



## 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.

## AUTHORS

**Steven Piotrowski**, MSc MPAS  
CCPA  
**Émélie Braschi**, MD PhD CCFP  
**Samantha Moe**, PharmD.

*Authors do not have any  
conflicts of interest to declare.*

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, Hosseinfard 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.

TOOLS FOR PRACTICE  
PROVIDED BY



IN PARTNERSHIP WITH



**Tools for Practice** are peer reviewed and summarize practice-changing medical evidence for primary care. Coordinated by **Dr. Adrienne Lindblad**, the articles are developed by the Patients, Experience, Evidence, Research (PEER) team, and supported by the College of Family Physicians of Canada, and the Alberta, Ontario, and Saskatchewan Colleges of Family Physicians. Feedback is welcome and can be sent to [toolsforpractice@cfpc.ca](mailto:toolsforpractice@cfpc.ca). Archived articles can be found at [www.toolsforpractice.ca](http://www.toolsforpractice.ca)

*This communication reflects the opinion of the authors and does not necessarily mirror the perspective and policy of the College of Family Physicians of Canada.*