Medical Management of Osteoporosis

Toolbox for treatment and optimizing outcomes

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Objectives

- Discuss current and potential pharmacologic management strategies for patient with or at risk for osteoporosis

- Discuss decision making in treatment selection; patient assessment; implications of treatment options, and patient education.

FDA-Approved Medications

- Keep in mind the goals of treatment
  - Strengthen bones
  - Reduce risk for future fracture

  All FDA approved treatments will do these things, however some are better than others

- **Antiresorptives**: slow osteoclastic activity down
- **Anabolics**: stimulate bone formation as part of the remodeling cycle

Class/Drug Name	Brand Name	Form	Frequency	Gender
ANTIRESORPTIVE AGENTS				
Bisphosphonates				
Alendronate	Fosamax®, Fosamax® Plus D	Oral (Tablet, Solution)	Daily/Weekly	Women & Men
Alendronate	Binosto®	Oral (Effervescent Tablet)	Weekly	Women & Men
Ibandronate	Boniva®	Oral (Tablet)	Monthly	Women
Ibandronate	Boniva®	Intravenous (IV) Injection	Every 3 Months	Women
Risedronate	Actonel®	Oral (Tablet)	Daily/Weekly/Twice Monthly/Monthly	Women & Men
Risedronate	Atelvia®	Oral (Tablet)	Weekly	Women
Zoledronic Acid	Reclast®	Intravenous (IV) Infusion	Once A Year/Once Every Two Years	Women & Men
RANK ligand (RANKL) inhibitor				
Denosumab	Prolia®	Injection	Every 6 months	Women & Men
Calcitonin				
Calcitonin	Fortical®, Miacalcin®	Nasal Spray	Daily	Women
Calcitonin	Miacalcin®	Injection	Varies	Women
Estrogen* (Hormone Therapy)				
Estrogen	Multiple Brands	Oral (Tablet)	Daily	Women
Estrogen	Multiple Brands	Transdermal (Skin Patch)	Twice Weekly/ Weekly	Women
Estrogen Agonist/Antagonist *also called selective estrogen receptor modulators (SERMs)*				
Raloxifene	Evista®	Oral (Tablet)	Daily	Women
Tissue Specific Estrogen Complex (TSEC)				
Conjugated Estrogens/ Bazodoxifene	Duavee®	Oral (Tablet)	Daily	Women

Class/Drug Name	Brand Name	Form	Frequency	Gender
ANABOLIC AGENTS				
Parathyroid Hormone (PTH) Analog				
Teriparatide	Forteo®	Injection	Daily	Women & Men
Parathyroid Hormone-Related Protein (PTHrp) Analog				
Abaloparatide	Tymlos®	Injection	Daily	Women
Sclerostin Inhibitor				
Romosozumab-aqqg	Evenity®	Injection	2 injections once monthly for 12 months	Women

Non-pharmacological treatments

- Calcium 1200 mg daily combined in both diet and supplements
- Vitamin D3 1000-2000 units daily or patient need specific
- Weight bearing exercises 3-4 days per week for 30-40 minutes (jogging, stair climbing, regular exercise)
- Resistance and muscle strengthening exercises 2-3 days per week (resistance bands, light weight, core exercises) This includes balance exercises for falls prevention
- Adequate diet in proteins, calories and nutrients

Decision Making: Patient Assessment and Treatment selection

- Workup completed: NOW WHAT?

- Different Medical World views affect the clinician and the patient in decision making

  - **Challenges for the clinician** include uncertainty of best treatment plan based on competing guidelines, indecisiveness, inconsistent clinical decision
  - **Challenges for the patient**: Distrust, Fear, Amusement

Highest Level of Evidence: Level 1

- When RCTs and systematic reviews agree on an outcome, we have achieved the highest level of medical evidence.
- **Does that guarantee we have the answer we need? Maybe, maybe not**
- **Truth is elusive, certainty is not absolute, and patient care is complex.**
- What does this mean?

Dr. Mike Lewiecki, ISO 2021

Medical Evidence plus Clinical Judgement

- Dr. Michael Lewiecki ISO 2021 quoted: "**All Clinical Guidelines are wrong but good ones are useful"**
- We must all be conscientious of the fine line between guidelines that are scientifically rigorous and those that are clinically useful
- This requires individualized osteoporosis treatment plans that may or may not fall into any specific guideline
- **As we all know: Unfortunately, healthcare payers may not see it that way**

Evidence-Based Medicine

- EBM = “conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients”*
- “What is the most likely outcome when I give this drug to my patient?”

- *Term coined by Gordon Guyatt, MD, in 1992

Osteoporosis: Consider Risk

- **Untreated:** probability of fracture and consequences of fracture vs. avoidance of medication side effects [feared side effects]
- **Treated**: expected benefits vs. possible adverse effects and events attributed to medication but not causally related
- **Risk tolerance is highly variable** - some people are terrified by things that are very unlikely to cause serious harm [osteoporosis medication?] but not bothered by things that kill many people [cars, fractures, COVID?]

Dr. Michael Lewiecki, ISO 2021

Choosing Approved Therapies

- Overall goals of treatment are to reduce the complications of this chronic disease and recommend good bone health maintenance efforts.
- Nonpharmacological treatments, smoking cessation, limited alcohol use, decreased drug use and optimization of comorbid conditions that harm the bone.
- Approved pharmacological treatments for those at high fracture risk

Balanced Decision Making

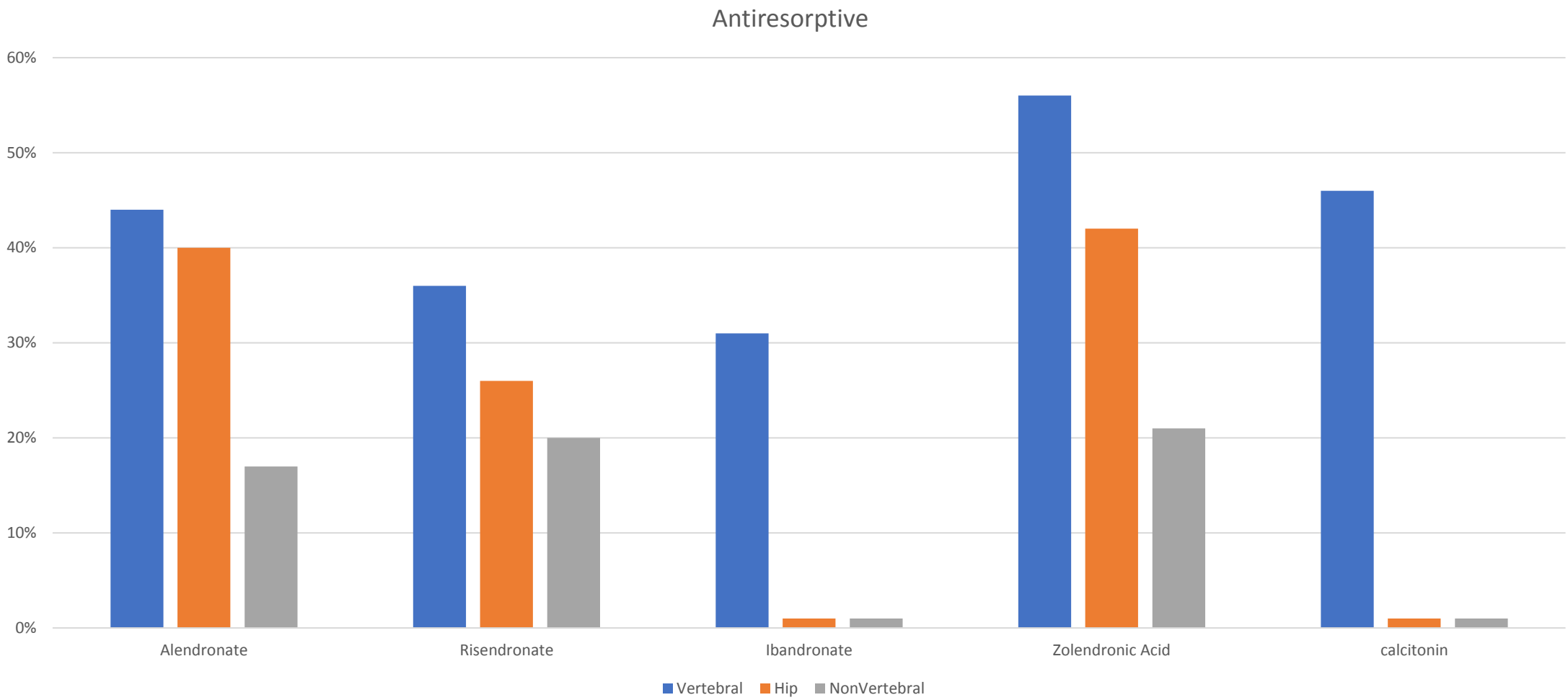
- Weigh risk and benefits of treatment
- Preferences based on individual preference
- Patient characteristics may help to determine which treatment is optimal
- Decision to switch treatment from one therapy to another may be based on availability, tolerability, costs, and preferences, compliance issues, failed therapy
- Alternative to decision making: “treat to target”. Choosing proper treatment sequencing that will most likely achieve a target BMD

Treatment sequencing considerations

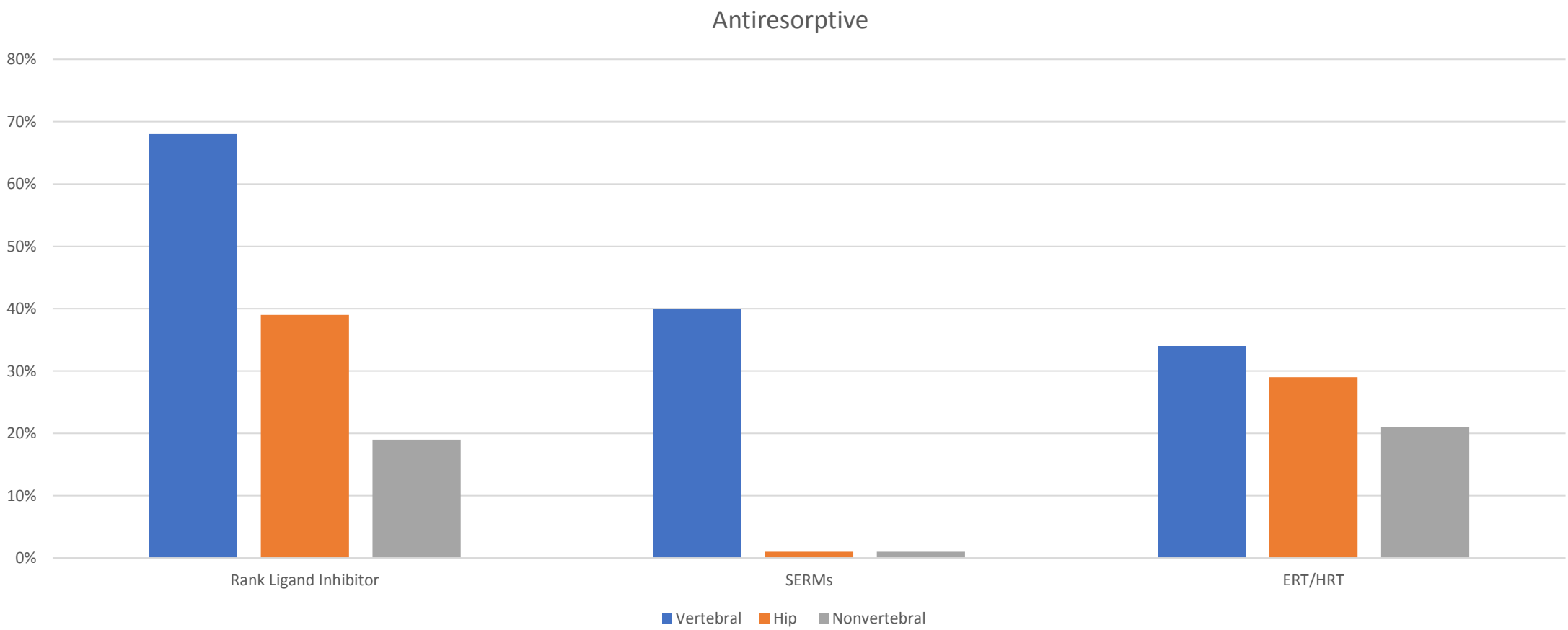
- Treatment sequence matters: Anabolic and Antiresorptive Therapy for Osteoporosis
  - **Comparison of Switching From Antiresorptive to TPTD Versus Adding Antiresorptive to TPTD**
  - **Effects of Sequential Treatment at the Tissue Level (cancellous envelope and cortical bone envelope**

- Effects of anabolic medications (TPTD) and parathyroid hormone (PTH) differ in patients who have received recent treatment with potent antiresorptive
- For treatment naïve patients, anabolic therapy should be considered first
- Evidence suggest that TPTD stimulates bone formation rapidly in the femoral neck and sites with predominate cortical bone
- Consider older protocols may not be optimal utilization of anabolic treatment
- Timing of fracture is important as to when treatment is initiated. Combination Therapy?

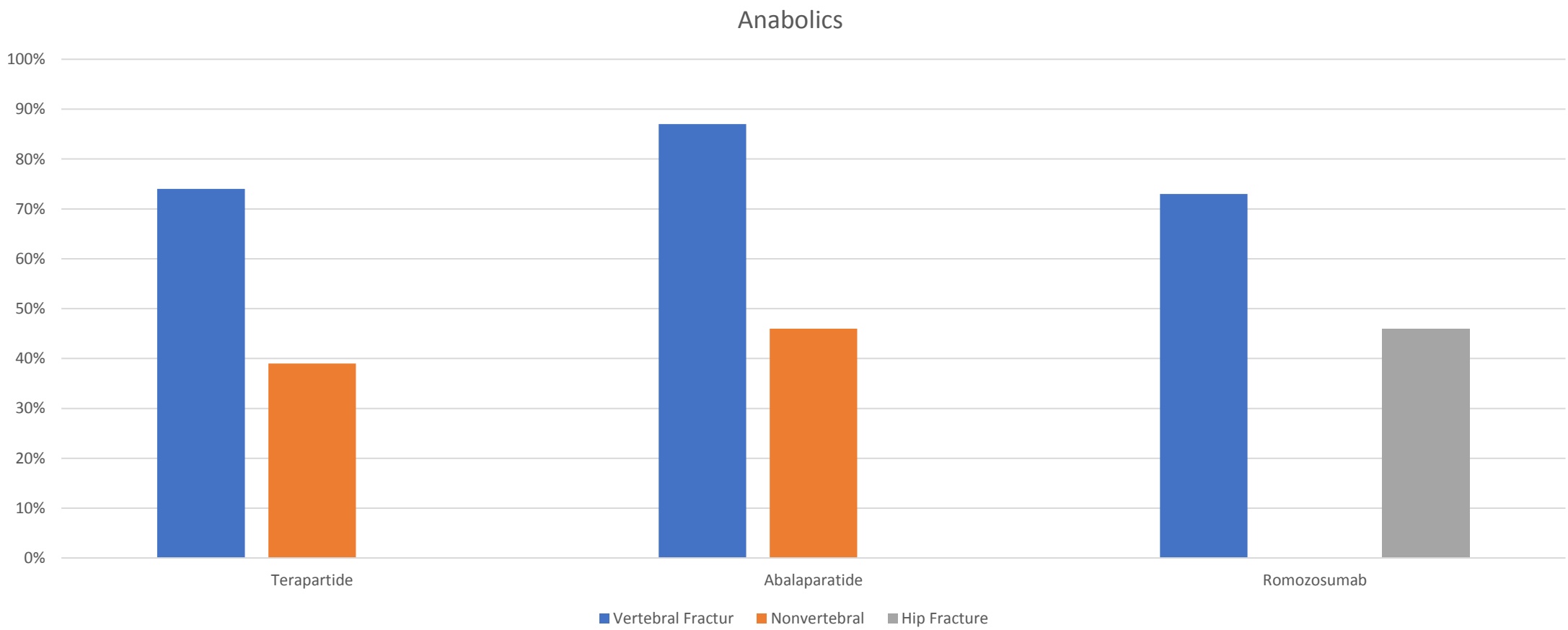
Antiresorptives and Fracture Efficacy



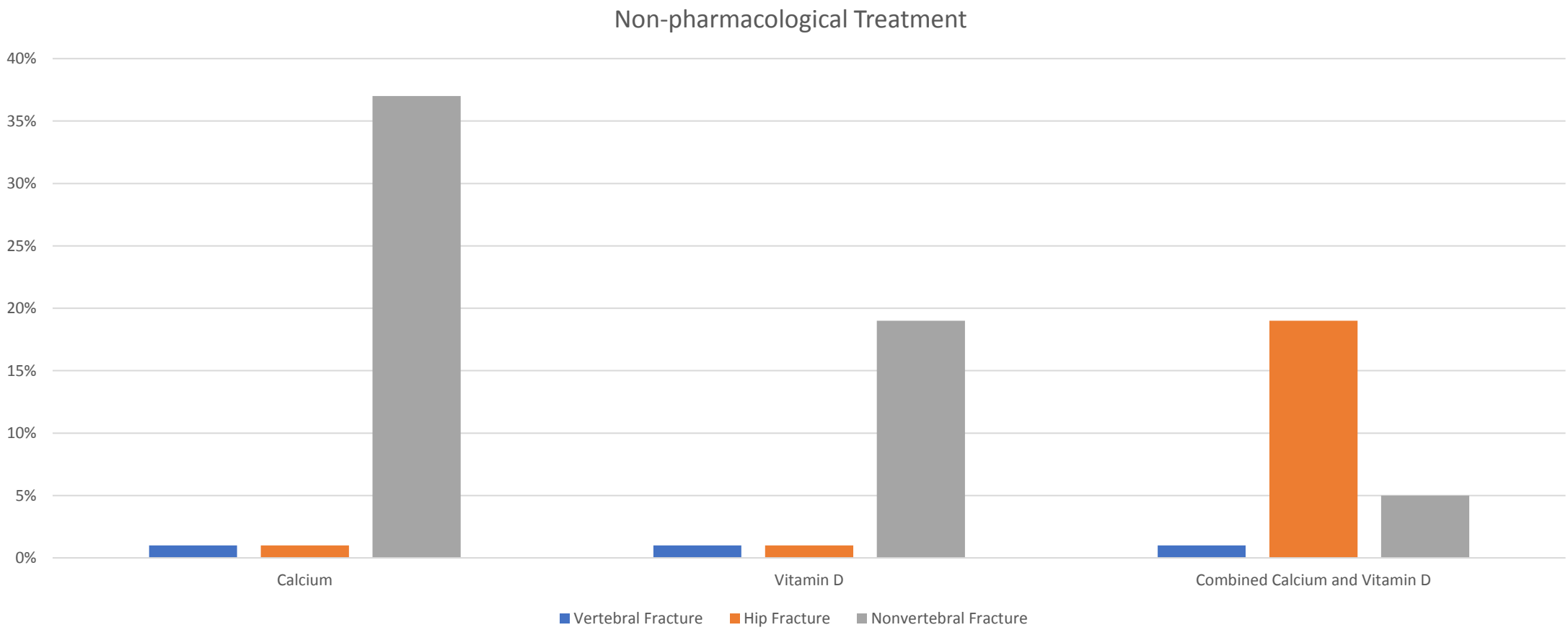
Antiresorptives and Fracture Efficacy



Anabolics and Fracture Efficacy



Non-Pharmacological Treatment and Fracture Efficacy



Medication Options

Medication	How it Works	How it is Given	Side Effects	Efficacy
Alendronate (Fosamax)	Decreases bone breakdown, decreases fracture risk	1 pill once weekly 30 minutes before breakfast and other medications	Heartburn, stomach pain, bone pains, joint or muscle pains; caution if decreased kidney function, don't use after certain stomach surgeries	✔✔✔✔✔
Risedronate (Actonel, Atelvia)	Decreases bone breakdown, decreases fracture risk	1 pill once weekly (Actonel 35 mg) or once monthly (Actonel 150 mg) 30 minutes before breakfast and other medications, or 1 pill once weekly after breakfast (Atelvia)	Heartburn, stomach pain, bone pains, joint or muscle pains; caution if decreased kidney function, don't use after certain stomach surgeries	✔✔✔✔✔
Ibandronate (Boniva)	Decreases bone breakdown, decreases fracture risk	1 pill once monthly 1 hour before breakfast	Heartburn, stomach pain, bone pains, joint or muscle pains; caution if decreased kidney function, don't use after certain stomach surgeries	✔✔✔
Zoledronic Acid (Reclast)	Decreases bone breakdown, decreases fracture risk	Intravenous (IV) infusion once yearly	Mild to moderate flu like symptoms, generalized bone, joint, or muscle pains; caution if decreased kidney function	✔✔✔✔✔

Medication Options

Medication	How it Works	How it is Given	Side Effects	Efficacy
Denosumab (Prolia)	Decreases bone breakdown, decreases fracture risk	Subcutaneous injection ('shot') every 6 months	Bone pain, joint or muscle pains, and rare risk of skin rash/ problems, and low blood calcium	✓✓✓✓✓
Raloxifene (Evista)	Decreases bone breakdown, decreases spine (not hip) fracture risk	1 pill daily	Hot flashes, rare blood clots	✓✓
Calcitonin (Miacalcin)	Decreases bone breakdown, no benefit to prevent fractures	Nasal spray once daily, or subcutaneous injection ('shot') once daily	Nasal irritation, injection site reaction	✓
Teriparatide (Forteo)	Increases bone formation and bone density, decreases fracture risk	Subcutaneous injection ('shot') once daily using an injection pen device	Injection site reaction, leg cramps	✓✓✓✓✓

Efficacy: ✓✓✓✓✓ is the most efficacious in decreasing fracture risk

Non-Pharmacologic Options

	How it Works	Recommended Dose/Frequency	Side Effects	Efficacy
Calcium (-Carbonate or -Citrate)	Main mineral component of bone	1000 mg daily (diet + supplement) in divided dose for all adults; 1200 mg daily in divided dose for postmenopausal women and men age >70 years	Bloating, constipation, gas	✔✔
Vitamin D	Increases calcium absorption	1000-2000 IU daily or higher doses in special situations	Generally well tolerated	✔✔
Exercise	Slight increase in bone density	30 minutes daily of weight bearing activity (walking or walking equivalent - treadmill, elliptical, etc.)	Muscle sprains if too much	✔

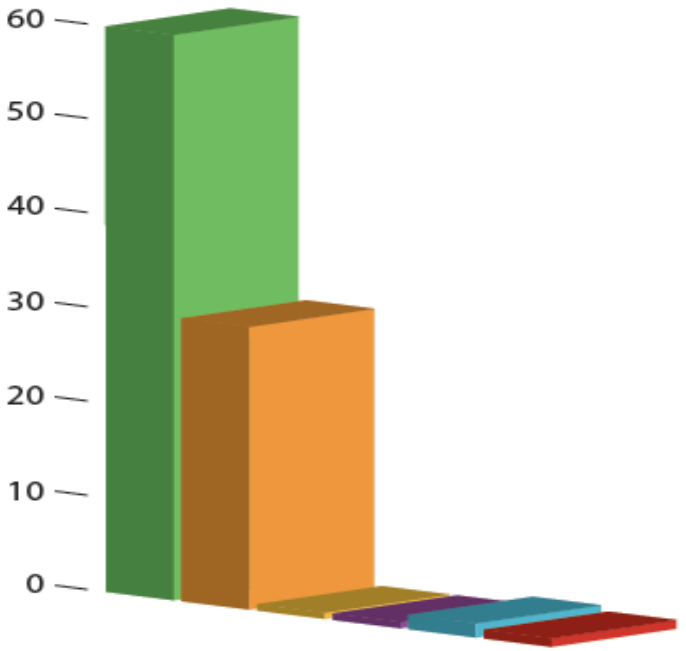
Efficacy is based on fracture risk reduction data (spine, non-spine and hip) as well as other endpoints

Balancing Benefits vs Risks

10-Year Probabilities

80 year old with a FN T-score of -3.0, a maternal history of hip fracture and a prior fracture

- Fx Risk Untreated **(60%)**
  Includes 0.01% Atypical Femur Fracture Risk
- Fx Risk Treated **(30%)**
  Includes 0.5% Atypical Femur Fracture Risk
- Atypical Fracture Risk **(0.01%)**
- ONJ Treated **(0.01%)**
- Fatal MVA **(0.11%)**
- Murder **(0.06%)**



Untreated probability of major osteoporotic fracture calculated by FRAX. ONJ estimate is ~1/100,000 patient-treatment-years from ASBMR Task Force by Khosla S et al. *J Bone Miner Res* 2007;22:1479–149. AFF estimate untreated is ~0.01/10,000 and treated is ~5/10,000 patient-years from Schilcher J et al. *N Eng J Med*. 2011;364:1728–1737. Risk estimates assume long-term bisphosphonate therapy resulting in 50% reduction in fracture risk. MVA and murder data from the CDC at http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_10.pdf.

Approach to PharmacologicalTreatment: Consider the 3 C's

A. **Cost/Coverage**: Commercial insurance, Medicare, Medicare Advantage, Tri Care for Life
   - Prior authorization, Patient Assistance programs, Specialty Pharmacy, Appeals, Request for Exception to tier
   - Keep open access to reimbursement specialist and pharmaceutical representative to stay up to date on resources.

B. **Compliance**: Should be determined at the initial visit between the patient and provider. Communication critical.

C. **Convenience**: Patient's level of independence, care needs, disposition, transportation, and any other disparities

Decision Making Summary

- Recognize that most clinical decisions are made with evidence that is insufficient, conflicting, or absent
- Understand that clinical practice guidelines and RCTs can be helpful but may not the final answer
- Accept the presence of uncertainty – it will never go away
- Reduce uncertainty by advancing your knowledge
- Individualize patient management decisions
- Stay Humble and Stay Connected: Colleagues, Project ECHO, Medical Liaisons, etc.

Dr. Michael Lewiecki, ISO 2021

Updates and potential pharmacologic management

Current Information

Eli Lilly's Teriparatide no longer on patent

Still available

Early 2021 FDA removed the boxed warning regarding osteosarcoma so now can be used longer than 24 months if appropriate

Current Information

- Alvogen's Teriparatide
- It is a brand, not generic but using the non formulary name
  - Started circulating last year
  - Same as Eli Lilly's teriparatide molecule
  - Same delivery mechanism by self injection
  - 20 mcg sub q daily for 24 months
  - Must be refrigerated

Updates and potential pharmacologic management

Current Information

- Radius is/has completed phase 3 testing in these areas:
  - **Abaloparatide patch for women**
  - **Abaloparatide indication for men**

  Data should be available by 4th quarter of 2021(both were 12-month studies)

  Fracture Healing studies with Evenity™ looking a hip and tibial fractures was neutral

On the Horizon

- Potential investigator-initiated studies around fracture healing in two areas
  - Nonunions
  - Spinal Fusions

- Entera Pharmaceuticals: markets oral equivalent for biological therapies and currently studying oral PTH for hypoparathyroidism

Resources and References

- National Osteoporosis Foundation.org
- NOF Bone Basics guidelines under professional resources
- Clinician's guide to treatment and management of osteoporosis
- AACE patient decision tool
- Cosman F, Nieves J, Dempster, D Treatment Sequence Matters: Anabolic and Antiresorptive Therapy for Osteoporosis. JBMR 2016 Vol 32, Issue 2
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Resources and References

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Thank you!