|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Drug** | **Dosing** | **Route of administration** | **Phase III study** | **Fractures intervention** | **Contraindications** | **Side effects** |
| **Biphosphonates** |  |  |  |  |  |  |
| Alendronate | 70mg, weekly | Oral *bioavailability impaired by food* | FIT Extension FLEX | Vertebral (RR 0.53) and non vertebral fractures, hip (RR 0.49) | ClCr < 35ml/min, Pregnancy, hypersensivity, hypocalcemia | Flu-like symptoms (IV infusion), hypocalcemia,  |
| Risendronate | 35mg, weekly | Oral | VERT  | Vertebral (RR 0.59) and non vertebral fractures, hip (RR 0.60) |  | Mild GI disturbances, rarely esophagitis, Esophagealcancer (?),Atrial fibrillation  |
| Ibandronate | 2.5mg daily OR 150mg monthly3mg, quartly per yer | OralIV | BONEDIVA | Vertebral fractures (RR 0.38 ), Non vertebral fractures (adhoc analysis)  |  | (possible causal relation), Osteonecrosis of the jaw (+cancer patients), |
| Zoledronate | 5mg, yearly | IV | HORIZON | Vertebral (RR 0.30) and non vertebral fractures, hip (RR 0.59) |  | Subtrochanteric fractures (causal relation not established) |
|  |  |  |  |  |  |  |
| **Strotium ranelate** | 2g, daily | Oral, 2h after the last meal | SOTITROPOS | Vertebral (RR 0.59) and non vertebral fractures, hip (RR 0.85) | ClCr < 30ml/min, history of VTE, hypersensivity | Nausea and diarrhoea, increased risk VTE (possible relation), DRESS syndrome, Increased CDV risk. |
| **Denosumab** | 60mg, every 6 months | SC | FREEDOM (against placebo)DECIDE (against alendronate) | Vertebral (RR 0.32) and non vertebral fractures, hip (RR 0.6) | CLCr<30ml/min, Pregnancy, hypersensivity, pre-existing hypocalcemia | Rash, musculosketelal pain, hypocalcemia, osteonecrosis of the jaw. |
| **PTH analogs** |  |  |  |  |  |  |
| Teriparatide (1-34 PTH) | 20ug, daily | SC | TOWEREUROFORS | Vertebral (RR 0.35) and non vertebral fractures (RR 0.47) | Hyperparathyroidism, Hypercalcemia, metabolic bone diseases, skeletal malignancies or bone methatasis | Nausea, headache, dizziness, transient ortosthatic hypotension, Hypercalcemia, Exacerbation of urolythiasis |
| 1-84 PTH | 100ug,daily | SC | TOP | Vertebral fractures (RR 0.39) |  | in patients with recent crisis. |
| **SERMS** |  |  |  |  |  |  |
| Raloxifene | 60mg, daily | Oral | MORE | Vertebral fractures (RR 0.70) | Pregnancy, lactation, history of VTE events | Increased risk of VTE |
| Hormonal replacement therapy |  |  |  | Not approved for OP therapy |  | According to WHI: increased risk coronary heart disease, stroke and breast cancer |

Table 3: Drugs used in OP treatment.

CDV - cardiovascular, DRESS Drug rash with eosinophilia and systemic symptoms, VTE – venous thromboembolic event, WHI women’s health initiative