Sequential Therapy in Osteoporosis

(Case Presentation)

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Agenda

- **Why do we need sequential therapy**
- **Case presentation**
- **Concept of risk stratification**
- **Switching between pharmacological classes**

Why do we need sequential therapy

- Each pharmacologic agent might be incapable of addressing all the pathophysiological perturbations that occur in osteoporosis
- Patients at higher fracture risk are candidates for more aggressive therapy
- Concerns of serious side effects
- Restrictions on duration of use of certain medications
- Treatment failure
- Better compliance

Case presentation

A 61-year-old woman with postmenopausal osteoporosis has sutained multiple low-trauma vertebral fractures. She was previously healthy and had no prior fractures. There is no family history of osteoporosis or fractures. Menopause was at age 50 years, and she has not taken hormone therapy. On physical examination, she has moderate kyphosis. Other secondary causes of osteoporosis are ruled out during her evaluation.

DXA

spine T-score of **-3.3**

left femoral neck T-score of -2.3

left total hip T-score of -2.1

Given this patients findings, which treatment sequence is most appropriate to optimize her bone mineral density, taking into account the drugs mechanisms of action?

A. Abaloparatide> denosumab>drug holiday
B. Alendronate> Abaloparatide >drug holiday
C. Denosumab >teriparatide > zoledronate
D. Romosozumab > drug holiday > zoledronate
E. Romosozumab >zoledronate > drug holiday

Very High Risk

At least one of the following applies:

- Newly-diagnosed major osteoporotic fracture (MOF) within past 12 months and T-score ≤ –1
- Multiple major fractures (≥2)
- Fractures while medication used for other reasons is harmful to bone, e.g: glucocorticosteroids , aromatase inhibitors or others
- Very low T-score <–3
- FRAX > 15% for MOF or > 4.5% for hip

Guidelines for the diagnosis and management of osteoporosis in Poland. Update 2022

High Risk

At least one of the following applies:

- Major osteoporotic fracture in the last 2 years
- T-score≤–2.5
- FRAX 10 to 15% for MOF or 3 to 4,5% for hip

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Medium / Low Risk

If present:

- Age > 50 or postmenopausal No fracture and T-score > –2.5
- FRAX: 5 to < 10% for MOF medium RF, FRAX: < 5% for MOF low RF

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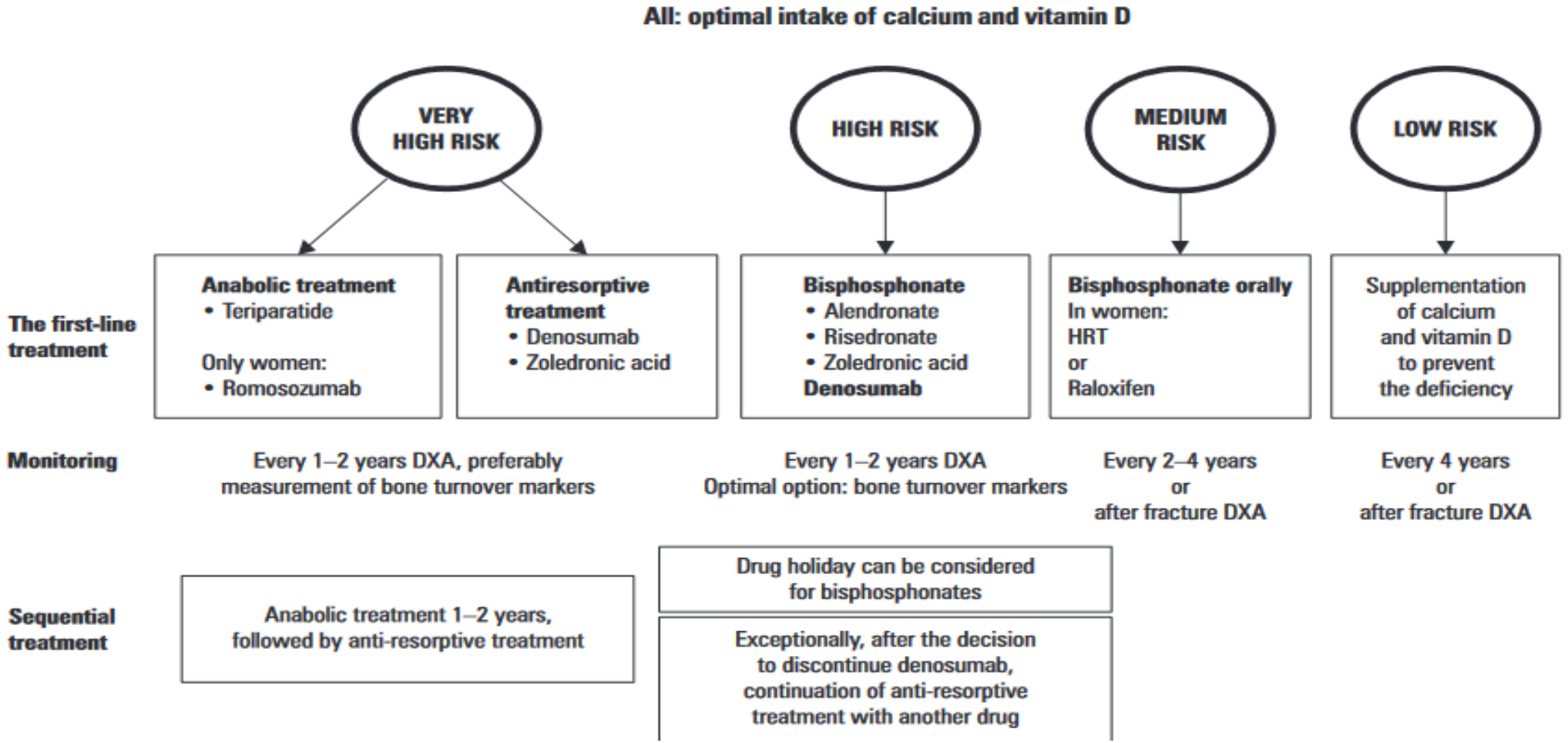
A proposed treatment algorithm for suspected for osteoporosis



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Sequence of Therapy Matters

Consider **anabolic** before **anti resorptive**
therapy for very high risk patients

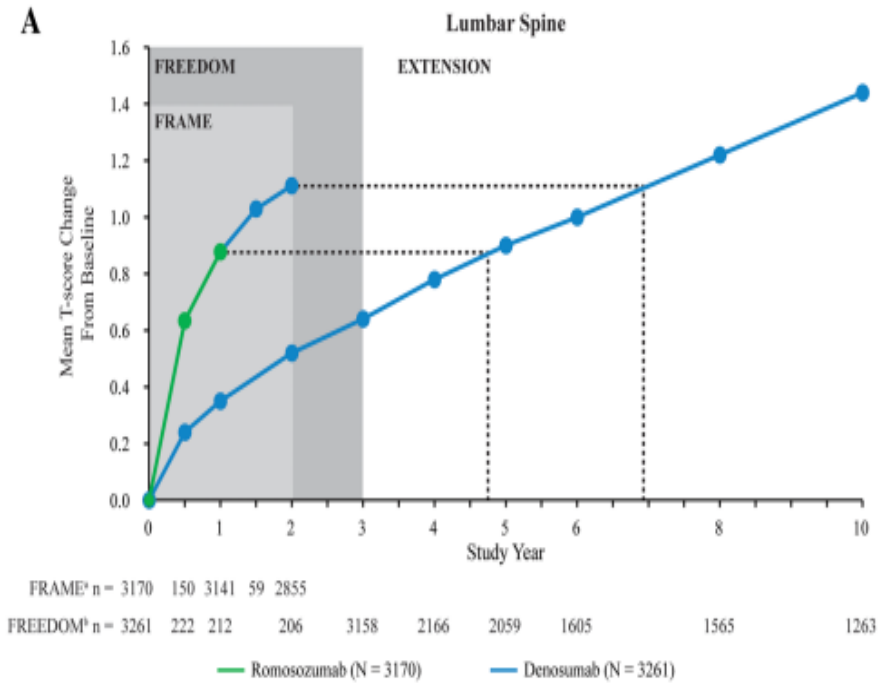
Romo → Dmab

FRAME vs

FREEDOM+ FREEDOM Extension

1 year of Romo followed by

1 year of Dmab gives same BMD increase as 7 years of continuous Dmab



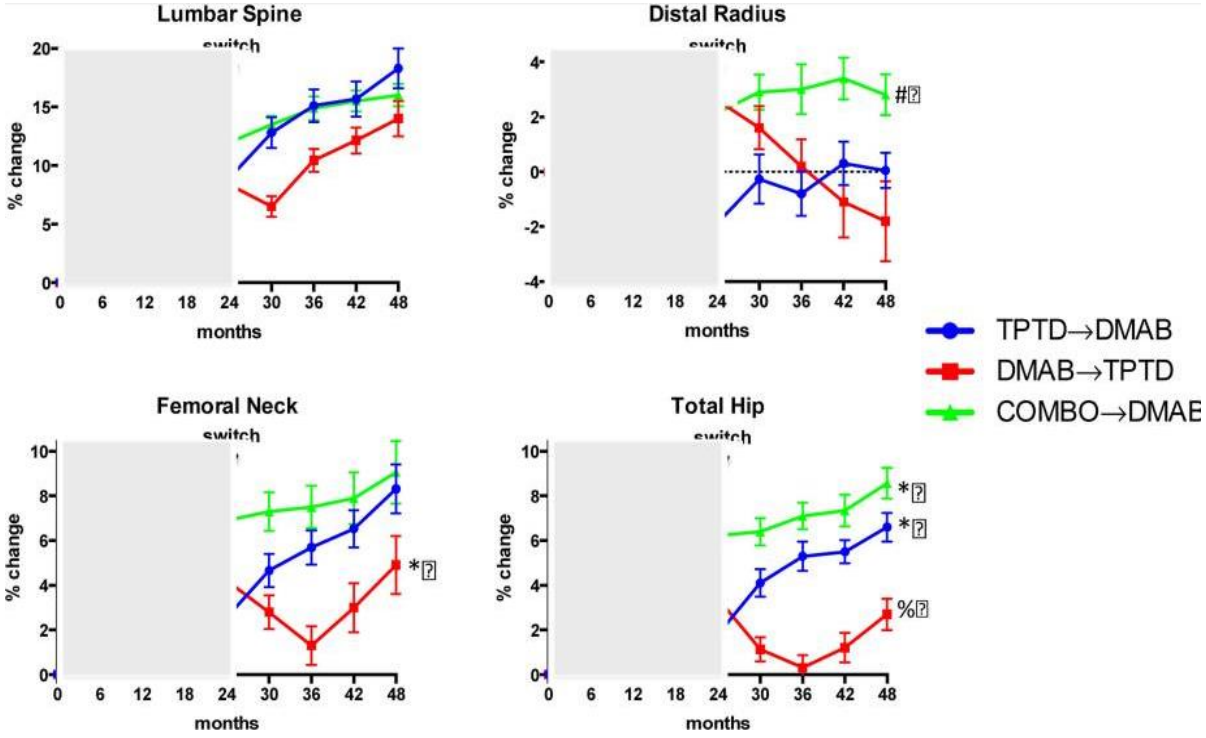
Cosman Fet al. j Bone and Mineral Research .2018;33:1219-1226

BMD Decrease Dmab → TPT (but not with Dmab →Romo)

77 women who completed **DATA study**
were randomized as follows

- TPT 2 year → Dmab 2 year
- Dmab 2 year → TPT 2 year
- TPT 2+ Dmab →Dmab 2 year

Result : Transient BMD decrease at Spine and hip and sustained BMD decrease at radius with Dmab → TPT



DATA Switch. leder BZ et al. Lancet. 2015 September 19; 386(9999): 1147–1155.

Dmab →Romo

- 22 women received PBO for 2 years followed by Dmab for 1 year, then Romo for 1 year

- Result : BMD is maintained at the hip and increased at LS with Dmab → Romo

	1 year Gain with Romo	Cumulative Gain with 1 yr Dmab followed by 1 yr Romo
TH	0.9%	3.8%
LS	5.3%	11.5%

Romo phase 2.kindler Dl et al. osteoporosis int.2019:30:2437-2448

BMD Decrease with ALN,RIS,Dmab → TPT

Study	Sample size	Treatment paradigm	% Change in total hip BMD during TPTD/PTH treatment			
			6 mo	12 mo	18 mo	24 mo
Ettinger et al.[27]	33	Alendronate (mean 29.3 mo) → TPTD (18 mo)	−1.8%	−1.0%	+0.3%	–
Boonen et al.[24]	107	Alendronate (median 29.2 mo) → TPTD (24 mo)	−1.2%	−0.6%	+0.6%	+2.1%
Boonen et al.[24]	59	Risedronate (median 23.4 mo) → TPTD (24 mo)	−1.6%	−0.4%	+0.9%	+2.9%
Miller et al.[30]	158	Risedronate (mean 37.2 mo) → TPTD (12 mo)	−1.2%	−0.3%	–	–
Miller et al.[30]	166	Alendronate (mean 38.0 mo) → TPTD (12 mo)	−1.9%	−1.7%	–	–
Cosman et al.[26]	50	Alendronate (mean 45.7 mo) → TPTD (18 mo)	−0.8%	–	+0.9%	–
Leder et al.[28]	27	Denosumab (24 mo) → TPTD (24 mo)	−1.7%	−2.7%	−1.7%	−0.7%

sustained BMD decrease with denosumab followed by teriparatide

Cosman Fet al. j Bone and Mineral Research .2017;32:198-202

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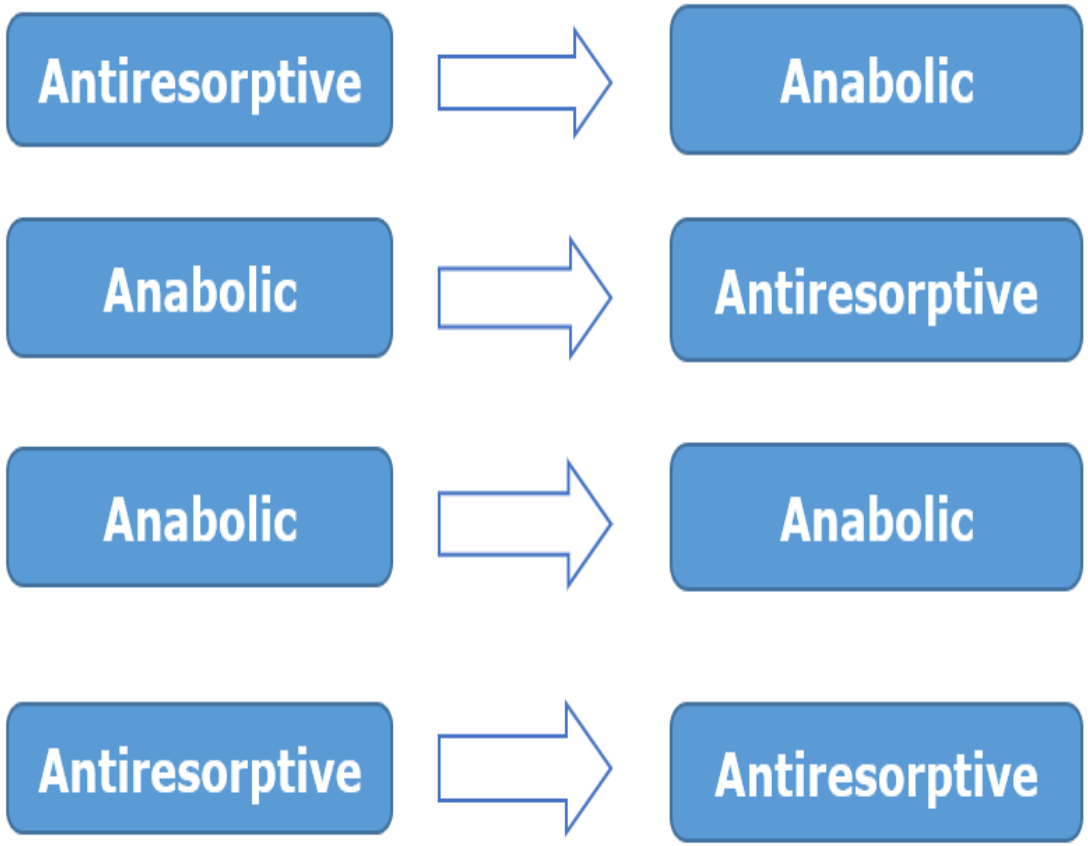
Summery of Treatment Sequences



Delay or attenuation of anabolic effect; Decreased BMD with TPT after Dmab

Antiresorptive is essential after anabolic; initial therapy with anabolic is best choice for very high risk patients

Probably neutral

Greater BMD effect with more robust antiresorptive, especially Dmab after BP

Thank you for your attention