



# Tony Romo-sozumab: Winning touchdown in osteoporosis or interception for the loss?

## CLINICAL QUESTION

**What is the efficacy and safety of romosozumab in postmenopausal women with osteoporosis?**

## BOTTOM LINE

**In a single randomized, controlled trial (RCT) of postmenopausal women with fracture history, romosozumab was more effective than alendronate at reducing major osteoporotic fractures (7% versus 10%) including hip fractures (2% versus 3%) but increased cardiovascular events (0.8% versus 0.3%) at 2.7 years. High cost and potential cardiovascular harm may limit use.**

## EVIDENCE

- Differences statistically significant unless noted.
- Efficacy: Two main RCTs of romosozumab 210mg subcutaneous monthly (mean age: 70).<sup>1-2</sup>
  - Versus alendronate 70mg weekly for 12 months, followed by open-label alendronate for additional 12 months in both groups. 4093 women (96%: vertebral fracture; baseline FRAX ~20%).<sup>1</sup> At 24-32 months:

- Major osteoporotic fractures: 7.1% versus 10% (alendronate), number needed to treat (NNT)=35.
    - Hip fracture: 2.0% versus 3.2% (alendronate), NNT=84.
    - Clinical vertebral fracture: 0.9% versus 2.1% (alendronate), NNT=79.
  - Versus placebo for 12 months, followed by denosumab subcutaneously 60mg every 6 months for one year in both groups. 7180 women with T-score -2.5 to -3.5 at hip/femoral neck (~20% previous fracture, baseline FRAX ~13%) at 12 months:<sup>2</sup>
    - Major osteoporotic fracture: 1.1% versus 1.8% (placebo), NNT=143.
    - Hip, non-vertebral fracture: No difference.
    - Vertebral fracture: 0.5% versus 1.8% (placebo), NNT=77.
    - Systematic reviews with additional small RCTs: Similar.<sup>3,4</sup>
- Adverse Events: Nine systematic reviews, romosozumab versus placebo.<sup>5-13</sup> Most comprehensive review (nine RCTs, 12,796 postmenopausal women):<sup>7</sup>
  - Injection site reactions: 5.3% versus 2.9% (placebo), number needed to harm (NNH)=44 at 6-12 months.
  - Osteonecrosis of jaw, atypical femur fracture: <1%, no statistical difference.
  - Consistent with other reviews.<sup>5,6,8,9,14-16</sup>
  - Cardiovascular risk: Focusing on above main RCTs:
    - Cardiac ischemic events:<sup>1</sup> 0.8% versus 0.3% (alendronate), NNH=206
      - Not reported in placebo-controlled trial.<sup>2</sup>
- Limitations: Industry funded;<sup>1-2</sup> few non-vertebral fractures in placebo-controlled RCT;<sup>2</sup> no comparisons versus denosumab.

## CONTEXT

- Guideline: Consider romosozumab first-line if:<sup>14</sup>
  - Vertebral fracture (within last two years) with vertebral height loss >40%, or
  - >1 vertebral fracture and T-score ≤ -2.5.
- Duration: Approved for one year, then anti-resorptive agent.<sup>14</sup>
- Yearly cost:<sup>15,16</sup>
  - Romosozumab ~ \$8200.
  - Risedronate/alendronate: ~\$480.
  - Denosumab: ~\$800.

## REFERENCES

1. Saag K, Petersen J, Brandi ML *et al.* *New Engl J Med.* 2017; 377:1417-1427.
2. Cosman F, Crittenden DB, Adachi JD, *et al.* *New Engl J Med.* 2016; 375:1532-43.
3. Davis S, Simpson E, Hamilton J, *et al.* *Health Technol Assess.* 2020; 24(29):1-314.
4. Simpson EL, Martyn-St James M, Hamilton J, *et al.* *Bone.* 2020; 130: 115081.

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*Authors do not have any  
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5. Ayers C, Kansagara D, Lazur B, *et al.* Ann Intern Med. 2023; 176(2): 182-195.
6. Händel MN, Cardoso I, von Bülow C, *et al.* BMJ. 2023; 381; e068033.
7. Huang W, Nagao M, Yonemoto N, *et al.* Pharmacoepidemiol Drug Saf. 2023; 32:671-684.
8. Singh S, Dutta S, Khasbage S, *et al.* Osteoporos Int. 2022; 33(1): 1-12.
9. Kaveh S, Hosseinifard H, Nashmil G, *et al.* Clin Rheumatol. 2020; 39: 3261-3276.
10. Lv F, Xiaoling C, Wenjia Y, *et al.* Bone. 2020; 130: <https://doi.org/10.1016/j.bone.2019.115121>.
11. Mariscal G, Nuñez HJ, Bhatia S, *et al.* Monoclon Antib Immunodiagn Immunother. 2020; 39(2): 29-36.
12. Poutoglidou F, Samolada E, Nikolaos R, *et al.* J Clin Densitom. 2022; 25:401-415.
13. Tian A, Jia H, Zhu S, *et al.* Orthop Surg. 2021; 13:1941-1950.
14. Morin S, Feldman S, Funnell L, *et al.* CMAJ. 2023; 195:E1333-E1348.
15. RxFiles. Osteoporosis. 2024. Available at: <https://www.rxfiles.ca/RxFiles/uploads/documents/members/Chart-osteoporosis.pdf>. Accessed August 6, 2024.
16. Moe SM, Allan GM. Tools for Practice #282: Osteoporosis treatment for post-menopausal women. Available at: <https://cfpclearn.ca/tfp282/> Accessed: August 6, 2024.

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