Table . Summary of Clinical Trials

Ref	Drug Regimens	n	Time	Demographics	Design*	End Points/Results/Comments
2	1. Placebo QD 2. Risedronate 2.5mg QD 3. Risedronate 5mg QD (All patients also took Ca 1g QD and vitamin D up to 500 IU QD)	408 410 408	3 yrs Rx (2.5mg group DC'd after 2 yrs when 5mg showed superior efficacy & no loss of tolerability	**Postmenopausal Osteoporosis:** Ambulatory women ≤85 yrs old 5+ yrs post-menopause who had ≥2 vertebral fractures No vitamin D analogs in last mo; no estrogens last 3 mos; no bisphosphonates last 6 mos	Double-masked, PC, PG, DB, RCT (80 study centers in Europe and Australia)	**Primary endpt:** % pts w/new vert fx: Placebo 2.5mg QD 5mg QD After 1 yr 13% 7.1% 5.6% RRR 5mg QD vs. placebo: 0.49 (p<0.001) After 3 yrs 29.0% N/A 18.1% RRR 5mg QD vs. placebo: 0.61 (p=0.001) NNT: 10 over 3 yrs; 14 over 1 yr (treated with 5mg QD) 44% of patients completed study; dropouts were evenly distributed among treatment groups (except discontinued 2.5mg group); Side effects: no sig differences among treatment group
3	1. Placebo QD 2. Risedronate 2.5mg QD 3. Cyclical 15mg risedronate (15mg risedronate daily during 2 wks followed by placebo daily during 10 wks)	40 40 40	2 yrs Rx 3 yrs F/U	**Glucocorticoid Induced Osteoporosis:** Postmenopausal women with rheumatoid arthritis who required long-term (>6 months) treatment with oral glucocorticoids (>2.5mg prednisolone)	Double-masked, PC, PG, RCT two centers (Sheffield, UK & Brussels, Belgium)	**Primary endpoint:** BMD: mean % change at lumbar spine from baseline at wk 97 Placebo QD drug Cyclical drug -1.6%* 1.4%## - 0.05% *p<0.05 from baseline; ##p<0.01 from placebo **Secondary endpoints:** mean BMD % change att femoral neck and trochanter Placebo QD drug Cyclical drug -3.6%** -1.0% 0.9% -4.0%** -0.4%# 1.3%## **p<0.01 from baseline;#p<0.05 from placebo; ##p<0.01 from placebo Study dropout rate not noted Side effects: abdominal pain (20% risedronate groups vs. 2.5% placebo)

Ref	Drug Regimens	n	Time	Demographics	Design*	End Points/Results/Comments
4	1. Placebo QD 2. Risedronate 2.5mg QD 3. Risedronate 5mg QD (All patients also took Ca 1g QD + vitamin D 400 IU QD)	96 94 100	1 yr Rx	**Glucocorticoid Induced Osteoporosis:** Men (109) and women (181, 14% premenopausal) aged 18-85 receiving long-term (>6 months) treatment with oral corticosteroids (≥7.5mg prednisone)	PC, PG, DB, RCT MC (23 centers in Europe	**Primary endpoint**:: BMD: mean % change at lumbar spine from baseline at12 months Placebo 2.5mg QD 5mg QD p-value 0.4% 1.9% 2.9% <0.001 **Secondary endpoints:** At femoral neck Placebo 2.5mg QD 5mg QD p-value -0.3% -0.2% 1.8% 0.004 Fem trochanter Placebo 2.5mg QD 5mg QD p-value 1.0% 0.1% 2.4% 0.01 Vert fracture Placebo 2.5mg QD 5mg QD p-value 15% 5% 5% 0.125 • 78% of patients completed study; dropouts were evenly distributed among treatment groups • NNT: 10 (to prevent fracture); however ARR not statistically significant • Side effects: back pain (23% 5mg group vs. 10% placebo); arthralgia (24% 5mg group vs. 15% placebo)
5	1. Placebo QD 2. Risedronate 2.5mg QD 3. Risedronate 5mg QD (All patients also took Ca 1g QD and vitamin D up to 500 IU QD)	815 811 813	3 yrs Rx (2.5mg group DC'd after 2 yrs when 5mg showed superior efficacy with no loss of tolerability)	**Postmenopausal Osteoporosis:** Ambulatory women ≤85 yrs old at least 5 yrs post-menopause who had ≥2 vertebral fractures, or 1 vertebral fracture and BMD T-score ≤2 No vitamin D analogs in last month; no estrogens in last 3 months; no bisphosphonates in last 6 months	PC, PG, DB, RCT conducted in 110 centers in North America	**Primary endpoint**:: New vertebral fractures:% of pts with ≥1 fracture over 3 yrs Placebo 2.5mg QD 5mg QD 16.3% N/A 11.3% RRR 5mg vs placebo: 0.65 (p<0.001) Over 1 yr 6.4% 3.8% 2.4% RRR 5mg vs placebo: 0.41 (p=0.003) NNT: 20 over 3 yrs; 25 over 1 yr (treated with 5mg QD) • 38% of patients completed study; 2.5mg group discontinued significantly more placebo dropouts than 5mg group dropouts had new vertebral fractures • Side effects: no significant differences among treatment groups

Evidence table abbreviations: DB = double-blind; RCT = randomized controlled trial; PC = placebo-controlled; PG = parallel-group; MC = multi-center; XO = crossover; F/U = follow-up; N/A = not applicable; ARR = absolute risk reduction; RRR = relative risk reduction; NNT = number needed to treat; BMD = Bone Mineral Density; qd = daily; Ca = calcium; IU = international units; mos = months; DC'd = discontinued; fem = femoral; vert = vertebral