# Year in Review


May 6, 2022

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## Disclosure

- Institutional research support - Amgen, Radius
- Consultant and speaker - Amgen

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## Objectives

- Describe recent advances in the care of patients with osteoporosis and other metabolic bone diseases
- Identify potential new-label and off-label uses of osteoporosis drugs
- Discuss management of rare adverse effects of osteoporosis drugs

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## Considerations

- Clinical trials, reviews, editorials, perspectives, commentaries, guidelines, position statements, abstracts, and presentations at medical congresses and Bone Health TeleECHO in 2021 and 2022
- Solicited input from colleagues of different specialties and perspectives
- Final selections highly subjective, presented in random order
- Many superb articles not included
- Primary criterion: Must address a relevant clinical question or provide insights on important clinical issues

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New therapeutic targets  Nothing

- "Because effective treatments are available, trials of new osteoporosis medications must use active controls or limit enrolment to low-risk patients, markedly increasing trial size, duration, and cost."
- "Regulatory agencies require a primary outcome of fracture in phase 3 trials, leading to the need for large, costly studies for drug approval."
- "Because of these high trial costs, no new osteoporosis drugs are in development."
- "A surrogate outcome, such as BMD, could greatly reduce the size, duration, and cost of trials needed for new drug development."

Black DM et al. Lancet. 2020;8:672-682.

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## Big Question

Until the osteoporosis drug pipeline reopens, how can we make better use of the treatments we have?

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## Monitoring Patients on a BP Holiday

- ASBMR suggests consideration of a BP holiday after 3-5 years of BP treatment if fracture risk is low, and resuming treatment when risk is high, possibly using BMD and BTMs to monitor (Adler RA et al. JBMR. 2016)
- Although BMD decreases and BTMs increase after stopping BP (FLEX, HORIZON), it remains unclear how to use these measurements to monitor patients
- What is the predictive value of BTMs after discontinuing ALN?

Sølling AS et al. Osteoporos Int. 2021;32:1557-1556.

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## PROSA Study

(**PR**edictive Value **O**f Bone Turnover Markers During Di**S**continuation With **A**lendronate)

- Cohort study at Aarhus University Hospital in Denmark in 136 women and men age > 50 who stopped ALN after median of 7 years (range 5-20 years), with TH T-score > -2.5 and LS T-score > -4.0 and no osteoporotic fracture in the past 5 years
- Primary endpoint: correlation between CTX 3 and 6 months after stopping ALN and TH BMD after 1 year
- Other endpoints included correlation between CTX and P1NP at 3 and 6 months with BMD and TBS after 1 year and 2 years

Sølling AS et al. Osteoporos Int. 2021;32:1557-1566.

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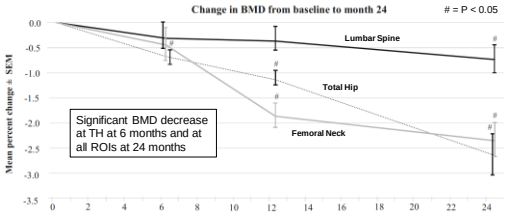
# PROSA Results: BMD Decrease




Sølling AS et al. Osteoporos Int. 2021;32:1557-1566.

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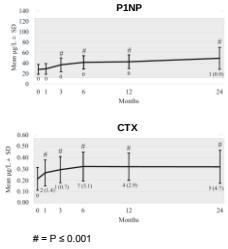
# PROSA Results: BTMs Increase




- BTMs increased after stopping ALN but remained within the reference range for most patients
- Significant CTX increase at 3 months (LSC 30%/50%) was associated with significant BMD decrease at months 12 and 24
- Conclusion: maintenance of BMD after stopping ALN is dependent on continued suppression of bone turnover
- **Suggested algorithm: monitor treatment discontinuation with BTM after 3 and 6 months; if increase ≥ LSC [ ~ 100 ng/L for CTX] or > premenopausal mean [~280 ng/L for CTX], consider resuming treatment [needs validation in clinical trials]**

Sølling AS et al. Osteoporos Int. 2021;32:1557-1566.

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# Teriparatide, Osteosarcoma, and Rats

- Due to the finding of high risk of osteosarcoma with Fischer 344 rats given high doses of teriparatide, the pivotal fracture trial in humans was terminated early, with a mean duration of treatment about 18 months and median observation time of 21 months
- When approved, the product label contained a boxed warning about osteosarcoma risk and 24 month lifetime limitation of treatment
- Patients are sometimes reluctant to take this medication due to fear of cancer and it has rarely been used beyond 24 months
- Does teriparatide cause osteosarcoma in humans and should it be limited to 24 months lifetime use?

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# 10-Year Cancer Surveillance Study

- 75,247 patients in Forteo Patient Registry (2009-2019) representing 361,763 cumulative person-years
- Linked with 6180 patients with osteosarcoma in 42 participating state cancer registries
- No patients in Forteo registry were identified with osteosarcoma
- Totality of evidence with this study, the Osteosarcoma Surveillance Study, and the Medicare comparative cohort study, showed **no increase in risk of osteosarcoma in patients treated with teriparatide**

Gilsenan A et al. Osteoporos Int. 2021;32:645-651.

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## Teriparatide Label Change

- Boxed warning on "Potential Risk of Osteosarcoma" was removed and statement to avoid use in patients at high risk for osteosarcoma was placed in "Warnings and Precautions" and . . .
- Restriction of 24 months lifetime use was changed to "Use of FORTEO for more than 2 years during a patient's lifetime should only be considered if a patient remains at or has returned to having a high risk for fracture."
- How do we identify patients who could benefit from treatment longer than 2 years?

FORTEO product label. Updated 11/2020.

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## Commentary on Identifying Patients for Long-term Use of Teriparatide

- Candidates for long-term use when fracture risk is high or very high
  - **Unable to come off long-term glucocorticoid therapy**
  - **P1NP remains high after 2 years on TPT**
  - **Multiple VFs before TPT and none while on TPT**
  - **Severe COPD with VFs**
  - **Adynamic renal bone disease**
- P1NP may be best test to monitor continuing anabolic effect
- Clinical investigation is needed to validate the benefits and risks of long-term TPT and other anabolic agents

Miller PD et al. Cleve Clin J Med. 2021;88:489-493.

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## Clinical Use of Bisphosphonates

- Oral BPs are widely available, safe, inexpensive, and can be prescribed by any provider, but may not used due to fear of adverse effects (AFF, ONJ, GI upset) and inconvenience of dosing; when prescribed and tolerated, adherence is poor and BP "holidays" commonly misused
- IV ZOL provides treatment for at least 1 year, but there may be bureaucratic barriers, referral to an infusion center may be required, and there is uncertainty about optimal dose and dosing interval
- How effective are different doses of ZOL and for how long?

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## BMD and BTMs 10 Years After ZOL

- Core trial (years 0-2): 180 postmenopausal women (mean age ~65) with osteopenia randomized to single dose ZOL 1 mg, 2.5 mg, 5 mg, or PBO
  - BMD increased with all ZOL doses vs. PBO; effect of 2.5 mg and 5 mg > 1 mg
  - BTMs trough with ZOL at ~3 mo. with slow rise; similar with 2.5 mg and 5 mg
- First extension (years 2-5): 160 participants, no additional therapy
  - BMD increased with all ZOL doses vs. PBO, with 5 mg > 2.5 mg > 1 mg
  - BTMs with ZOL continued to rise in dose dependent fashion
- **Second extension** (years 5-10): 116 participants
  - Women who received ZOL 5 mg or PBO at baseline received no further treatment
  - Women who received ZOL 1 mg or 2.5 mg at baseline received ZOL 5 mg at 5 years

Grey A et al. J Bone Miner Res. 2022;37:3-11.

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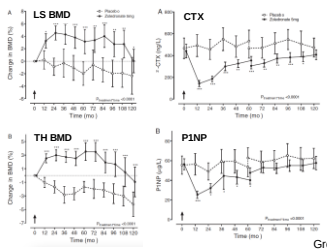
# 10-year Data with ZOL 5 mg vs. PBO




- BMD increased with ZOL vs. PBO throughout 10 years and at or above baseline for 8-9 years
- BTMs decreased with ZOL vs. PBO throughout 10 years
- Similar pattern for BMD and BTMs with ZOL 1 mg and 2.5 mg at baseline and 5 years
- **Long duration of action and slow offset of effect suggests that very infrequent doses of ZOL may be clinically useful**
- Limitations: no fracture data, these women had osteopenia not osteoporosis
- But what about adverse effects, such as APR?

Grey A et al. J Bone Miner Res. 2022;37:3-11.

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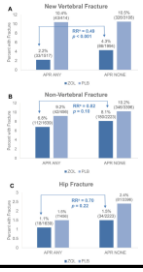
# Benefits of APR with ZOL?



- APR is common and disturbing when severe/prolonged, but may have benefits
- HORIZON-PFT found 42% incidence of APR with first dose ZOL vs. 12% with PBO
- APR more common with younger patients, NSAIDs, and Asians; less common with smokers, DM, and prior BP users
- This post hoc analysis found that **ZOL patients with APR had 51% fewer VFs than ZOL patients without APR (P<0.001), with a trend toward fewer NVFs and HFs**

Black DM et al. J Bone Miner Res. 2021;37:21-28.

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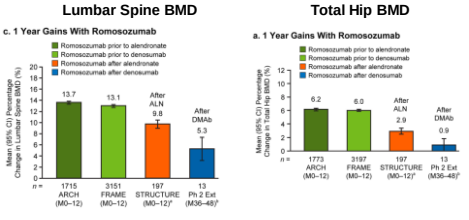
# Sequence of Therapy Matters




Cosman F et al. Osteoporos Int. 2022. Epub.

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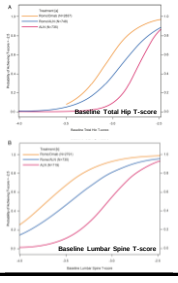
# Sequence and Achievement of Treatment Goal




- Achievement of target T-score > -2.5 has been suggested when baseline T-score is ≤ -2.5
- Post hoc analyses of FRAME and ARCH data in 3234 women with PMO
- Primary outcome measure: probability of reaching T-score > -2.5 at TH or LS over 3 years with 3 treatment sequences:
  - Romo 1 yr → Dmab 2 yrs
  - Romo 1 yr → ALN 2 yrs
  - ALN 3 yrs.
- Results according to baseline T-score
  - **-2.5 to -2.7: > 50% chance of success with all regimens**
  - **< -2.7 to -3.5: < 10% chance with ALN alone, with much higher chance of success with Romo followed by antiresorptive, especially Dmab**
- This methodology may be useful in evaluating other current and future drugs and sequences

Cosman F et al. JBMR Plus. 2021;5:e10546.

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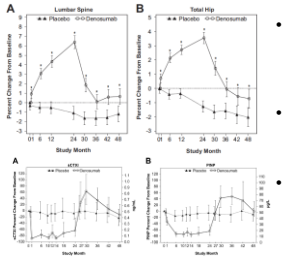
## Denosumab Discontinuation




- Rapid decrease of BMD with rapid rise and overshoot of BTMs with discontinuation of Dmab after 24 months
- Return of fracture risk to baseline and apparent increase in risk of multiple VFs
- Why is this happening?

Bone HG et al. J Clin Endocrinol Metab. 2011;96:972-980.

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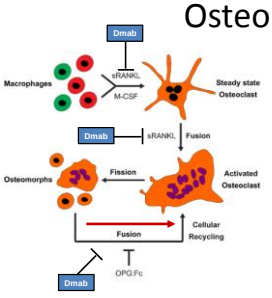
## Osteomorphs




- Osteoclasts have been thought to undergo apoptosis after bone resorption is complete
- Alterative fate is fission into daughter cells called "osteomorphs"
- Inhibiting RANKL blocks recycling resulting in accumulation of osteomorphs
- Withdrawal of RANKL inhibition results in rebound increase of activated osteoclasts
- Might explain bone loss and increase of BTMs with Dmab discontinuation

McDonald MM et al. Cell. 2021;184:1940.

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## What to do when Dmab is stopped

Switch to something else, probably a bisphosphonate, but . . . uncertainty on how best to do this

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## Denosumab → Bisphosphonate

*Effect may depend on duration of Dmab treatment*

- **After 1 year** of Dmab (DAPS) – BMD stable with ALN
  - ALN started 6 months after last dose of Dmab prevented bone loss over the following year
  - Freemantle N et al. Osteoporos Int. 2012;23:317-326.
- **After 2.2 years** (mean) of Dmab – BMD stable after ZOL
  - ZOL given 6 months after last dose of Dmab prevented bone loss for at least 2 years
  - Anastasilakis AD et al. J Bone Miner Res. 2019;34:2220-2228.
- **After 4.6 years** (mean) of Dmab – BMD loss after ZOL
  - ZOL given 6 months, 9 months, or when CTX increased after last dose of Dmab was followed by bone loss over next 12 months
  - Sølling AS et al. J Bone Miner Res. 2020;35:1858-1870.
- **After 7 years** of Dmab (post-FREEDOM data) – BMD loss after ZOL
  - ZOL given 6 months after last dose of Dmab was followed by bone loss over next 18-23 months
  - Reid IR et al. Calcif Tissue Int. 2017;101:371-374.

What's new?

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# ZOL after Single Dose Dmab

- Case series from osteoporosis registry of Swiss Society of Rheumatology in patients receiving a single dose Dmab followed by ZOL 6 months later (n=32) compared with those receiving 5 doses Dmab over 2.5 years followed by ZOL (n=110)
- All patients had DXA at baseline (prior to first dose of Dmab) and about 18 months after ZOL
- Primary endpoint: % change in BMD

Everts-Graber J et al. J Clin Densitom. 2022. Epub.

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# Results for ZOL after 1 Dose Dmab

| BMD | Dmab x 1 → ZOL | Dmab x 5 → ZOL | P-value |
|---|---|---|---|
| Lumbar Spine | + 7.6% | +5.6% | 0.014 |
| Total Hip | + 3.5% | +2.3% | 0.010 |

- Greater BMD increase with ZOL after 1 dose of Dmab than after 5 doses
- Limitations: small sample size, possible selection bias, retrospective, observational, no group with only Dmab or only ZOL, no fracture data
- If confirmed, offers possibility of alternative treatment regimen for appropriate patients (i.e., if we are going to switch from Dmab to ZOL at some point, sooner might be better than later)

Everts-Graber J et al. J Clin Densitom. 2022. Epub.

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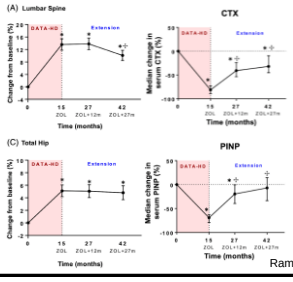
# ZOL after Combined Dmab/TPT




DATA-HD Study Extension (Denosumab and High-Dose Teriparatide Administration)

76 women with PMO received TPT 20 or 40 mcg/day for 9 months + Dmab at mo. 3 and 9

IV ZOL 5 mg given 6-9 mo. after last dose Dmab

BMD and BTMs followed for next 27 mo.

Results: **Single dose ZOL maintained BMD for at least 12 mo. and prevented overshoot of BTMs after short-term overlapping treatment with TPT/Dmab**

Ramchand SK et al. J Bone Miner Res. 2021;36:921-930.

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# More on ZOL after Long-term Dmab

- 2-year randomized open-label study of 61 postmenopausal women and men age > 50 discontinuing Dmab after mean of 4.6 years
- Year 1 report, 3 groups, ↓ BMD and ↑ BTMs 1 year after ZOL for all (Sølling AS et al. J Bone Miner Res. 2020; 35:1858-1870)
  - ZOL 5 mg 6 months after last dose Dmab (6 months group)
  - ZOL 5 mg 9 months after last dose Dmab (9 months group)
  - ZOL 5 mg when (1) CTX increased (> 1260 pg/mL) or (2) BMD decreased ≥ 5% at LS or TH or (3) VF/HF or (4) 12 months passed after last Dmab (OBS group)
- **Year 2**
  - All women were followed for 2 years after 1st dose ZOL
  - They received 2nd dose ZOL if CTX increased (> 1260 pg/mL) at 16, 20, or 24 months after ZOL or BMD decreased (≥ 5%) 24 months after ZOL or VF/HF after ZOL
  - Primary endpoint: % of women who failed to maintain BMD (≥3% loss at LS or ≥5% loss at TH or FN)

Sølling AS et al. J Bone Miner Res. 2021; 36:1245-1254.

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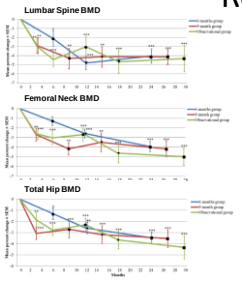
# Results




BMD decreased in all groups after 1st dose ZOL

47% of women completing the 1-year study met BMD criteria for 2nd dose ZOL (none met CTX or fracture criteria), mostly in the 6-month group

Average bone loss over 24 months was 4.2% at LS and 3.8% at TH

BMD was generally maintained in the 2nd year

Bone loss with ZOL after Dmab was less than expected without follow-up treatment

Conclusion: **use BP after Dmab and monitor closely**

Sølling AS et al. J Bone Miner Res. 2021; 36:1245-1254.

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# Treatment after Denosumab Discontinuation: ECTS Position Statement

- Short-term Dmab treatment (≤ 2 years) and fracture risk is low
  - Oral BP or ZOL for 1-2 years
  - Monitor BMD and BTM
- Long-term Dmab treatment (> 2 years) and/or fracture risk is high
  - Continue Dmab for up to 10 years (no data beyond 10 years), or
  - ZOL 6 months after last Dmab, measure BTM at 6 and 12 months, repeat ZOL if BTM persistently increased, or
  - If ZOL is not an option, consider oral BP
- VF within 2 years of Dmab discontinuation
  - Resume Dmab, ZOL or oral BP, or Dmab+TPT followed by ZOL
  - Avoid TPT monotherapy

Tsourdi E et al. J Bone Miner Res. 2021;106:264-281.

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# Persistence is poor with oral BPs, but what about Dmab?

- Retrospective cohort study in a dataset of 41,901 patients (mean age ~77) from 44 general practices in Ireland
- Analysis of those with a first prescription of oral BP (n=1569) or Dmab (n=1615) after 12 observation time with no treatment
- Persistence defined as time from initiation to discontinuation
- Discontinuation defined as > 90 day gap in prescription coverage
- Patients switching to another bone-health medication were excluded from analysis

Walsh ME et al. Arch Osteoporos. 2021;16:71.

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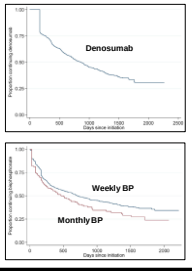
# Similar Persistence with Dmab and Oral BP




- Denosumab
  - 54% continued for 2 years
  - **Only 6% of patients stopping Dmab were switched to another bone-health medication**
- Oral BP
  - 49% continued for 2 years
  - Persistence better with weekly than monthly dosing
- State-funded healthcare and medication coverage was associated with better persistence with Dmab and BP
- Take-home points: persistence is poor with Dmab and oral BP, and **far too many patients are stopping Dmab without follow-up treatment**

Walsh ME et al. Arch Osteoporos. 2021;16:71.

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## Spine Surgery and Bone Health

- Survey of 349 spine surgeons found that only 20% screened patients for osteoporosis prior to surgery
- Another study showed that 91% of patients having arthroplasty or spine surgery had indications for osteoporosis drug treatment
- Patients with poor bone health are at increased risk of pedicle screw loosening, instrumentation failure, pseudoarthosis, VFs, proximal junctional kyphosis, and revision surgery
- Pre-op evaluation and treatment can reduce the risk of these complications
- How can we improve outcomes with spine surgery?

Sarder ZM et al. Spine. 2021;47;128-135.

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## Best Practice Guidelines Evaluation for Elective Adult Spine Reconstruction Surgery

**Formal bone health evaluation for**

- All patients age ≥ 65
- Patients age 50-64 with any 1 of 12 risk factors*
- Patients age < 50 with any 1 of 5 risk factors**

*glucocorticoids, fracture, MBD, CKD, low D, high FRAX, smoker, failed spine surgery, alcohol excess, limited mobility, cancer Rx, cancer treatment, DM.

**glucocorticoids, fracture, MBD, cancer treatment, CKD

**Assessment tools**

- Spine and hip DXA with TBS and VFA for all
- Lateral spine X-ray screening for VF if VFA not available
- Opportunistic lumbar spine CT Hounsfield Units may be useful if available (DXA if ≤ 150)
- 25-OH-D
- All patients with poor bone health should be evaluated by an experienced bone health provider

Sarder ZM et al. Spine. 2021;47;128-135.

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## Best Practice Guidelines Treatment for Elective Adult Spine Reconstruction Surgery

- Optimize non-pharmacologic measures
- For patients with poor bone health
  - **1st choice: anabolic with TPT or ABL starting 2-6 months pre-op and continuing at least 8 months post-op, followed by antiresorptive**
  - **2nd choice: antiresorptive with Dmab or BP**
  - **No need to withhold treatment in the immediate post-op period**

Sarder ZM et al. Spine. 2021;47;128-135.

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## Best Practice Guidelines Benefits for Elective Adult Spine Reconstruction Surgery

**Anabolic benefits (TPT vs. BP or no Rx)**

- ↓ pedicle screw loosening
- ↑ fusion rates
- Shorter time to union
- ↑ rate of union
- ↓ rod breakage
- ↑ insertional torque
- ↓ adjacent segment disease

**Antiresorptive benefits**

- ALN, ZOL: mixed reports of efficacy for improving fusion and decreasing complications vs. no treatment
- TPT+Dmab superior to TPT alone in a single study

ABL: no data but assumed to be similar to TPT
Romo: no data reported
[classified here as antiresorptive]

Sarder ZM et al. Spine. 2021;47;128-135.

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## Anabolic Therapy and Fracture Healing

- Preclinical and clinical data show that PTH receptor agonists may improve bone union, hasten fracture healing, and improve physical function after fractures
- One non-randomized study showed that 100% of pelvic fracture patients given PTH (1-84) healed with 12 weeks vs. 68% of controls, with reduced pain and better TUG performance
- Post hoc analysis of RCT showed shorter healing time in 3 of 4 cortices by X-ray after distal radius fractures with TPT 20 mcg (but not 40 mcg) vs. PBO
- Despite these studies and others, uncertainty remains on the benefit of anabolic therapy for fracture healing
- Does anabolic therapy improve fracture healing, or not?

Nieves JW et al. Osteoporos Int. 2022. 33:239-250.

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## Teriparatide and Pelvic Fracture Healing

- 6% of fractures in Medicare patients are at the pelvis
- 60% of these require hospitalization, with median stay of 9 days
- 42% have another fracture with the next 2 years
- 20% 1 year mortality
- 92% are NOT treated with osteoporosis medication
- For these reasons, a 3-month phase 2 RCT was conducted to evaluate the effect of TPT vs PBO in acute pelvic fracture patients (N=35) on fracture healing by CT, pain, and physical performance

Nieves JW et al. Osteoporos Int. 2022. 33:239-250.

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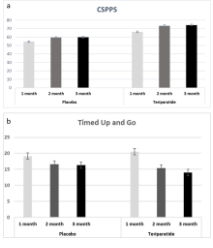
## Improved Physical Performance with TPT




- No difference in healing time for cortical bridging by CT
- No difference in pain scores
- **Improvement in CSPPS and TUG (P<0.01)**
- Poor physical function is a factor associated with imminent fracture risk
- Limitation: Underpowered to detect TPT effect on fracture healing due to small N (goal of 100 subjects not achieved due to withdrawal of study drug supply during recruitment)

CSPPS = combined score for 4 min walk speed, timed repeated chair stands, and balance

Nieves JW et al. Osteoporos Int. 2022. 33:239-250.

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## Stress Fractures in Athletes and Military Recruits

Rafael Nadal
Indian Wells
March 20, 2022
Stress Fracture Left 3rd Rib

Chris Sale
Red Sox Pitcher
March 2022
Stress Fracture Right Rib

US Army Recruits, 5th Squadron, 1st Cavalry Regiment, 1st Stryker Brigade Combat Team, 25th Infantry Division, 26.2-mile foot march
High Risk for Stress Fractures

**What do these people have in common?** **RETURN TO WORK FAST!**

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## Does anabolic therapy improve fracture healing in young healthy adults?

- Anecdotal case reports and small clinical trials faster healing time and return to work using TPT in young adults with stress fractures
- TPT is sometimes used off-label for elite athletes with fractures but uncertainty of effectiveness continues
- RCTs in progress
  - **STRONG Study** [https://clinicaltrials.gov/ct2/show/NCT04589819, updated 9/28/2021]
    - US Army recruits with tibia stress fractures randomized 1:1 to TPT 20 mcg daily or PBO
    - Primary endpoint: time to full return to activity (passing score on Army Combat Fitness Test)
  - **RETURN Study** [Carswell AT et al. Trials. 2021.22:580]
    - UK Army recruits (men and women, age 18-40) with lower body stress fractures randomized 1:1 to open label TPT 20 mcg daily for up to 24 weeks vs. standard Army care
    - Primary endpoint: improvement in healing at 8 weeks by MRI (Fredericson grading)
    - Secondary endpoints include MRI healing for up to 24 weeks, time to clinical healing, time to discharge from rehab, health related quality of life

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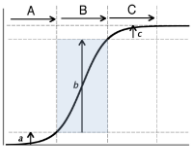
## Nutrition and Skeletal Health

- Geoffrey Rose "prevention paradox" – a community-based approach producing a small benefit to an individual may confer a large benefit to the community
- Robert Heaney "quality of clinical trials" – RCTs in nutrition often fail to show an effect because the dose is insufficient (A) and/or the population is sufficient at baseline (C)
- Can better nutrition prevent fractures in an at-risk population?




"Only intakes in the (B) region produce responses large enough adequately to test the hypothesis that the nutrient concerned elicits the response in question."

Iuliano S et al. BMJ. 2021;375;n2364.
Rose G. Br Med J (Clin Res Ed). 1981;282:1847-1851.
Lappe JM, Heaney RP. Dermato-Endocrinology. 2012;4:95-100.

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## Underserved Population: Institutionalized Elderly

- Osteosarcopenia – frailty and weak bones associated with physical inactivity and poor nutrition
- Falls and fall-related injuries are common
- 30% of hip fractures
- Calcium intake typically low (< 700 mg/day), likely resulting in obligatory calcium loss
- Protein intake typically low (< 1 g/kg/day), predisposing to loss of lean muscle mass

Iuliano S et al. BMJ. 2021;375;n2364.

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## Study Design

- 2-year cluster RCT of 7195 mostly ambulatory vitamin D replete residents in 60 "aged care facilities" in Australia, 68% female, mean age 86
- 30 facilities randomized to provide residents with total dietary calcium intake of 1141 mg and total dietary protein intake of 1.1 g/kg. vs. 30 control facilities with usual menus (calcium 700 mg, protein 0.9 g/kg)
- Outcomes measures: falls, fractures, all cause mortality

Iuliano S et al. BMJ. 2021;375;n2364.

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## Effect of Diet on Falls, Fractures, Mortality

- 90,557 person-months of follow-up with 4,302 falls, 324 fractures of all types, 135 hip fractures, and 1,974 deaths
- Dietary calcium and protein intervention vs. control
  - 11% RRR of falls (P=0.04) with NNT = 17
  - 33% RRR of all fractures (P=0.02) with NNT = 52
  - 46% RRR of hip fractures (P=0.005) with NNT = 82
  - No difference in mortality

Iuliano S et al. BMJ. 2021;375:n2364.

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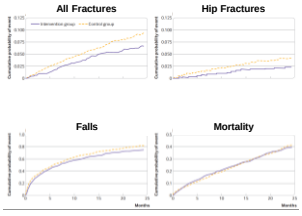
## Reduced Risk of Falls and Fractures




- Fall risk reduction was significant at 3 months (P=0.004)
- Hip fracture risk reduction was significant at 5 months (P=0.02)
- **RRR of fractures similar to that reported in clinical trials with antiresorptive agents in high risk patients with osteoporosis**
- Implications for nutritional public health measures in the elderly

Iuliano S et al. BMJ. 2021;375:n2364.

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## Isolated Osteoporosis at the Forearm

- Patients with T-score ≤ -2.5 at the 1/3 (33%) radius and much better T-score at LS and hip represent a therapeutic dilemma
- Although this qualifies for diagnostic classification of osteoporosis, there is uncertainty regarding fracture risk and treatment decisions
- Pivotal fracture trials have not enrolled such patients and we have very little data to inform us on how to manage them
- Meanwhile, what should we do?

Chukir T et al. J Clin Densitom. 2021 Aug 13:S1094-6950(21)00069-X.

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## Retrospective Cohort Study at HSS

- Postmenopausal women having DXA between 2/2016 and 11/2019 were screened
- Those being treated for osteoporosis were excluded
- 3 groups, mean age = 71, mostly non-Hispanic white
  - PMO: T-score ≤ -2.5 at spine or hip, regardless of 1/3R, n=214
  - 1/3RO: T-score ≤ -2.5 at 1/3R only (isolated 1/3R osteoporosis), n=107
  - Controls: T-score > -2.5 at spine, hip, and 1/3R, n=214
- Hypothesis: women with 1/3RO would have fracture risk similar to those with PMO and higher than controls

Chukir T et al. J Clin Densitom. 2021 Aug 13:S1094-6950(21)00069-X.

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# Results

- Prevalence of osteoporotic fractures was 25% in the cohort as a whole, with no significance differences comparing the groups (31% for PMO, 21% for 1/3RO, 28% for controls), and no differences in fracture types (spine, hip, wrist, etc)
- Women with 1/3RO had similar prevalence of PHPT, insufficient calcium and vitamin D intake, and other comorbidities
- Older age was the only clinical characteristic associated with increased fracture risk with 1/3RO (P=0.05)
- Conclusion: **older women with 1/3RO should be considered for treatment**, no age threshold could be identified, more data needed
- My take: diagnosis ≠ treatment, consider all clinical risk factors, we still have much to learn, still a clinical conundrum

Chukir T et al. J Clin Densitom. 2021 Aug 13:S1094-6950(21)00069-X.

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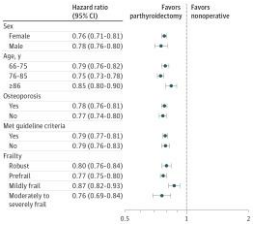
# Does PTX Prevent Fractures in Patients with PHPT?

- PHPT is associated with low BMD and increased fracture risk
- PTX is followed in improvement in BMD
- Most older adults with PHPT do not have PTX
- Longitudinal cohort study of 210,206 Medicare patients with PHPT with mean follow-up time of 4.9 years
- 30% had PTX, 70% did not
- Results: 22% lower risk of any clinical fracture and 24% lower risk of hip fracture with PTX, including all subgroups
- Conclusion: **lower risk of fracture after PTX in older patients**




Seib CD et al. JAMA Intern Med. 2022;182:10-18.

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# Clinician's Guide to Prevention and Treatment of Osteoporosis

Updates since 2014 include fracture risk stratification, sequence of therapy, imminent fracture risk, new therapeutic agents (abaloparatide, romosozumab), osteoporosis as a lifelong disease, crisis in osteoporosis care, consequences of underdiagnosis and undertreatment

Osteoporos Int. 2022. In press.

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