 6.7%(2/30) |
| Mok et al., 2008500  Risedronate (Actonel) | Placebo + Elemental calcium 1000 mg/day vs Risedronate 5 mg/day + Elemental calcium 1000 mg/day: Allergic skin rash: 0.0%(0/60) vs 1.7%(1/60) Confirmed esophagitis: 0.0%(0/60) vs 0.0%(0/60) Death: 5.0%(3/60) vs 3.3%(2/60) Diarrhea: 0.0%(0/60) vs 5.0%(3/60) Dizziness: 1.7%(1/60) vs 0.0%(0/60) Dyspepsia/epigastric pain: 5.0%(3/60) vs 16.7%(10/60) Endoscopic gastritis: 5.0%(3/60) vs 5.0%(3/60) Heartburn: 0.0%(0/60) vs 1.7%(1/60) Nausea: 1.7%(1/60) vs 0.0%(0/60) Skin itching: 1.7%(1/60) vs 1.7%(1/60) Transient urticaria: 1.7%(1/60) vs 0.0%(0/60) Withdrawals: 13.3%(8/60) vs 15.0%(9/60) Withdrawals due to adverse events: 0.0%(0/60) vs 3.3%(2/60) |
| Palomba et al., 200875  Risedronate (Actonel) | Placebo + 1,500 mg/d 1,25 dihydroxyvitamin 800 UI/d vs Risedronate 35 mg/week + 1,500 mg/d 1,25 dihydroxyvitamin 800 UI/d: Abdominal pain: 8.9%(4/45) vs 6.7%(3/45) Constipation: 2.2%(1/45) vs 2.2%(1/45) Death from MI: 2.2%(1/45) vs 0.0%(0/45) Dyspepsia: 4.4%(2/45) vs 4.4%(2/45) Dysphagia: 0.0%(0/45) vs 2.2%(1/45) Flatulence: 6.7%(3/45) vs 4.4%(2/45) Headache: 0.0%(0/45) vs 2.2%(1/45) Heartburn: 2.2%(1/45) vs 6.7%(3/45) Leg cramps: 2.2%(1/45) vs 0.0%(0/45) Withdrawals: 8.9%(4/45) vs 11.1%(5/45) |
| Ringe et al., 200973  Risedronate (Actonel) | Placebo + Calcium + Vitamin D 800 IU/day vs Risedronate 5 mg/day + Calcium + Vitamin D 800 IU/day: Withdrawals: 6.3%(10/158) vs 3.8%(6/158) Withdrawals due to adverse events: 0.0%(0/158) vs 0.0%(0/158) |
| Ste-Marie et al., 2009501  Risedronate (Actonel) | Risedronate 100 mg/mo + Elemental Calcium 1000 mg/day + Vitamin D 400 IU/day vs Risedronate 150 mg/mo + Elemental Calcium 1000 mg/day + Vitamin D 400 IU/day vs Risedronate 200 mg/mo + Elemental Calcium 1000 mg/day + Vitamin D 400 IU/day vs Risedronate 5 mg/day + Elemental Calcium 1000 mg/day + Vitamin D 400 IU/day: Any adverse event: 52.7%(48/91) vs 61.4%(54/88) vs 56.8%(50/88) vs 51.5%(53/103) Abdominal pain: 2.2%(2/91) vs 6.8%(6/88) vs 9.1%(8/88) vs 3.9%(4/103) Abdominal pain upper: 4.4%(4/91) vs 11.4%(10/88) vs 8.0%(7/88) vs 6.8%(7/103) Any serious adverse event: 1.1%(1/91) vs 5.7%(5/88) vs 3.4%(3/88) vs 2.9%(3/103) Arthralgia: 4.4%(4/91) vs 9.1%(8/88) vs 5.7%(5/88) vs 5.8%(6/103) Back pain: 3.3%(3/91) vs 6.8%(6/88) vs 3.4%(3/88) vs 1.9%(2/103) Cervical spine stenosis: 0.0%(0/91) vs 1.1%(1/88) vs 0.0%(0/88) vs 0.0%(0/103) Chest pain: 0.0%(0/91) vs 0.0%(0/88) vs 0.0%(0/88) vs 1.0%(1/103) Chronic bronchitis: 0.0%(0/91) vs 1.1%(1/88) vs 0.0%(0/88) vs 0.0%(0/103) Coronary artery atherosclerosis: 0.0%(0/91) vs 0.0%(0/88) vs 0.0%(0/88) vs 1.0%(1/103) Coronary artery disease: 0.0%(0/91) vs 0.0%(0/88) vs 1.1%(1/88) vs 0.0%(0/103) Death: 0.0%(0/91) vs 0.0%(0/88) vs 0.0%(0/88) vs 0.0%(0/103) Diarrhea: 7.7%(7/91) vs 4.5%(4/88) vs 10.2%(9/88) vs 2.9%(3/103) Dyspepsia: 7.7%(7/91) vs 5.7%(5/88) vs 5.7%(5/88) vs 2.9%(3/103) Erosive esophagitis: 0.0%(0/91) vs 0.0%(0/88) vs 0.0%(0/88) vs 1.0%(1/103) Headache: 2.2%(2/91) vs 6.8%(6/88) vs 5.7%(5/88) vs 4.9%(5/103) Hypertension: 0.0%(0/91) vs 0.0%(0/88) vs 1.1%(1/88) vs 0.0%(0/103) Malignant lung neoplasm: 0.0%(0/91) vs 1.1%(1/88) vs 0.0%(0/88) vs 0.0%(0/103) Moderate or severe upper GI event: 2.2%(2/91) vs 9.1%(8/88) vs 6.8%(6/88) vs 3.9%(4/103) Myalgia: 4.4%(4/91) vs 3.4%(3/88) vs 4.5%(4/88) vs 0.0%(0/103) Nasopharyngitis: 2.2%(2/91) vs 5.7%(5/88) vs 5.7%(5/88) vs 3.9%(4/103) Nausea: 3.3%(3/91) vs 3.4%(3/88) vs 8.0%(7/88) vs 1.9%(2/103) Ovarian cyst: 0.0%(0/91) vs 1.1%(1/88) vs 0.0%(0/88) vs 0.0%(0/103) Paraparesis: 0.0%(0/91) vs 1.1%(1/88) vs 0.0%(0/88) vs 0.0%(0/103) Pheochromocytoma: 1.1%(1/91) vs 0.0%(0/88) vs 0.0%(0/88) vs 0.0%(0/103) Pneumonia: 0.0%(0/91) vs 1.1%(1/88) vs 0.0%(0/88) vs 0.0%(0/103) Supraventricular tachycardia: 0.0%(0/91) vs 0.0%(0/88) vs 1.1%(1/88) vs 0.0%(0/103) Tendon rupture: 0.0%(0/91) vs 1.1%(1/88) vs 0.0%(0/88) vs 0.0%(0/103) Upper GI event: 13.2%(12/91) vs 22.7%(20/88) vs 19.3%(17/88) vs 18.4%(19/103) Upper respiratory tract infection: 5.5%(5/91) vs 9.1%(8/88) vs 9.1%(8/88) vs 3.9%(4/103) Urinary tract infection: 3.3%(3/91) vs 1.1%(1/88) vs 2.3%(2/88) vs 5.8%(6/103) |
| Boonen et al., 2008502  Zoledronic acid (Zometa) | Placebo + Calcium + Vitamin D vs Zoledronic Acid 5 mg + Calcium + Vitamin D: AEs: all: 93.9%(3,618/3,852) vs 95.5%(3,687/3,862) AEs: deaths: 2.9%(112/3,852) vs 3.4%(131/3,862) AEs: serious AE: 30.1%(1,160/3,852) vs 29.2%(1,127/3,862) Apical granuloma: 0.0%(1/3,852) vs 0.0%(0/3,862) Bone fistula: 0.0%(1/3,852) vs 0.0%(0/3,862) Bone infarction: 0.0%(0/3,852) vs 0.0%(1/3,862) Bone lesion: 0.0%(0/3,852) vs 0.0%(1/3,862) Bone lesion excision: 0.0%(1/3,852) vs 0.0%(0/3,862) Dental Caries: 0.6%(23/3,852) vs 0.5%(18/3,862) Dental alveolar anomaly: 0.0%(1/3,852) vs 0.0%(0/3,862) Dental necrosis: 0.1%(3/3,852) vs 0.0%(0/3,862) Dry socket: 0.1%(3/3,852) vs 0.0%(0/3,862) Estimated creatinine clearance < 30 ml/min: overall: 4.2%(152/3,658) vs 4.4%(160/3,621) Estimated creatinine clearance decreased by ≥ 30%: ml/min: overall: 4.8%(177/3,658) vs 5.0%(182/3,621) Exostosis: 0.5%(19/3,852) vs 0.4%(17/3,862) Increase in serum creatinine > 0.5 mg/100ml: overall: 2.0%(77/3,767) vs 2.8%(104/3,752) Mouth ulceration: 0.3%(10/3,852) vs 0.3%(11/3,862) Osteitis: 0.2%(7/3,852) vs 0.2%(7/3,862) Osteitis deformans: 0.0%(1/3,852) vs 0.0%(1/3,862) Osteolysis: 0.0%(0/3,852) vs 0.0%(1/3,862) Osteomyelitis: 0.0%(0/3,852) vs 0.1%(2/3,862) Osteomyelitis chronic: 0.0%(0/3,852) vs 0.0%(1/3,862) Osteonecrosis of jaw: 0.0%(1/3,852) vs 0.0%(1/3,862) Osteonecrosis of the hip: 0.1%(2/3,852) vs 0.1%(5/3,862) Periodontitis: 0.3%(12/3,852) vs 0.2%(7/3,862) Periostitis: 0.1%(2/3,852) vs 0.0%(0/3,862) Sinusitis: 2.7%(103/3,852) vs 2.2%(86/3,862) Sinusitis bacterial: 0.0%(1/3,852) vs 0.0%(1/3,862) Sinusitis fungal: 0.0%(0/3,852) vs 0.0%(1/3,862) Soft tissue inflammation: 0.0%(0/3,852) vs 0.0%(1/3,862) Soft tissue injury: 0.3%(12/3,852) vs 0.3%(11/3,862) Soft-tissue disorder: 0.0%(1/3,852) vs 0.0%(0/3,862) Soft-tissue infection: 0.0%(1/3,852) vs 0.0%(0/3,862) Tooth abscess: 0.5%(18/3,852) vs 0.6%(23/3,862) Urinary protein level > 2+: overall: 0.5%(19/3,758) vs 0.5%(19/3,749) Discontinuation: due to AE: 1.8%(69/3,852) vs 2.1%(81/3,862) Discontinuation: total: 15.3%(590/3,852) vs 16.2%(625/3,862) |
| Chapman et al., 2009114  Zoledronic acid (Zometa) | Zoledronic acid IV 2mg vs Placebo: Fever, rigor, bone pain in legs and chest: 10.0%(1/10) vs 0.0%(0/12) Flu-like illness: 80.0%(8/10) vs 8.3%(1/12) Musculoskeletal pain: 40.0%(4/10) vs 16.7%(2/12) Severe pain restricting movement requiring hospitalization: 10.0%(1/10) vs 0.0%(0/12) |
| Grey et al., 2010418  Zoledronic acid (Zometa) | Zoledronic acid vs Placebo: Atrial fibrillation: 0.0%(0/25) vs 0.0%(0/25) Ocular inflammation: 0.0%(0/25) vs 0.0%(0/25) Osteonecrosis of the jaw: 0.0%(0/25) vs 0.0%(0/25) Other fracture: 16.0%(4/25) vs 8.0%(2/25) Symptomatic hypocalcemia: 0.0%(0/25) vs 0.0%(0/25) |
| Lyles et al., 2007113  Zoledronic acid (Zometa) | Zoledronic acid vs Placebo: Any AE: 82.3%(867/1,054) vs 80.6%(852/1,057) Adjudicated hypocalcemia: 0.3%(3/1,054) vs 0.0%(0/1,057) Any serious AE: 38.3%(404/1,054) vs 41.2%(436/1,057) Arrhythmia: 2.3%(24/1,054) vs 3.7%(39/1,057) Arthralgia: 3.1%(33/1,054) vs 2.2%(23/1,057) Atrial fibrillation: any event: 2.8%(29/1,054) vs 2.6%(27/1,057) Bone pain: 3.2%(34/1,054) vs 1.0%(11/1,057) Death: 9.6%(101/1,054) vs 13.3%(141/1,057) Death from cardiovascular causes: 3.4%(36/1,054) vs 4.9%(52/1,057) Death from cardiovascular disease: 1.0%(11/1,054) vs 1.7%(18/1,057) Death from cerebrovascular disease: 0.7%(7/1,054) vs 0.7%(7/1,057) Falls: 9.7%(102/1,054) vs 11.4%(120/1,057) Headache: 1.5%(16/1,054) vs 0.9%(9/1,057) Influenza-like symptoms: 0.6%(6/1,054) vs 0.3%(3/1,057) Musculoskeletal pain: 3.1%(33/1,054) vs 1.2%(13/1,057) Myalgia: 4.9%(52/1,054) vs 2.7%(29/1,057) Myocardial infarction: 1.2%(13/1,054) vs 1.6%(17/1,057) Ocular events possibly related to a study drug: 0.4%(4/1,054) vs 0.1%(1/1,057) Pyrexia: 8.7%(92/1,054) vs 3.1%(33/1,057) Renal event: increase in serum creatinine>0.5 mg/dl: 6.2%(55/886) vs 5.6%(50/900) Stroke: fatal event: 0.9%(9/1,054) vs 0.6%(6/1,057) Stroke: serious adverse event: 4.4%(46/1,054) vs 3.6%(38/1,057) Withdrawals: due to AE: 2.0%(21/1,054) vs 1.7%(18/1,057) Withdrawals: total: 18.3%(193/1,054) vs 29.9%(316/1,057) |
| McClung et al., 2007503  Zoledronic acid (Zometa) | Alendronate 70 mg/wk vs Zoledronic acid 5mg/wk: AEs: any: 95.5%(107/112) vs 114.2%(129/113) AEs: serious AE: 9.8%(11/112) vs 10.6%(12/113) Arthralgia: 10.7%(12/112) vs 17.7%(20/113) Back pain: 11.6%(13/112) vs 7.1%(8/113) Bronchitis: 1.8%(2/112) vs 5.3%(6/113) Cough: 5.4%(6/112) vs 2.7%(3/113) Death: 0.0%(0/112) vs 0.0%(0/113) Diarrhea: 1.8%(2/112) vs 5.3%(6/113) Fatigue: 1.8%(2/112) vs 9.7%(11/113) Headache: 13.4%(15/112) vs 16.8%(19/113) Hypocalcemia: 0.0%(0/112) vs 0.0%(0/113) Lab renal abnormality: 0.0%(0/112) vs 1.8%(2/113) Pain: 2.7%(3/112) vs 6.2%(7/113) Pain in extremity: 5.4%(6/112) vs 7.1%(8/113) Sinusitis: 4.5%(5/112) vs 6.2%(7/113) Upper respiratory tract infection: 12.5%(14/112) vs 8.0%(9/113) Urinary tract infection: 6.3%(7/112) vs 8.0%(9/113) Withdrawals: due to AE: 0.9%(1/112) vs 3.5%(4/113) |
| McClung et al., 2009421  Zoledronic acid (Zometa) | Placebo at randomization and at month 24 vs Zoledronic acid 5 mg at randomization and at month 24 vs Zoledronic acid 5 mg at randomization and placebo at month 24: Arthralgia: 19.3%(39/202) vs 27.3%(54/198) vs 18.8%(34/181) Atrial fibrillation: 0.0%(0/202) vs 0.0%(0/198) vs 0.0%(0/181) Back pain: 11.9%(24/202) vs 18.2%(36/198) vs 16.6%(30/181) Chills: 3.0%(6/202) vs 18.2%(36/198) vs 18.2%(33/181) Chills 3 or < days after an infusion: 1.5%(3/202) vs 16.7%(33/198) vs 18.2%(33/181) Chills >3 days after an infusion: 1.5%(3/202) vs 1.5%(3/198) vs 1.1%(2/181) Death due to sepsis: 0.0%(0/202) vs 0.5%(1/198) vs 0.0%(0/181) Fatigue: 4.0%(8/202) vs 14.6%(29/198) vs 9.9%(18/181) Headache: 11.4%(23/202) vs 14.6%(29/198) vs 20.4%(37/181) Long-term effects on renal function: 0.0%(0/202) vs 0.0%(0/198) vs 0.0%(0/181) Myalgia: 6.9%(14/202) vs 19.2%(38/198) vs 22.7%(41/181) Myalgia 3 or < days after an infusion: 2.0%(4/202) vs 15.7%(31/198) vs 20.4%(37/181) Myalgia >3 days after an infusion: 5.4%(11/202) vs 4.5%(9/198) vs 4.4%(8/181) Nasopharyngitis: 11.4%(23/202) vs 13.6%(27/198) vs 9.4%(17/181) Nausea: 7.9%(16/202) vs 17.7%(35/198) vs 11.6%(21/181) Nausea 3 or < days after an infusion: 2.0%(4/202) vs 12.1%(24/198) vs 8.8%(16/181) Nausea >3 days after an infusion: 5.9%(12/202) vs 6.6%(13/198) vs 3.9%(7/181) Osteonecrosis of the jaw: 0.0%(0/202) vs 0.0%(0/198) vs 0.0%(0/181) Pain: 3.5%(7/202) vs 24.2%(48/198) vs 14.9%(27/181) Pain 3 or < days after an infusion: 2.0%(4/202) vs 19.7%(39/198) vs 13.8%(25/181) Pain >3 days after an infusion: 1.5%(3/202) vs 6.1%(12/198) vs 1.1%(2/181) Pain in extremity: 9.9%(20/202) vs 11.1%(22/198) vs 16.0%(29/181) Pyrexia: 4.5%(9/202) vs 21.7%(43/198) vs 21.0%(38/181) Pyrexia 3 or < days after an infusion: 1.5%(3/202) vs 17.2%(34/198) vs 19.3%(35/181) Pyrexia >3 days after an infusion: 3.0%(6/202) vs 5.1%(10/198) vs 4.4%(8/181) Serious adverse event: 11.4%(23/202) vs 8.6%(17/198) vs 11.6%(21/181) Total number of participants with an AE: 92.1%(186/202) vs 93.9%(186/198) vs 95.6%(173/181) Total number of participants with an AE 3 or < days after an infusion: 24.8%(50/202) vs 61.6%(122/198) vs 63.0%(114/181) Total number of participants with an AE >3 days after an infusion: 91.6%(185/202) vs 90.9%(180/198) vs 89.5%(162/181) Upper respiratory tract infection: 11.4%(23/202) vs 13.6%(27/198) vs 10.5%(19/181) Urinary tract infection: 12.4%(25/202) vs 11.1%(22/198) vs 8.8%(16/181) |
| Etminan et al., 2008504  Alendronate (Fosamax), Etidronate (Didronel) | Oral Bisphosphonate: Aseptic osteonecrosis: 28.3%(58/205) |
| Emkey et al., 2009505  Alendronate (Fosamax), Ibandronate (Boniva)  Trial: MOTION | Alendronate 70 mg weekly + Calcium 500 mg + Vitamin D 400 IU vs Ibandronate 150 mg monthly + Calcium 500 mg + Vitamin D 400 IU: Any adverse event: 73.6%(632/859) vs 75.4%(659/874) All GI adverse events: 28.9%(248/859) vs 30.3%(265/874) Arthralgia: 5.7%(49/859) vs 5.4%(47/874) Back pain: 5.2%(45/859) vs 6.9%(60/874) Death: 0.5%(4/859) vs 0.2%(2/874) Duodenal ulcer: 0.1%(1/859) vs 0.0%(0/874) Dyspepsia: 5.6%(48/859) vs 6.9%(60/874) Erosive duodenitis: 0.1%(1/859) vs 0.0%(0/874) Esophagitis ulcerative: 0.1%(1/859) vs 0.0%(0/874) GI hemorrhagic: 0.1%(1/859) vs 0.0%(0/874) Gastric ulcer: 0.2%(2/859) vs 0.1%(1/874) Gastritis erosive: 0.2%(2/859) vs 0.1%(1/874) Gastritis hemorrhagic: 0.1%(1/859) vs 0.0%(0/874) Hypertension: 5.9%(51/859) vs 7.8%(68/874) Influenza: 4.2%(36/859) vs 5.6%(49/874) Intestinal hemorrhagic: 0.1%(1/859) vs 0.0%(0/874) Musculoskeletal and general disorders: 3.0%(26/859) vs 6.8%(59/874) Nasopharyngitis: 4.8%(41/859) vs 5.8%(51/874) Perforations, ulcers and bleeding: 0.9%(8/859) vs 0.5%(4/874) Rectal hemorrhage: 0.1%(1/859) vs 0.2%(2/874) Serious adverse event: 6.4%(55/859) vs 4.5%(39/874) Upper-GI adverse event: 17.2%(148/859) vs 17.5%(153/874) Upper-GI hemorrhage: 0.1%(1/859) vs 0.0%(0/874) |
| Hadji et al., 2008506  Alendronate (Fosamax), Ibandronate (Boniva)  Trial: BALTTO II | Alendronate 70 mg weekly + Calcium + Vitamin D vs Ibandronate 150 mg monthly + Calcium + Vitamin D: Any adverse event: 34.6%(117/338) vs 37.5%(126/336) Constipation: 1.2%(4/338) vs 3.0%(10/336) Death: 0.0%(0/338) vs 0.0%(0/336) Diarrhea: 3.3%(11/338) vs 1.5%(5/336) Dyspepsia: 1.8%(6/338) vs 0.9%(3/336) GI disorder: 8.6%(29/338) vs 8.3%(28/336) Gastro-esophageal reflux disease: 0.6%(2/338) vs 1.2%(4/336) General disorders: 2.1%(7/338) vs 1.5%(5/336) Infections and infestations: 1.2%(4/338) vs 2.1%(7/336) Musculoskeletal and connective tissue disorder: 4.7%(16/338) vs 3.3%(11/336) Nervous system disorders: 1.2%(4/338) vs 2.1%(7/336) Serious AE: 1.8%(6/338) vs 2.4%(8/336) Severe GI events: 2.7%(9/338) vs 0.3%(1/336) Upper GI event: 7.1%(24/338) vs 5.7%(19/336) Withdrawals due to AE: 0.9%(3/338) vs 0.3%(1/336) |
| Li et al., 2009507  Alendronate (Fosamax), Ibandronate (Boniva) | Alendronate 70 mg/week + Calcium 500 mg/day + Vitamin D 200 IU/day vs Intravenous ibandronate 2 mg every 3mo + Calcium 500 mg/day + Vitamin D 200 IU/day: Acute renal failure: 0.0%(0/79) vs 0.0%(0/79) Bone pain after 1 month: 3.8%(3/79) vs 2.5%(2/79) Bone pain after 2-12 months: 0.0%(0/79) vs 0.0%(0/79) Fever after 1 month: 1.3%(1/79) vs 3.8%(3/79) Fever after 2-12 months: 0.0%(0/79) vs 0.0%(0/79) Influenza-like symptoms after 1 month: 7.6%(6/79) vs 12.7%(10/79) Influenza-like symptoms after 2-12 months: 3.8%(3/79) vs 0.0%(0/79) Muscle pain after 1 month: 5.1%(4/79) vs 29.1%(23/79) Muscle pain after 2-12 months: 3.8%(3/79) vs 0.0%(0/79) Osteonecrosis of jaw after 1 month: 0.0%(0/79) vs 0.0%(0/79) Osteonecrosis of jaw after 2-12 months: 0.0%(0/79) vs 0.0%(0/79) Other after 1 month: 0.0%(0/79) vs 3.8%(3/79) Other after 2-12 months: 0.0%(0/79) vs 0.0%(0/79) Peptic side effects after 1 month: 3.8%(3/79) vs 1.3%(1/79) Peptic side effects after 2-12 months: 2.5%(2/79) vs 0.0%(0/79) Withdrawals: 3.8%(3/79) vs 5.1%(4/79) Withdrawals due to adverse events: 1.3%(1/79) vs 2.5%(2/79) |
| Cadarette et al., 2009508  Alendronate (Fosamax), Risedronate (Actonel) | Alendronate vs Risedronate: Any upper GI diagnosis or procedure: 18.2%(1,058/5,818) vs 18.8%(867/4,602) Gastroprotective treatment: 31.7%(1,843/5,818) vs 34.5%(1,588/4,602) Hospitalization for upper GI bleed: 0.3%(16/5,818) vs 0.3%(15/4,602) Switched between therapies: 1.9%(111/5,818) vs 1.3%(60/4,602) Upper GI disease: 10.5%(612/5,818) vs 11.0%(508/4,602) Upper GI endoscopy: 2.3%(134/5,818) vs 2.0%(90/4,602) Upper GI symptom: 11.4%(662/5,818) vs 11.2%(516/4,602) |
| Reid et al., 2006509  Alendronate (Fosamax), Risedronate (Actonel)  Trial: FACTS-INT'L | Alendronic acid 10 mg/day + Elemental calcium 1000 mg + Vitamin D 400 IU vs Risedronic acid 5mg/day + Elemental calcium 1000 mg + Vitamin D 400 IU: Any adverse event: 65.4%(306/468) vs 67.1%(314/468) Any serious adverse event: 5.1%(24/468) vs 10.0%(47/468) Death: 0.4%(2/468) vs 0.9%(4/468) Serious upper GI event: 0.4%(2/468) vs 0.9%(4/468) Upper GI event: 20.3%(95/468) vs 20.1%(94/468) Withdrawals: 8.1%(38/468) vs 9.4%(44/468) |
| Breart et al., 2009510  Alendronate (Fosamax), Strontium ranelate | Alendronate sodium vs Control: Venous thromboembolism: 0.7%(140/20,084) vs 0.5%(61/11,546) |
| Saag et al., 2007511  Alendronate (Fosamax), Zoledronic acid (Zometa) | Alendronate vs Zoledronic acid: Any AE: 78.0%(46/59) vs 79.7%(55/69) Abdominal distension: 6.8%(4/59) vs 2.9%(2/69) Abdominal pain: 5.1%(3/59) vs 1.4%(1/69) Arthralgia: 10.2%(6/59) vs 5.8%(4/69) Back pain: 0.0%(0/59) vs 5.8%(4/69) Chest pain: 1.7%(1/59) vs 1.4%(1/69) Chills: 1.7%(1/59) vs 1.4%(1/69) Clinical remarkable changes in vital signs: 0.0%(0/59) vs 0.0%(0/69) Constipation: 5.1%(3/59) vs 1.4%(1/69) Death: 0.0%(0/59) vs 0.0%(0/69) Diarrhea: 0.0%(0/59) vs 2.9%(2/69) Dizziness: 5.1%(3/59) vs 0.0%(0/69) Dyspepsia: 5.1%(3/59) vs 10.1%(7/69) Elevation in alanine aminotransferase (ALT): 3.4%(2/59) vs 18.8%(13/69) Eructation: 5.1%(3/59) vs 1.4%(1/69) Fatigue: 5.1%(3/59) vs 2.9%(2/69) Flatulence: 3.4%(2/59) vs 1.4%(1/69) Headache: 15.3%(9/59) vs 8.7%(6/69) Hypocalcemia: 0.0%(0/59) vs 0.0%(0/69) Influenza-like illness: 1.7%(1/59) vs 1.4%(1/69) Low calcium levels: 0.0%(0/59) vs 0.0%(0/69) Muscle spasms: 6.8%(4/59) vs 4.3%(3/69) Myalgia: 3.4%(2/59) vs 7.2%(5/69) Nasopharyngitis: 3.4%(2/59) vs 10.1%(7/69) Nausea: 6.8%(4/59) vs 1.4%(1/69) Osteoarthritis: 5.1%(3/59) vs 5.8%(4/69) Pain: 0.0%(0/59) vs 0.0%(0/69) Pain in extremity: 6.8%(4/59) vs 2.9%(2/69) Pyrexia: 1.7%(1/59) vs 0.0%(0/69) Rash: 1.7%(1/59) vs 1.4%(1/69) Serious AE: 5.1%(3/59) vs 2.9%(2/69) Shoulder pain: 5.1%(3/59) vs 0.0%(0/69) Sinusitis: 5.1%(3/59) vs 4.3%(3/69) Upper respiratory tract infection: 11.9%(7/59) vs 7.2%(5/69) Withdrawals: 8.5%(5/59) vs 8.7%(6/69) |
| Reid et al., 2009512  Risedronate (Actonel), Zoledronic acid (Zometa) | Intravenous Zoledronic acid 5 mg + 1 g Calcium + Vitamin D 400-1200 IU/day + oral placebo vs Oral risedronate 5 mg/day + 1 g Calcium + Vitamin D 400-1200 IU/day + Intravenous placebo: Any adverse event: 77.4%(322/416) vs 66.9%(279/417) Abdominal pain: 2.4%(10/416) vs 1.9%(8/417) Acute renal failure: 0.2%(1/416) vs 0.5%(2/417) Allergic dermatitis: 0.5%(2/416) vs 1.9%(8/417) Anemia: 2.4%(10/416) vs 2.9%(12/417) Anxiety: 1.0%(4/416) vs 1.2%(5/417) Any serious adverse event: 18.3%(76/416) vs 18.5%(77/417) Arthralgia: 9.9%(41/416) vs 7.4%(31/417) Asthenia: 3.8%(16/416) vs 3.6%(15/417) Asymptomatic hypocalcemia: 0.2%(1/416) vs 0.0%(0/417) Atrial fibrillation: 0.7%(3/416) vs 0.0%(0/417) Back pain: 4.3%(18/416) vs 6.2%(26/417) Baseline creatinine clearance </= 30% after given drug: 0.2%(1/416) vs 0.5%(2/417) Baseline creatinine clearance ≤ 60ml/min and ≥ 30% after given drug: 0.2%(1/416) vs 0.5%(2/417) Blepharitis: 0.2%(1/416) vs 0.0%(0/417) Blurred vision: 0.0%(0/416) vs 0.5%(2/417) Bone pain: 3.1%(13/416) vs 2.2%(9/417) Bronchitis: 1.2%(5/416) vs 1.4%(6/417) Cataract: 1.7%(7/416) vs 1.7%(7/417) Chest pain: 0.5%(2/416) vs 0.7%(3/417) Chills: 3.4%(14/416) vs 0.7%(3/417) Conjunctivitis: 1.2%(5/416) vs 0.2%(1/417) Constipation: 2.2%(9/416) vs 2.4%(10/417) Contusion: 1.9%(8/416) vs 0.5%(2/417) Creatinine clearance < 30 mL/min after given drug: 1.0%(4/416) vs 1.0%(4/417) Death: 1.0%(4/416) vs 0.7%(3/417) Depression: 1.7%(7/416) vs 1.7%(7/417) Diarrhea: 3.6%(15/416) vs 2.4%(10/417) Diplopia: 0.0%(0/416) vs 0.2%(1/417) Dizziness: 2.4%(10/416) vs 1.0%(4/417) Dyspepsia: 5.5%(23/416) vs 4.3%(18/417) Episcleritis: 0.0%(0/416) vs 0.2%(1/417) Fall: 1.7%(7/416) vs 1.0%(4/417) Fatigue: 3.1%(13/416) vs 1.4%(6/417) Gastritis: 1.2%(5/416) vs 1.4%(6/417 |
| Reid et al., 2009512  Continued | Intravenous Zoledronic acid 5 mg + 1 g Calcium + Vitamin D 400-1200 IU/day + oral placebo vs Oral risedronate 5 mg/day + 1 g Calcium + Vitamin D 400-1200 IU/day + Intravenous placebo: Gastro-esophageal reflux: 1.2%(5/416) vs 1.4%(6/417) Headache: 5.3%(22/416) vs 2.4%(10/417) Hypertension: 4.3%(18/416) vs 4.1%(17/417) Increase of lacrimation: 0.0%(0/416) vs 0.2%(1/417) Influenza: 3.4%(14/416) vs 1.9%(8/417) Influenza-like illness: 6.0%(25/416) vs 1.0%(4/417) Insomnia: 1.9%(8/416) vs 1.4%(6/417) Joint swelling: 1.0%(4/416) vs 0.5%(2/417) Keratoconjunctivitis sicca: 0.7%(3/416) vs 0.0%(0/417) Musculoskeletal chest pain: 1.9%(8/416) vs 0.0%(0/417) Musculoskeletal pain: 1.4%(6/416) vs 1.7%(7/417) Musculoskeletal stiffness: 1.2%(5/416) vs 0.2%(1/417) Myalgia: 9.1%(38/416) vs 3.4%(14/417) Nasopharyngitis: 2.9%(12/416) vs 2.6%(11/417) Nausea: 9.6%(40/416) vs 8.4%(35/417) Edema peripheral: 2.9%(12/416) vs 2.2%(9/417) Osteonecrosis of long bones: 0.2%(1/416) vs 0.0%(0/417) Osteonecrosis of the jaw: 0.0%(0/416) vs 0.0%(0/417) Pain in limbs: 3.1%(13/416) vs 1.2%(5/417) Palpitations: 1.0%(4/416) vs 0.7%(3/417) Paresthesia: 1.4%(6/416) vs 0.5%(2/417) Pneumonia: 1.4%(6/416) vs 1.9%(8/417) Proteinuria: 1.0%(4/416) vs 0.7%(3/417) Pyrexia: 12.7%(53/416) vs 3.6%(15/417) Rash: 0.7%(3/416) vs 1.9%(8/417) Rectal Haemorrhage: 1.0%(4/416) vs 0.0%(0/417) Sciatica: 2.4%(10/416) vs 0.2%(1/417) Serum creatinine increase by >44 umol/L: 1.9%(8/416) vs 1.4%(6/417) Sinusitis: 1.2%(5/416) vs 2.2%(9/417) Supraventricular tachycardia: 0.2%(1/416) vs 0.0%(0/417) Upper abdominal pain: 5.0%(21/416) vs 3.1%(13/417) Upper respiratory tract infection: 2.4%(10/416) vs 1.9%(8/417) Urinary tract infection: 5.0%(21/416) vs 4.1%(17/417) Vertigo: 1.9%(8/416) vs 1.2%(5/417) Vomiting: 4.8%(20/416) vs 2.4%(10/41 |
| Grosso et al., 2009513  Alendronate (Fosamax), Bisphosphonates, Risedronate (Actonel) | Bisphosphonates (either Alendronate 10mg daily or 70mg weekly OR Risedronate 5mg daily or 35mg weekly): Atrial fibrillation or atrial flutter: 8.3%(3,335/40,253) |
| Hong et al., 2009514  Alendronate (Fosamax), Bisphosphonates, Risedronate (Actonel) | Bisphosphonates: Osteonecrosis of the jaw (BRONJ): 0.1%(7/9,882) |
| Blumentals et al., 2009515  Alendronate (Fosamax), Ibandronate (Boniva), Risedronate (Actonel) | Alendronate/Risedronate weekly vs Ibandronate 150 mg/mo: Severe GI events: during the follow-up period: 0.8%(70/8,608) vs 0.5%(45/8,608) Use of healthcare services: GI drugs: 24.6%(2,115/8,608) vs 25.7%(2,209/8,608) Use of healthcare services: GI endoscopy: 1.6%(139/8,608) vs 1.8%(158/8,608) Use of healthcare services: GI specialist visits: 5.7%(487/8,608) vs 6.2%(535/8,608) Use of healthcare services: X-ray use: 0.4%(34/8,608) vs 0.3%(23/8,608) Use of healthcare services: emergency care: 7.1%(611/8,608) vs 6.5%(562/8,608) Use of healthcare services: hospitalization: 4.2%(365/8,608) vs 3.8%(325/8,608) Use of healthcare services: outpatient visits: 69.2%(5,959/8,608) vs 71.5%(6,155/8,608) Use of healthcare services: outpatient visits related to GI diagnoses: 2.3%(201/8,608) vs 2.7%(233/8,608) Use of healthcare services: outpatient visits related to musculoskeletal diagnoses: 25.9%(2,230/8,608) vs 26.1%(2,246/8,608) |
| Ideguchi et al., 2007294  Alendronate (Fosamax), Bisphosphonates, Etidronate (Didronel), Risedronate (Actonel) | Bisphosphonates: Any adverse event: 9.5%(124/1,307) Diarrhea and/or constipation: 0.9%(12/1,307) Elevated liver function: 0.2%(3/1,307) Gastric pain: 4.6%(60/1,307) Heartburn: 0.5%(6/1,307) Increase of creatine kinase: 0.1%(1/1,307) Increase of creatinine: 0.3%(4/1,307) Laboratory abnormalities: 0.6%(8/1,307) Stomatitis: 0.6%(8/1,307) |
| Bonnick et al., 2007226  Alendronate (Fosamax), Calcium | Alendronate 10 mg/d vs Alendronate 10mg/d +Ca 1000 mg/d vs Calcium 100 mg/d: Clinical AEs: any: 93.2%(262/281) vs 87.9%(248/282) vs 91.3%(126/138) Clinical AEs: deaths: 0.4%(1/281) vs 0.7%(2/282) vs 0.0%(0/138) Clinical AEs: drug-related: 39.1%(110/281) vs 34.8%(98/282) vs 35.5%(49/138) Clinical AEs: serious: 10.7%(30/281) vs 14.2%(40/282) vs 19.6%(27/138) Upper GI AEs: any: 34.9%(98/281) vs 34.8%(98/282) vs 38.4%(53/138) Upper GI AEs: drug-related: 21.0%(59/281) vs 20.6%(58/282) vs 21.0%(29/138) Upper GI AEs: serious: 0.7%(2/281) vs 0.0%(0/282) vs 1.4%(2/138) Withdrawals: total: 29.5%(83/281) vs 32.6%(92/282) vs 30.4%(42/138) |
| Brown et al., 2009275  Alendronate (Fosamax), Denosumab  Trial: DECIDE | Alendronate 70 mg/wk vs Denosumab 60 mg/6 mos: AEs: all AEs: 82.3%(482/586) vs 80.9%(480/593) AEs: serious AE: 6.3%(37/586) vs 5.7%(34/593) Arthralgia: 9.6%(56/586) vs 12.6%(75/593) Asymptomatic grade 2 decrease in albumin-adjusted serum calcium concentrations: 0.0%(0/586) vs 0.2%(1/593) Benign neoplasms of the breast: 0.0%(0/586) vs 0.3%(2/593) Benign neoplasms of the kidney: 0.0%(0/586) vs 0.3%(2/593) Benign neoplasms of the thyroid gland: 0.3%(2/586) vs 0.2%(1/593) Deaths: 0.2%(1/586) vs 0.2%(1/593) GI disorders: 28.7%(168/586) vs 27.7%(164/593) Infections - bronchitis: 3.6%(21/586) vs 3.2%(19/593) Infections - influenza: 7.2%(42/586) vs 6.9%(41/593) Infections - nasopharyngitis: 7.3%(43/586) vs 7.6%(45/593) Infections - serious: 1.0%(6/586) vs 1.5%(9/593) Infections - serious abscessed limb: 0.2%(1/586) vs 0.0%(0/593) Infections - serious diverticulitis: 0.0%(0/586) vs 0.5%(3/593) Infections - serious ear infection: 0.0%(0/586) vs 0.2%(1/593) Infections - serious infected cyst: 0.2%(1/586) vs 0.0%(0/593) Infections - serious localized infection (finger): 0.0%(0/586) vs 0.2%(1/593) Infections - serious pneumonia: 0.5%(3/586) vs 0.2%(1/593) Infections - serious pseudomembranous colitis: 0.0%(0/586) vs 0.2%(1/593) Infections - serious pyelonephritis: 0.0%(0/586) vs 0.2%(1/593) Infections - serious sepsis: 0.0%(0/586) vs 0.2%(1/593) Infections - serious upper respiratory tract infection: 0.2%(1/586) vs 0.0%(0/593) Infections - serious urosepsis: 0.0%(0/586) vs 0.2%(1/593) Infections - upper respiratory tract infection: 4.4%(26/586) vs 6.1%(36/593) Infections - urinary tract infection: 2.9%(17/586) vs 3.0%(18/593) Malignant neoplasm - serious breast cancer: 0.2%(1/586) vs 0.3%(2/593) Malignant neoplasm - serious gastric cancer: 0.0%(0/586) vs 0.2%(1/593) Malignant neoplasm - serious metastases to liver: 0.0%(0/586) vs 0.2%(1/593) Malignant neoplasm - serious metastatic neoplasm: 0.2%(1/586) vs 0.0%(0/593) Malignant neoplasm - serious mycosis fungoides: 0.0%(0/586) vs 0.2%(1/593) Malignant neoplasm - serious ovarian cancer recurrent: 0.2%(1/586) vs 0.0%(0/593) Malignant neoplasm - serious renal cell carcinoma stage unspecified: 0.0%(0/586) vs 0.2%(1/593) Malignant neoplasm - serious small cell lung cancer metastatic: 0.2%(1/586) vs 0.0%(0/593) Malignant neoplasm - serious squamous cell carcinoma: 0.0%(0/586) vs 0.2%(1/593) Malignant neoplasm - serious vaginal cancer: 0.2%(1/586) vs 0.0%(0/593) Neoplasms (benign or malignant): 2.6%(15/586) vs 3.5%(21/593) Withdrawals: due to all AE: 1.7%(10/586) vs 1.3%(8/593) Withdrawals: total: 9.2%(54/586) vs 6.1%(36/593) |
| Kendler et al., 2009516  Alendronate (Fosamax), Denosumab  Trial: STAND | Alendronate 70 mg weekly + Calcium 1000 mg + Vitamin D 400 IU vs Subcutaneous denosumab 60 mg/6 months + Calcium 1000 mg + Vitamin D 400 IU: Any adverse event: 78.7%(196/249) vs 77.9%(197/253) Arthralgia: 10.4%(26/249) vs 5.9%(15/253) Back pain: 11.6%(29/249) vs 10.7%(27/253) Bronchitis: 5.6%(14/249) vs 6.3%(16/253) Clinical fractures: 1.6%(4/249) vs 3.2%(8/253) Constipation: 4.8%(12/249) vs 5.1%(13/253) Death: 0.0%(0/249) vs 0.4%(1/253) GI disorder: 24.1%(60/249) vs 22.9%(58/253) Infections: 37.3%(93/249) vs 43.9%(111/253) Nasopharyngitis: 10.8%(27/249) vs 13.4%(34/253) Neoplasms (benign or malignant): 3.6%(9/249) vs 3.6%(9/253) Pain in an extremity: 8.4%(21/249) vs 4.7%(12/253) Serious adverse event: 6.4%(16/249) vs 5.9%(15/253) Serious infection: 1.2%(3/249) vs 0.4%(1/253) Serious neoplasms (benign or malignant): 1.2%(3/249) vs 1.2%(3/253) Withdrawals: total: 4.4%(11/249) vs 4.0%(10/253) |
| Miller et al., 2008517  Alendronate (Fosamax), Denosumab | Alendronate + Calcium 1000mg/day + Vitamin D 400 IU/day vs Denosumab + Calcium 1000mg/day + Vitamin D 400 IU/day vs Placebo + Calcium 1000mg/day + Vitamin D 400 IU/day: Any adverse event: 95.7%(44/46) vs 93.3%(293/314) vs 93.5%(43/46) Adverse event requiring hospitalization: 0.0%(0/46) vs 3.2%(10/314) vs 0.0%(0/46) Anemia: 13.0%(6/46) vs 1.6%(5/314) vs 2.2%(1/46) Arthralgia: 17.4%(8/46) vs 23.6%(74/314) vs 30.4%(14/46) Back pain: 15.2%(7/46) vs 20.1%(63/314) vs 13.0%(6/46) Bronchitis: 8.7%(4/46) vs 8.3%(26/314) vs 10.9%(5/46) Constipation: 13.0%(6/46) vs 6.4%(20/314) vs 2.2%(1/46) Death due to Adenocarcinoma: 0.0%(0/46) vs 0.3%(1/314) vs 0.0%(0/46) Death due to Brain neoplasm: 0.0%(0/46) vs 0.3%(1/314) vs 0.0%(0/46) Death due to Cerebral vascular accident: 0.0%(0/46) vs 0.3%(1/314) vs 0.0%(0/46) Death due to gastric cancer: 0.0%(0/46) vs 0.3%(1/314) vs 0.0%(0/46) Development of neutralizing antibodies to denosumab: 0.0%(0/46) vs 0.0%(0/314) vs 0.0%(0/46) Diarrhea: 8.7%(4/46) vs 8.9%(28/314) vs 13.0%(6/46) Dyspepsia: 26.1%(12/46) vs 12.4%(39/314) vs 6.5%(3/46) Gastroesophageal reflux disease: 15.2%(7/46) vs 12.7%(40/314) vs 4.3%(2/46) Headache: 10.9%(5/46) vs 12.1%(38/314) vs 17.4%(8/46) Hypertension: 10.9%(5/46) vs 15.3%(48/314) vs 4.3%(2/46) Infections: 69.6%(32/46) vs 66.2%(208/314) vs 67.4%(31/46) Influenza-like illness: 15.2%(7/46) vs 13.1%(41/314) vs 10.9%(5/46) Muscle spasms: 10.9%(5/46) vs 10.2%(32/314) vs 15.2%(7/46) Nasopharyngitis: 13.0%(6/46) vs 19.1%(60/314) vs 15.2%(7/46) Nausea: 21.7%(10/46) vs 12.1%(38/314) vs 4.3%(2/46) Osteoarthritis: 13.0%(6/46) vs 4.1%(13/314) vs 8.7%(4/46) Pain in extremity: 15.2%(7/46) vs 17.5%(55/314) vs 17.4%(8/46) Peripheral edema: 6.5%(3/46) vs 4.8%(15/314) vs 10.9%(5/46) Serious Infections: 0.0%(0/46) vs 3.2%(10/314) vs 0.0%(0/46) Serious adverse events: 17.4%(8/46) vs 17.8%(56/314) vs 10.9%(5/46) Shoulder pain: 8.7%(4/46) vs 9.6%(30/314) vs 15.2%(7/46) Sinusitis: 13.0%(6/46) vs 11.8%(37/314) vs 19.6%(9/46) Symptomatic hypocalcemia: 0.0%(0/46) vs 0.0%(0/314) vs 0.0%(0/46) Upper respiratory tract infection: 30.4%(14/46) vs 28.0%(88/314) vs 23.9%(11/46) Urinary tract infection: 13.0%(6/46) vs 13.1%(41/314) vs 4.3%(2/46) Withdrawals: 37.0%(17/46) vs 36.9%(116/314) vs 37.0%(17/46) |
| Tseng et al., 2006265  Alendronate (Fosamax), Estrogen | Alendronate 10 mg + Equine estrogen .625 mg + Medroxyprogesterone 5 mg + Calcium carbonate 500 mg/d vs Placebo + Equine estrogen .625 mg + Medroxyprogesterone 5 mg + Calcium carbonate 500 mg/d: Back pain: 1.3%(1/79) vs 1.4%(1/72) Epigastralgia: 1.3%(1/79) vs 0.0%(0/72) Epigastric discomfort: 0.0%(0/79) vs 2.8%(2/72) Esophageal irritation: 2.5%(2/79) vs 0.0%(0/72) General discomfort: 0.0%(0/79) vs 1.4%(1/72) Hemoptysis: 0.0%(0/79) vs 1.4%(1/72) Intolerance to menopausal hormone therapy: 2.5%(2/79) vs 1.4%(1/72) Light stroke: 0.0%(0/79) vs 1.4%(1/72) Withdrawals: 36.7%(29/79) vs 38.9%(28/72) Withdrawals due to adverse events: 7.6%(6/79) vs 9.7%(7/72) |
| Saag et al., 2009224  Alendronate (Fosamax), PTH (Teriparatide) (Forteo) | Alendronate 10 mg/day + Calcium + Vitamin D vs Teriparatide 20 ug/day + Calcium + Vitamin D: Any adverse event: 86.0%(184/214) vs 90.7%(194/214) Anemia: 7.9%(17/214) vs 5.1%(11/214) Any serious adverse event: 29.9%(64/214) vs 32.7%(70/214) Death: 7.0%(15/214) vs 4.2%(9/214) Dyspepsia: 7.0%(15/214) vs 4.2%(9/214) Dyspnea: 2.8%(6/214) vs 7.5%(16/214) Fatigue: 1.9%(4/214) vs 4.2%(9/214) Gastritis: 3.7%(8/214) vs 7.9%(17/214) Headache: 6.5%(14/214) vs 8.9%(19/214) Influenza: 11.2%(24/214) vs 8.4%(18/214) Insomnia: 1.4%(3/214) vs 5.6%(12/214) Joint injury: 2.8%(6/214) vs 0.5%(1/214) Nasopharyngitis: 6.1%(13/214) vs 3.3%(7/214) Nausea: 8.4%(18/214) vs 16.8%(36/214) Rash: 4.7%(10/214) vs 1.9%(4/214) Urinary tract infection: 13.6%(29/214) vs 10.3%(22/214) Viral infection: 0.0%(0/214) vs 2.3%(5/214) Weight loss: 4.2%(9/214) vs 0.0%(0/214) Withdrawals: 44.9%(96/214) vs 42.5%(91/214) |
| Antoniucci et al., 2007518  Alendronate (Fosamax), PTH184 (Preos)  Trial: PATH | PTH 100 ug/d alone vs PTH 100 ug/d +alendronate 10 mg/d: AE other than hypercalciuria: 1.7%(2/119) vs 3.4%(2/59) Concurrent serum and urinary calcium elevations: 1.7%(2/119) vs 0.0%(0/59) Hypercalcemia: 13.4%(16/119) vs 15.3%(9/59) Hypercalciuria: 8.4%(10/119) vs 11.9%(7/59) |
| Huang et al., 2009519  Alendronate (Fosamax), Raloxifene (Evista) | Alendronate 10 mg/day OR 70 mg/weekly vs Raloxifene 60 mg: Acute myocardial infarction: 5.8%(1,216/21,037) vs 4.7%(294/6,220) Atrial fibrillation: 3.2%(663/21,037) vs 2.5%(158/6,220) |
| Sanad et al., 2011409  Alendronate (Fosamax), Raloxifene (Evista) | Alendronate vs Raloxifene: Chest pain: 6.8%(3/44) vs 2.2%(1/46) Constipation: 2.3%(1/44) vs 0.0%(0/46) Deep vein thrombosis: 0.0%(0/44) vs 2.2%(1/46) Diarrhea: 2.3%(1/44) vs 2.2%(1/46) Epigastric pain: 6.8%(3/44) vs 4.3%(2/46) Heartburn: 6.8%(3/44) vs 2.2%(1/46) Hot flashes: 6.8%(3/44) vs 8.7%(4/46) Sweating: 4.5%(2/44) vs 4.3%(2/46) Urticaria: 0.0%(0/44) vs 2.2%(1/46) |
| Binkley et al., 2009264  Alendronate (Fosamax), Vitamin D | Alendronate 70 mg +Vitamin D 2800 IU vs Alendronate 70 mg +Vitamin D 5600 IU: Clinical AE: with ≥1 AE: 51.5%(168/326) vs 47.2%(154/326) Clinical AE: with drug related AE: 4.0%(13/326) vs 5.2%(17/326) Clinical AE: with serious AE: 4.0%(13/326) vs 4.9%(16/326) Clinical AE: with serious drug related AE: 0.3%(1/326) vs 0.0%(0/326) Death (due to cerebellar hemorrhage): 0.3%(1/326) vs 0.0%(0/326) Lab AE: with ≥1 AE: 8.3%(27/326) vs 7.7%(25/326) Lab AE: with drug related AE: 0.3%(1/326) vs 2.8%(9/326) Lab AE: with serious AE: 0.0%(0/326) vs 0.0%(0/326) Lab AE: with serious drug related AE: 0.0%(0/326) vs 0.0%(0/326) Withdrawals: 2.8%(9/326) vs 4.6%(15/326) |
| Ringe et al., 200756  Alendronate (Fosamax), Vitamin D  Trial: AAC TRIAE | Alendronate 70 mg/week + Calcium 1000 mg/day + Vitamin D 1,000 IU/day vs Alfacalcidol 1 ug/day + Alendronate 70 mg/week + Calcium 500 mg/day vs Alfacalcidol 1 ug/day + Vitamin D 1,000 IU/day: Arthralgia: 3.3%(1/30) vs 0.0%(0/30) vs 0.0%(0/30) Back pain: 70.0%(21/30) vs 20.0%(6/30) vs 56.7%(17/30) Bone pain: 0.0%(0/30) vs 0.0%(0/30) vs 3.3%(1/30) Epigastric pain: 6.7%(2/30) vs 3.3%(1/30) vs 0.0%(0/30) Headache: 0.0%(0/30) vs 0.0%(0/30) vs 6.7%(2/30) Heartburn: 3.3%(1/30) vs 0.0%(0/30) vs 0.0%(0/30) Hypercalcemia: 0.0%(0/30) vs 0.0%(0/30) vs 0.0%(0/30) Hypercalciuria: 0.0%(0/30) vs 3.3%(1/30) vs 13.3%(4/30) Meteoric: 0.0%(0/30) vs 0.0%(0/30) vs 3.3%(1/30) Nausea: 0.0%(0/30) vs 3.3%(1/30) vs 0.0%(0/30) Obstipation: 6.7%(2/30) vs 6.7%(2/30) vs 6.7%(2/30) Soft bowels: 3.3%(1/30) vs 0.0%(0/30) vs 0.0%(0/30) Withdrawals due to adverse events: 0.0%(0/30) vs 0.0%(0/30) vs 0.0%(0/30) |
| de Nijs et al., 200657  Alendronate (Fosamax), Vitamin D  Trial: STOP | Alendronate 10 mg + Elemental Calcium 500 mg + Vitamin D 400 IU vs Placebo (alfacalcidol) + Elemental Calcium 500 mg + Vitamin D 400 IU: Abdominal pain: 5.0%(5/100) vs 4.0%(4/101) Adverse events: 68.0%(68/100) vs 66.3%(67/101) Adverse events related to the study: 21.0%(21/100) vs 13.9%(14/101) Death: 2.0%(2/100) vs 1.0%(1/101) Death: Perforated sigmoid colon due to diverticulitis: 1.0%(1/100) vs 0.0%(0/101) Death: cerebrovascular accident: 0.0%(0/100) vs 1.0%(1/101) Death: non-Hodgkin's lymphoma: 1.0%(1/100) vs 0.0%(0/101) Death: stroke: 0.0%(0/100) vs 1.0%(1/101) Diarrhea: 3.0%(3/100) vs 6.9%(7/101) Dyspepsia: 7.0%(7/100) vs 7.9%(8/101) Gastrointestinal adverse event: 35.0%(35/100) vs 51.5%(52/101) Headache: 7.0%(7/100) vs 7.9%(8/101) Hypercalcemia ( calcium > 10.8 mg/dl): 3.0%(3/100) vs 6.9%(7/101) Hypocalcemia (calcium <8.8 mg/dl): 36.0%(36/100) vs 20.8%(21/101) Increase in creatinine (>.2 mg/dl): 8.0%(8/100) vs 15.8%(16/101) Laboratory Adverse events: 47.0%(47/100) vs 43.6%(44/101) Nausea: 2.0%(2/100) vs 7.9%(8/101) Other adverse events: 18.0%(18/100) vs 16.8%(17/101) Other symptoms: 18.0%(18/100) vs 24.8%(25/101) Skin disorder: 11.0%(11/100) vs 8.9%(9/101) Withdrawals: 21.0%(21/100) vs 16.8%(17/101) Withdrawals due to adverse events: 6.0%(6/100) vs 6.9%(7/101) |
| Obermayer-Pietsch et al., 2008520  Bisphosphonates, PTH (Teriparatide) (Forteo)  Trial: EUROFORS | Teriparatide 20 ug/day + Calcium 500 mg/day + Vitamin D 400-800 IU/day: Any adverse event: 78.2%(394/504) Abdominal pain upper: 3.8%(19/504) Any serious adverse event: 17.5%(88/504) Arthralgia: 11.7%(59/504) Back pain: 5.2%(26/504) Bronchitis: 4.6%(23/504) Constipation: 4.2%(21/504) Contusion: 3.0%(15/504) Depression: 3.0%(15/504) Diarrhea: 6.2%(31/504) Dizziness: 5.0%(25/504) Dyspepsia: 3.0%(15/504) Edema peripheral: 3.0%(15/504) Headache: 6.9%(35/504) Hypercalcemia: 5.0%(25/504) Hypertension: 8.9%(45/504) Influenza: 4.0%(20/504) Muscle cramp: 6.2%(31/504) Nasopharyngitis: 6.3%(32/504) Nausea: 12.5%(63/504) Pain in extremity: 7.3%(37/504) Urinary tract infection: 3.4%(17/504) Withdrawals: 5.6%(28/504) Withdrawals due to adverse events: 1.2%(6/504) |
| Kim et al., 2010432  Bisphosphonates, Raloxifene (Evista) | Bisphosphonates vs Raloxifene: Diaphyseal femur fracture: 0.1%(24/17,028) vs 0.1%(13/16,787) Subtrochanteric femur fracture: 0.2%(36/17,028) vs 0.2%(34/16,787) |
| Sato et al., 200772  Vitamin D, Risedronate (Actonel) | Placebo + Vitamin D2 vs Risedronate 2.5mg + Vitamin D2: Abdominal pain: 2.5%(3/121) vs 3.3%(4/121) Death or intercurrent illness: 3.3%(4/121) vs 3.3%(4/121) Esophagitis: 0.0%(0/121) vs 2.5%(3/121) Withdrawals: 7.4%(9/121) vs 8.3%(10/121) |
| McComsey et al., 2007521  Alendronate (Fosamax), Calcium, Vitamin D | Alendronate 70 mg weekly + Calcium carbonate 500 mg/2x day + Vitamin D 200 IU/2x day vs Placebo + Calcium carbonate 500 mg/2x day + Vitamin D 200 IU/2x day: Any adverse event: 69.0%(29/42) vs 57.5%(23/40) Abdominal pain: 0.0%(0/42) vs 2.5%(1/40) Cardiovascular system event: 2.4%(1/42) vs 10.0%(4/40) Chemistry abnormalities: 14.3%(6/42) vs 17.5%(7/40) Dyspepsia: 2.4%(1/42) vs 0.0%(0/40) Dysphagia: 2.4%(1/42) vs 0.0%(0/40) Endocrinology system event: 7.1%(3/42) vs 5.0%(2/40) GI event: 4.8%(2/42) vs 10.0%(4/40) General body event: 14.3%(6/42) vs 17.5%(7/40) Grade 3+ lab toxicities: 16.7%(7/42) vs 15.0%(6/40) Grade 3+ signs/symptoms: 0.0%(0/42) vs 15.0%(6/40) Hematological system event: 2.4%(1/42) vs 2.5%(1/40) Hepatic system event: 35.7%(15/42) vs 30.0%(12/40) Metabolic event: 11.9%(5/42) vs 10.0%(4/40) Neurological system event: 4.8%(2/42) vs 10.0%(4/40) Pain and burning in mouth: 2.4%(1/42) vs 0.0%(0/40) Pancreatic event: 7.1%(3/42) vs 7.5%(3/40) Renal event: 2.4%(1/42) vs 2.5%(1/40) Respiratory system event: 4.8%(2/42) vs 7.5%(3/40) Retrosternal pain: 0.0%(0/42) vs 2.5%(1/40) Serious adverse event: 19.0%(8/42) vs 35.0%(14/40) Skin event: 2.4%(1/42) vs 5.0%(2/40) Stomatitis: 2.4%(1/42) vs 0.0%(0/40) Swelling and pain in tongue: 2.4%(1/42) vs 0.0%(0/40) Urogenital system event: 0.0%(0/42) vs 5.0%(2/40) Withdrawals: 7.1%(3/42) vs 7.5%(3/40) |
| Vestergaard et al., 2010522  Alendronate (Fosamax), Etidronate (Didronel), Ibandronate (Boniva), Pamidronate (Aredia) (APD), PTH (Teriparatide) (Forteo), Raloxifene (Evista), Risedronate (Actonel) | Alendronate vs Clodronate vs Ibandronate vs Raloxifene vs Risedronate vs Teriparatide vs Zoledronic acid: Atrial fibrillation: 1.3%(729/55,090) vs 2.1%(12/566) vs 0.0%(0/612) vs 1.1%(55/4,831) vs 0.0%(0/1,452) vs 0.0%(0/303) vs 0.0%(0/22) |
| Vestergaard et al., 2009523  Alendronate (Fosamax), Etidronate (Didronel), Ibandronate (Boniva), Pamidronate (Aredia) (APD), PTH184 (Preos), Raloxifene (Evista), Risedronate (Actonel), Strontium | Alendronate vs Clodronate vs Ibandronate vs Raloxifene vs Risedronate vs Zoledronic acid vs Control: Deep venous thromboembolism or pulmonary embolism: 0.4%(200/55,090) vs 1.6%(9/566) vs 0.0%(0/612) vs 0.5%(24/4,831) vs 0.0%(0/1,452) vs 0.0%(0/22) vs 0.5%(1,528/310,683) |

| **Author, Year, Drug, Trial name** | **Adverse events reported** |
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| Gorai et al., 2009270  Raloxifene (Evista) | Alfacalcidol 1 ug/d vs Alfacalcidol 1 ug/d +Raloxifene 60 mg/d vs Raloxifene 60 mg/d: Alopecia areata: 0.0%(0/44) vs 0.0%(0/48) vs 2.2%(1/45) Angina attack: 0.0%(0/44) vs 2.1%(1/48) vs 0.0%(0/45) Calcaneodynia: 2.3%(1/44) vs 0.0%(0/48) vs 0.0%(0/45) Cramp of limb: 0.0%(0/44) vs 0.0%(0/48) vs 4.4%(2/45) Diaphoresis: 0.0%(0/44) vs 2.1%(1/48) vs 0.0%(0/45) Digestive symptom (nausea, gastralgia): 0.0%(0/44) vs 6.3%(3/48) vs 2.2%(1/45) Diverticula of the colon (abdominal pain lower): 2.3%(1/44) vs 0.0%(0/48) vs 0.0%(0/45) Dizziness: 2.3%(1/44) vs 0.0%(0/48) vs 2.2%(1/45) Gallstones: 0.0%(0/44) vs 2.1%(1/48) vs 0.0%(0/45) Headache: 2.3%(1/44) vs 0.0%(0/48) vs 2.2%(1/45) Hepatic function disorder: 0.0%(0/44) vs 2.1%(1/48) vs 2.2%(1/45) Hot flash: 2.3%(1/44) vs 0.0%(0/48) vs 2.2%(1/45) Hypercalciuria: 9.1%(4/44) vs 0.0%(0/48) vs 0.0%(0/45) Itching Paresthesia: 0.0%(0/44) vs 0.0%(0/48) vs 6.7%(3/45) Knee pain: 2.3%(1/44) vs 0.0%(0/48) vs 0.0%(0/45) Leg cramp: 0.0%(0/44) vs 4.2%(2/48) vs 4.4%(2/45) Leg edema: 0.0%(0/44) vs 0.0%(0/48) vs 2.2%(1/45) Myalgia: 2.3%(1/44) vs 0.0%(0/48) vs 2.2%(1/45) Numbness of lower extremities: 0.0%(0/44) vs 2.1%(1/48) vs 0.0%(0/45) Sweaty: 0.0%(0/44) vs 0.0%(0/48) vs 2.2%(1/45) Symptoms of menopause: 0.0%(0/44) vs 4.2%(2/48) vs 0.0%(0/45) Thoracic pain: 0.0%(0/44) vs 2.1%(1/48) vs 0.0%(0/45) Weigh increased: 0.0%(0/44) vs 0.0%(0/48) vs 2.2%(1/45) Withdrawals: due to AE: 11.4%(5/44) vs 12.5%(6/48) vs 15.6%(7/45) |
| Miller et al., 2008444  Raloxifene (Evista) | Bazedoxifene 10mg vs Bazedoxifene 20mg vs Bazedoxifene 40mg vs Raloxifene 60 mg/d vs Placebo: AEs: any: 95.3%(306/321) vs 96.0%(309/322) vs 94.4%(301/319) vs 92.3%(287/311) vs 95.8%(297/310) AEs: any serious AE: 9.0%(29/321) vs 11.5%(37/322) vs 10.3%(33/319) vs 9.3%(29/311) vs 9.0%(28/310) AEs: any treatment emergent AE: 93.1%(299/321) vs 94.4%(304/322) vs 91.5%(292/319) vs 89.7%(279/311) vs 93.2%(289/310) Breast cancer: 0.3%(1/321) vs 0.6%(2/322) vs 0.0%(0/319) vs 0.3%(1/311) vs 0.6%(2/310) Cerebral hemorrhage: 0.3%(1/321) vs 0.0%(0/322) vs 0.0%(0/319) vs 0.0%(0/311) vs 0.0%(0/310) Cerebral ischemia: 0.0%(0/321) vs 0.0%(0/322) vs 0.0%(0/319) vs 0.3%(1/311) vs 0.0%(0/310) Cerebrovascular accident: 0.0%(0/321) vs 0.0%(0/322) vs 0.3%(1/319) vs 0.0%(0/311) vs 0.0%(0/310) Deaths: 0.6%(2/321) vs 0.0%(0/322) vs 0.9%(3/319) vs 0.0%(0/311) vs 0.3%(1/310) Deep venous thrombosis: 0.0%(0/321) vs 0.6%(2/322) vs 0.0%(0/319) vs 0.0%(0/311) vs 0.3%(1/310) Endometrial cancer: 0.0%(0/321) vs 0.0%(0/322) vs 0.0%(0/319) vs 0.0%(0/311) vs 0.3%(1/310) Endometrial hyperplasia: 0.0%(0/321) vs 0.0%(0/322) vs 0.0%(0/319) vs 0.0%(0/311) vs 0.0%(0/310) Hot flushes: 19.6%(63/321) vs 20.8%(67/322) vs 24.1%(77/319) vs 18.6%(58/311) vs 14.2%(44/310) Leg cramps: 9.3%(30/321) vs 12.1%(39/322) vs 11.9%(38/319) vs 11.9%(37/311) vs 11.6%(36/310) Myocardial infarction: 0.0%(0/321) vs 0.6%(2/322) vs 0.3%(1/319) vs 0.0%(0/311) vs 0.3%(1/310) Phlebitis (superficial): 0.3%(1/321) vs 0.3%(1/322) vs 0.9%(3/319) vs 0.0%(0/311) vs 0.3%(1/310) Pulmonary embolus: 0.0%(0/321) vs 0.0%(0/322) vs 0.3%(1/319) vs 0.0%(0/311) vs 0.0%(0/310) Retinal vein thrombosis: 0.0%(0/321) vs 0.0%(0/322) vs 0.0%(0/319) vs 0.3%(1/311) vs 0.0%(0/310) Withdrawals: due to AE: 16.2%(52/321) vs 17.1%(55/322) vs 17.9%(57/319) vs 13.8%(43/311) vs 15.2%(47/310) Withdrawals: total: 32.1%(103/321) vs 30.4%(98/322) vs 30.4%(97/319) vs 28.0%(87/311) vs 27.4%(85/310) |
| Mok et al., 2010456  Raloxifene (Evista) | Raloxifene vs Placebo: Aching: 1.8%(1/57) vs 0.0%(0/57) Atypical chest pain: 0.0%(0/57) vs 7.0%(4/57) Depression: 0.0%(0/57) vs 3.5%(2/57) Dizziness/vertigo: 5.3%(3/57) vs 1.8%(1/57) Duodenal ulcer: 0.0%(0/57) vs 1.8%(1/57) Dyspepsia/heartburn: 5.3%(3/57) vs 8.8%(5/57) Flushing: 0.0%(0/57) vs 1.8%(1/57) Headache: 1.8%(1/57) vs 1.8%(1/57) Leg cramps: 7.0%(4/57) vs 0.0%(0/57) Skin rash: 1.8%(1/57) vs 1.8%(1/57) Tinnitus: 1.8%(1/57) vs 0.0%(0/57) |
| Mosca et al., 2009443  Raloxifene (Evista) | Raloxifene 60 mg/d vs Placebo: Atrial fibrillation: 6.4%(323/5,044) vs 6.6%(334/5,057) Deaths: VTE: 0.2%(10/5,044) vs 0.1%(5/5,057) Deaths: all cardiovascular deaths: 7.2%(362/5,044) vs 7.0%(355/5,057) Deaths: cerebrovascular (stroke): 1.2%(59/5,044) vs 0.8%(39/5,057) Deaths: hemorrhagic: 0.2%(10/5,044) vs 0.2%(12/5,057) Deaths: ischemic: 0.6%(29/5,044) vs 0.3%(16/5,057) Deaths: noncoronary deaths: 2.1%(107/5,044) vs 1.6%(81/5,057) Deaths: stroke undetermined: 0.4%(19/5,044) vs 0.2%(11/5,057) Stroke: Hemorrhagic: 0.4%(18/5,044) vs 0.6%(30/5,057) Stroke: Ischemic: 3.9%(198/5,044) vs 3.4%(171/5,057) Stroke: Undetermined: 0.8%(39/5,044) vs 0.6%(30/5,057) Stroke: all: 4.9%(249/5,044) vs 4.4%(224/5,057) Transient ischemic attacks: 1.7%(86/5,044) vs 1.8%(91/5,057) VTE event: all: 2.0%(103/5,044) vs 1.4%(71/5,057) VTE event: deep vein thrombosis: 1.3%(65/5,044) vs 0.9%(47/5,057) VTE event: intracranial (retinal vein) thrombosis: 0.2%(8/5,044) vs 0.1%(6/5,057) VTE event: other: 0.0%(2/5,044) vs 0.0%(1/5,057) VTE event: pulmonary embolism: 0.7%(36/5,044) vs 0.5%(24/5,057) |
| Silverman et al., 2008121  Raloxifene (Evista), Bazedoxifene | Bazedoxifene 20mg vs Bazedoxifene 40mg vs Raloxifene 60mg vs Placebo: AEs: any AE: 95.8%(1,806/1,886) vs 95.7%(1,792/1,872) vs 96.0%(1,775/1,849) vs 96.2%(1,813/1,885) AEs: any serious AE: 20.3%(382/1,886) vs 19.7%(368/1,872) vs 18.6%(344/1,849) vs 18.7%(353/1,885) Breast carcinoma: 0.3%(5/1,886) vs 0.2%(4/1,872) vs 0.4%(7/1,849) vs 0.4%(8/1,885) Breast cyst/fibrocystic breast disease: 0.7%(13/1,886) vs 0.6%(12/1,872) vs 1.7%(31/1,849) vs 1.0%(18/1,885) Deaths: 0.9%(17/1,886) vs 0.7%(13/1,872) vs 1.0%(19/1,849) vs 0.6%(11/1,885) Deep vein thrombosis: 0.4%(8/1,886) vs 0.5%(10/1,872) vs 0.4%(8/1,849) vs 0.1%(1/1,885) Endometrial carcinoma: 0.0%(0/1,886) vs 0.1%(2/1,872) vs 0.1%(2/1,849) vs 0.2%(3/1,885) Endometrial hyperplasia: 0.1%(1/1,886) vs 0.1%(1/1,872) vs 0.1%(1/1,849) vs 0.1%(1/1,885) Hemorrhagic stroke: 0.1%(1/1,886) vs 0.1%(1/1,872) vs 0.1%(2/1,849) vs 0.3%(5/1,885) Indeterminate: 0.4%(7/1,886) vs 0.2%(3/1,872) vs 0.2%(4/1,849) vs 0.2%(4/1,885) Ischemic stroke: 0.6%(11/1,886) vs 0.8%(15/1,872) vs 0.5%(9/1,849) vs 0.6%(11/1,885) Leg cramps: 10.9%(205/1,886) vs 10.9%(204/1,872) vs 11.7%(216/1,849) vs 8.2%(155/1,885) Myocardial infarction: 0.4%(8/1,886) vs 0.4%(8/1,872) vs 0.3%(6/1,849) vs 0.4%(8/1,885) Pulmonary embolus: 0.3%(5/1,886) vs 0.2%(3/1,872) vs 0.2%(4/1,849) vs 0.2%(4/1,885) Retinal vein thrombosis: 0.1%(2/1,886) vs 0.1%(1/1,872) vs 0.0%(0/1,849) vs 0.2%(3/1,885) Strokes: total: 1.0%(19/1,886) vs 1.0%(19/1,872) vs 0.8%(15/1,849) vs 1.1%(20/1,885) Vasodilatation: 12.6%(238/1,886) vs 13.0%(243/1,872) vs 12.0%(222/1,849) vs 6.3%(118/1,885) Venous thromboembolic events: 0.7%(13/1,886) vs 0.6%(12/1,872) vs 0.5%(10/1,849) vs 0.3%(5/1,885) Withdrawals: due to AE: 14.3%(269/1,886) vs 14.4%(270/1,872) vs 14.2%(262/1,849) vs 12.7%(240/1,885) Withdrawals: total: 33.5%(632/1,886) vs 34.3%(643/1,872) vs 32.3%(597/1,849) vs 33.4%(629/1,885) |
| Pelayo et al., 2008524  Calcium, Raloxifene (Evista) | Raloxifene (60 mg/d) +CC (600 mg/d) vs Raloxifene (60 mg/d) +OHC (712 mg/d): Constipation: 0.0%(0/42) vs 4.2%(2/48) Hot flashes: 7.1%(3/42) vs 8.3%(4/48) Mild leg swelling: 2.4%(1/42) vs 4.2%(2/48) Nephrolithiasis: 0.0%(0/42) vs 2.1%(1/48) Nonspecific GI problems: 7.1%(3/42) vs 6.3%(3/48) Withdrawals due to adverse events: 9.5%(4/42) vs 14.6%(7/48) Withdrawals: total: 11.9%(5/42) vs 16.7%(8/48) |
| Anastasilakis et al., 2008266  PTH (Teriparatide) (Forteo), Raloxifene (Evista) | Risedronate 35 mg/wk vs Teriparatide 20 ug/d: Total number of any AE: 31.8%(7/22) vs 50.0%(11/22) Bone pain: 4.5%(1/22) vs 13.6%(3/22) Dizziness: 0.0%(0/22) vs 9.1%(2/22) Epigastric pain: 9.1%(2/22) vs 0.0%(0/22) Flushes: 0.0%(0/22) vs 4.5%(1/22) Hypercalcaemia: 4.5%(1/22) vs 9.1%(2/22) Nausea: 0.0%(0/22) vs 9.1%(2/22) Renal colic: 0.0%(0/22) vs 4.5%(1/22) Substernal burn: 13.6%(3/22) vs 0.0%(0/22) |

| **Author, Year, Drug, Trial name** | **Adverse events reported** |
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| Miller et al., 2007460  PTH (Teriparatide) (Forteo)  Trial: TPTD  Study A | Teriparatide 20ug/d vs Teriparatide 40ug/d vs Placebo: Hematuria: 0.8%(4/527) vs 0.7%(4/541) vs 1.1%(6/536) Hypercalcemia at 4-h after a dose: 2.1%(11/527) vs 5.2%(28/541) vs 0.4%(2/536) Hypercalciuria: 12.0%(63/527) vs 7.0%(38/541) vs 10.1%(54/536) Kidney calculus: 0.4%(2/527) vs 0.0%(0/541) vs 0.4%(2/536) Kidney pain: 0.6%(3/527) vs 0.2%(1/541) vs 0.0%(0/536) Normal urinary calcium excretion and hypercalcemia: 0.9%(5/527) Predose (>16 h after injection) hypercalcemia: 0.2%(1/527) vs 0.0%(0/541) vs 0.2%(1/536) Urinary tract calcifications: 0.2%(1/527) vs 0.2%(1/541) vs 0.0%(0/536) Urolithiasis: 1.1%(6/527) vs 0.4%(2/541) vs 0.4%(2/536) |
| Miller et al., 2007460  PTH (Teriparatide) (Forteo)  Trial: TPTD  Study B | Teriparatide 20ug/d vs Teriparatide 40ug/d vs Placebo: Hypercalciuria at 1 month: 18.6%(27/145) vs 19.7%(26/132) vs 15.6%(22/141) Kidney calculus: 1.4%(2/145) vs 0.8%(1/132) vs 0.7%(1/141) Kidney pain: 0.0%(0/145) vs 0.8%(1/132) vs 0.0%(0/141) Urolithiasis: 3.4%(5/145) vs 3.8%(5/132) vs 3.5%(5/141) |
| Recker et al., 2009525  PTH (Teriparatide) (Forteo), Strontium ranelate | Teriparatide: ≥1 predose serum calcium level>2.75mM: 7.7%(3/39) AEs: ≥1 AE: 41.0%(16/39) AEs: serious AE: 2.6%(1/39) Above ULN in total alkaline phosphatase: 28.2%(11/39) Above ULN in uric acid: 30.8%(12/39) Cerebrovascular accident: 0.0%(0/39) Lymphoma: 0.0%(0/39) Parathyroid adenoma: 0.0%(0/39) Withdrawals: due to AE: 5.1%(2/39) Withdrawals: total: 15.4%(6/39) |

| **Author, Year, Drug, Trial name** | **Adverse events reported** |
| --- | --- |
| Bone et al., 2008117  Denosumab | Denosumab 60 mg/6 mos vs Placebo: Any AE: 94.0%(156/166) vs 94.6%(157/166) AE in >10% subjects: arthralgia: 24.7%(41/166) vs 25.3%(42/166) AE in >10% subjects: back pain: 19.9%(33/166) vs 19.9%(33/166) AE in >10% subjects: constipation: 10.8%(18/166) vs 4.8%(8/166) AE in >10% subjects: headache: 15.7%(26/166) vs 11.4%(19/166) AE in >10% subjects: influenza: 9.0%(15/166) vs 10.8%(18/166) AE in >10% subjects: nasopharyngitis: 21.7%(36/166) vs 18.7%(31/166) AE in >10% subjects: pain in extremity: 14.5%(24/166) vs 12.0%(20/166) AE in >10% subjects: pharyngolaryngeal pain (sore throat): 9.0%(15/166) vs 3.0%(5/166) AE in >10% subjects: rash: 8.4%(14/166) vs 3.0%(5/166) AE in >10% subjects: shoulder pain: 10.2%(17/166) vs 6.0%(10/166) AE in >10% subjects: sinusitis: 6.0%(10/166) vs 10.2%(17/166) AE in >10% subjects: upper respiratory tract infection: 11.4%(19/166) vs 13.3%(22/166) AE in >10% subjects: urinary tract infection: 10.8%(18/166) vs 10.2%(17/166) Deaths: 0.0%(0/166) vs 0.0%(0/166) Serious AE: gastrointestinal disorder: 1.2%(2/166) vs 0.0%(0/166) Serious AE: hepatobiliary disorder: 0.0%(0/166) vs 0.6%(1/166) Serious AE: infection: 4.8%(8/166) vs 0.6%(1/166) Serious AE: injury, poisoning, or procedural complication: 1.2%(2/166) vs 0.6%(1/166) Serious AE: musculoskeletal or connective tissue disorder: 1.8%(3/166) vs 1.2%(2/166) Serious AE: neoplasm - B cell lymphoma: 0.0%(0/166) vs 0.6%(1/166) Serious AE: neoplasm - breast cancer in situ: 0.6%(1/166) vs 0.0%(0/166) Serious AE: neoplasm - mycosis fungoides: 0.6%(1/166) vs 0.0%(0/166) Serious AE: neoplasm - ovarian cancer: 0.6%(1/166) vs 0.0%(0/166) Serious AE: neoplasm - uterine cancer: 0.6%(1/166) vs 0.0%(0/166) Serious AE: nervous system disorder: 0.0%(0/166) vs 0.6%(1/166) Serious AE: psychiatric disorder: 0.0%(0/166) vs 0.6%(1/166) Serious AE: reproductive system or breast disorder: 0.6%(1/166) vs 0.6%(1/166) Withdrawals: 6.0%(10/166) vs 9.0%(15/166) Withdrawals due to AE: 0.6%(1/166) vs 1.2%(2/166) |
| Cohen et al., 2008526  Denosumab  Trial: DENOSUMAB RA STUDY CORP | Denosumab 180 mg injections + Elemental Calcium 500-1000 mg + Vitamin D 400-800 IU vs Denosumab 60 mg injections + Elemental Calcium 500-1000 mg + Vitamin D 400-800 IU vs Subcutaneous placebo + Elemental Calcium 500-1000 mg + Vitamin D 400-800 IU: Any adverse event: 77.8%(56/72) vs 84.5%(60/71) vs 89.3%(67/75) Arthralgia: 5.6%(4/72) vs 8.5%(6/71) vs 2.7%(2/75) Bronchitis: 5.6%(4/72) vs 4.2%(3/71) vs 4.0%(3/75) Cough: 1.4%(1/72) vs 8.5%(6/71) vs 6.7%(5/75) Death: 0.0%(0/72) vs 0.0%(0/71) vs 0.0%(0/75) Infection requiring hospitalization: 2.8%(2/72) vs 1.4%(1/71) vs 1.3%(1/75) Influenza: 9.7%(7/72) vs 2.8%(2/71) vs 0.0%(0/75) Nasopharyngitis: 6.9%(5/72) vs 7.0%(5/71) vs 12.0%(9/75) Neoplasm: 1.4%(1/72) vs 1.4%(1/71) vs 2.7%(2/75) Rhematoid arthritis flare: 29.2%(21/72) vs 29.6%(21/71) vs 33.3%(25/75) Serious adverse event: 8.3%(6/72) vs 4.2%(3/71) vs 9.3%(7/75) Sinusitis: 11.1%(8/72) vs 5.6%(4/71) vs 10.7%(8/75) Upper respiratory tract infection: 12.5%(9/72) vs 15.5%(11/71) vs 8.0%(6/75) Urinary tract infection: 4.2%(3/72) vs 5.6%(4/71) vs 1.3%(1/75) Withdrawals due to adverse events: 1.4%(1/72) vs 0.0%(0/71) vs 1.3%(1/75) |
| Cummings et al., 2009118  Denosumab  Trial: FREEDOM | Denosumab 60 mg/6 mos vs Placebo: AEs: all: 92.8%(3,605/3,886) vs 93.1%(3,607/3,876) AEs: serious: 25.8%(1,004/3,886) vs 25.1%(972/3,876) Atrial fibrillation: 0.7%(29/3,886) vs 0.7%(29/3,876) Cancer: overall: 4.8%(187/3,886) vs 4.3%(166/3,876) Cancer: serious: 3.7%(144/3,886) vs 3.2%(125/3,876) Cardiovascular event: 4.8%(186/3,886) vs 4.6%(178/3,876) Cellulitis (including erysipelas): overall: 1.2%(47/3,886) vs 0.9%(36/3,876) Cellulitis (including erysipelas): serious: 0.3%(12/3,886) vs 0.0%(1/3,876) Concussion: 0.0%(1/3,886) vs 0.3%(11/3,876) Coronary heart disease: 1.2%(47/3,886) vs 1.0%(39/3,876) Deaths: 1.8%(70/3,886) vs 2.3%(90/3,876) Decrease in serum calcium to levels below 8mg: 0.1%(4/3,886) vs 0.1%(5/3,876) Delayed fracture healing: 0.1%(2/3,886) vs 0.1%(4/3,876) Development of neutralizing antibodies to denosumab: 0.0%(0/3,886) vs 0.0%(0/3,876) Eczema: 3.0%(118/3,886) vs 1.7%(65/3,876) Falling: 4.5%(175/3,886) vs 5.7%(219/3,876) Flatulence: 2.2%(84/3,886) vs 1.4%(53/3,876) Hypocalcemia: 0.0%(0/3,886) vs 0.1%(3/3,876) Infection: overall: 52.9%(2,055/3,886) vs 54.4%(2,108/3,876) Infection: serious: 4.1%(159/3,886) vs 3.4%(133/3,876) Local reactions: 0.8%(33/3,886) vs 0.7%(26/3,876) Opportunistic infections: 0.1%(4/3,886) vs 0.1%(3/3,876) Osteonecrosis of the jaw: 0.0%(0/3,886) vs 0.0%(0/3,876) Peripheral vascular disease: 0.8%(31/3,886) vs 0.8%(30/3,876) Stroke: 1.4%(56/3,886) vs 1.4%(54/3,876) Withdrawals: due to AE: 2.4%(93/3,886) vs 2.1%(81/3,876) |

| **Author, Year, Drug, Trial name** | **Adverse events reported** |
| --- | --- |
| Boone et al., 2006136  Estrogen | 17ß-estradiol (0.05 mg/d) then norethisterone acetate (0.24 mg/d) + 17ß-estradiol (0.05 mg/d)® vs Placebo: Withdrawals: total: 50.0%(8/16) vs 6.7%(1/15) |

| **Author, Year, Drug, Trial name** | **Adverse events reported** |
| --- | --- |
| Bolland et al., 2008469  Calcium | Calcium vs Placebo: Angina: 6.8%(50/732) vs 9.6%(71/739) Death: 4.6%(34/732) vs 3.9%(29/739) Myocardial infarction: 4.2%(31/732) vs 1.9%(14/739) Other chest pain: 2.2%(16/732) vs 2.0%(15/739) Stroke: 5.5%(40/732) vs 3.8%(28/739) Sudden death: 0.5%(4/732) vs 0.1%(1/739) Transient ischaemic attack: 4.5%(33/732) vs 2.8%(21/739) |
| Lewis et al., 2011527  Calcium  Trial: CAIFOS | Calcium vs Placebo: At least one vascular event: 13.2%(96/730) vs 14.0%(102/730) Deaths: Arrhythmia: 1.4%(10/730) vs 2.2%(16/730) Deaths: Cerebrovascular disease (excl. hemorrhage): 2.7%(20/730) vs 3.0%(22/730) Deaths: Heart failure: 1.9%(14/730) vs 3.7%(27/730) Deaths: Ischemic heart disease: 4.7%(34/730) vs 4.9%(36/730) Deaths: Peripheral arterial disease (excl. hemorrhage): 0.1%(1/730) vs 0.5%(4/730) Hospitalization: Arrhythmia: 5.3%(39/730) vs 5.5%(40/730) Hospitalization: Cerebrovascular disease (excl. hemorrhage): 6.2%(45/730) vs 7.8%(57/730) Hospitalization: Heart failure: 3.0%(22/730) vs 3.8%(28/730) Hospitalization: Ischemic heart disease: 11.6%(85/730) vs 11.6%(85/730) Hospitalization: Peripheral arterial disease (excl. hemorrhage): 2.6%(19/730) vs 2.5%(18/730) Total vascular deaths: 8.1%(59/730) vs 9.9%(72/730) Total vascular hospitalization: 21.9%(160/730) vs 23.2%(169/730) |
| Matsumoto et al., 2005470  Vitamin D | ED-71 0.5ug/d vs ED-71 0.75ug/d vs ED-71 1.0ug/d vs Placebo: ≥1 episode of hypercalcemia over 2.6mmol/liter: 7.3%(4/55) vs 5.5%(3/55) vs 23.2%(13/56) vs 0.0%(0/53) ≥1 episode of hypercalciuria over 0.1mmol/liter GF: 7.3%(4/55) vs 9.1%(5/55) vs 25.0%(14/56) vs 0.0%(0/53) AEs: any serious AE: 10.9%(6/55) vs 12.7%(7/55) vs 5.4%(3/56) vs 7.5%(4/53) Blood calcium increased: 7.3%(4/55) vs 5.5%(3/55) vs 23.2%(13/56) vs 0.0%(0/53) Conjunctivitis: 3.6%(2/55) vs 5.5%(3/55) vs 0.0%(0/56) vs 0.0%(0/53) Cystitis NOS: 7.3%(4/55) vs 10.9%(6/55) vs 1.8%(1/56) vs 1.9%(1/53) Headache: 1.8%(1/55) vs 5.5%(3/55) vs 5.4%(3/56) vs 0.0%(0/53) Stomachache NOS: 7.3%(4/55) vs 0.0%(0/55) vs 1.8%(1/56) vs 0.0%(0/53) Urine calcium increased: 7.3%(4/55) vs 9.1%(5/55) vs 25.0%(14/56) vs 1.9%(1/53) |
| Sanders et al., 2010164  Vitamin D  Trial: VIT. D | Vitamin D vs Placebo: Cancer: 0.6%(7/1,131) vs 0.9%(10/1,125) Cardiovascular events: 15.1%(171/1,131) vs 1.2%(13/1,125) Death nos: 3.5%(40/1,131) vs 4.2%(47/1,125) Injury including fracture: 15.2%(172/1,131) vs 12.1%(136/1,125) |
| Salovaara et al., 2010154  Calcium, Vitamin D  Trial: OSPRE | Vitamin D + calcium vs Placebo: Death NOS: 0.9%(15/1,586) vs 0.8%(13/1,609) |
| Xia et al., 2009227  Calcium, Vitamin D | Caltrate D (600 mg calcium and 125 iu vitamin D) vs Rocaltrol (0.25 ug/d) +Caltrate D (600 mg calcium and 125 iu vitamin D): Calcification: 0.0%(0/76) vs 0.0%(0/74) Renal lithiasis: 0.0%(0/76) vs 0.0%(0/74) Withdrawals: total: 5.3%(4/76) vs 5.4%(4/74) |

| **Author, Year, Drug, Trial name** | **Adverse events reported** |
| --- | --- |
| Korpelainen et al., 2010215  Physical activity | Exercise vs Placebo: Death due to cancer: 1.2%(1/84) vs 2.6%(2/76) Death due to cardiovascular disease: 0.0%(0/84) vs 6.6%(5/76) Death due to external cause: 0.0%(0/84) vs 1.3%(1/76) |

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| Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone |
| AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal |

| **Citations** | **Drugs** | **Primary Care** | **Inclusion/exclusion minimal\*** | **Outcome= fx** | **Duration>6mos/Adherence** | **Adverse events** | **Sample size\*\*** | **ITT** | **Total** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Bone, 2008117 | Denosumab | y | y | y | y/n | y | 332 | n | 5.5 out of 7 |
| Bonnick, 2007226 | alendronate vs. alendronate+calcium | y | y (many exclusion criteria) | n (fx reported as AEs) | y/y | y | 484 | y (modified) | 6 out of 7 |
| Boone, 2006136 | estrogen | n | n (PM women with primary biliary cirrhosis) | y | y/y | y | 31 | n | 3 out of 7 |
| Boonen, 200974 | risedronate | y | y (male) | y | y/n | y | 284 | y | 6.5 out of 7 but men |
| Campbell, 2009231 | estrogen (and etidronate) | y | n (GC users w/asthma) | y | y/n | n | 47 | n | 2.5 out of 7 |
| Chapman, 2009114 | zoledronic acid | n | n(CF) | y | y/y | y | 22 | y | 4 out of 7 |
| Cummings, 2009118 | Denosumab | y | y (many exclusion criteria) | y | y/y | y | 7,868 | y | 7 out of 7 |
| de Nijs, 200657 | alendronate and vitamin D | n | n (GC-users w/autoimmune diseases) | y | y/n | y | 163 | n | 3.5 out of 7 |
| Delmas, 200885 | risedronate | y | p (excl users of other osteoporosis meds and obese women) | y | y/y | y | 1,231 | n | 5 out of 7 |
| Delmas, 200886 | risedronate | y | p (excl users of other osteoporosis meds and many comorbidities) | y | y/y | y | 1,294 | n | 5 out of 7 |
| Ensrud, 2008120 | raloxifene | y | n (women w/CHD; many exclusion criteria) | y | y/y | y | 10,101 | y | 6 out of 7 |
| Fahrleitner-Pammer, 2009106 | ibandronate | n | n (male heart transplant) | y | y/n | y | 35 | n | 2.5 out of 7 |
| Frost, 2007157 | calcium | n | n (men with CHF) | y | y/n | y | 33 | n | 2.5 out of 7 |
| Fujita, 2004158 | calcium | n | n(hosp women) | y | y/n | n | 19 | n | 1.5 out of 7 |
| Ishani, 2008255 | raloxifene | y | y (stratification by renal failure status) | y | y/n | y | 7,492 | y | 6.5 out of 7 |
| Korpelainen, 2010215 | Physical activity | y | y (population based) | y | n/n | y | 160 | y | 6 out of 7 |
| Larsen, 2004150 | Calcium and Vitamin D | y | y | y | y/n | n | 9,605 | y | 5.5 out of 7 |
| Law, 2006163 | Vitamin D | y | y | y | y/n | n | 3,717 | y | 5.5 out of 7 |
| Lyles, 2007113 | zoledronic acid | y | y (prior hip fx) | y | y/nr (not relevant, once-yearly) | y | 2,127 | y | 7 out of 7 |
| Lyons. 2007203 | Vitamin D | y | y | y | y/y | y(mort only) | 3,440 | y | 7 out of 7 |
| Okada, 2008225 | alendronate and vitamin D | y | n (GC-users w/autoimmune diseases) | y | y/n | y | 47 | n | 4.5 out of 7 |
| Palomba, 200875 | risedronate | n | n (IBD pts) | y | y/y | y | 90 | y | 4 out of 7 |
| Papaioannou, 200855 | alendronate | n | n (CF) | y | y/y | y | 56 | y | 4 out of 7 |
| Ringe, 200756 | alendronate and vitamin D | y | y | y | y/n | y | 90 | y | 5.5 out of 7 |
| Ringe, 200973 | risedronate | y | n (male, small German clinic) | y | y/n | y | 316 | y | 5.5 out of 7 but men |
| Saag, 2009224 | alendronate and PTH | y | n (GC-users) | y | y/n | y | 428 | y | 5.5 out of 7 |
| Salovaara, 2010 154 | Calcium and vitamin D | y | y (population-based) | y | y/y | y | 3,195 | y | 7 out of 7 |
| Sanders, 2010 164 | Vitamin D | y | y | y | y/y | y | 2,256 | y | 7 out of 7 |
| Sato, 200772 | Risedronate and vitamin D | n | n (males with Parkinsons) | y | y/n | y | 223 | n | 3.5 out of 7 |
| Shiraki, 1996161 | Vitamin D | y | y | y | y/n | n | 113 | y | 5.5 out of 7 |
| Silverman, 2008121 | raloxifene | y | n (many exclusion criteria, incl vitamin D use) | y | y/n | y | 7,492 | y | 5.5 out of 7 |
| Smith, 2007162 | Vitamin D | y | y | y | y/y | y | 9,440 | y | 7 out of 7 |
| Xia, 2009227 | Calcium and Vitamin D | y | y (Chinese women) | y | y/n | y | 150 | y | 6.5 out of 7 |

\*p=probably

\*\*n<100 considered "no"