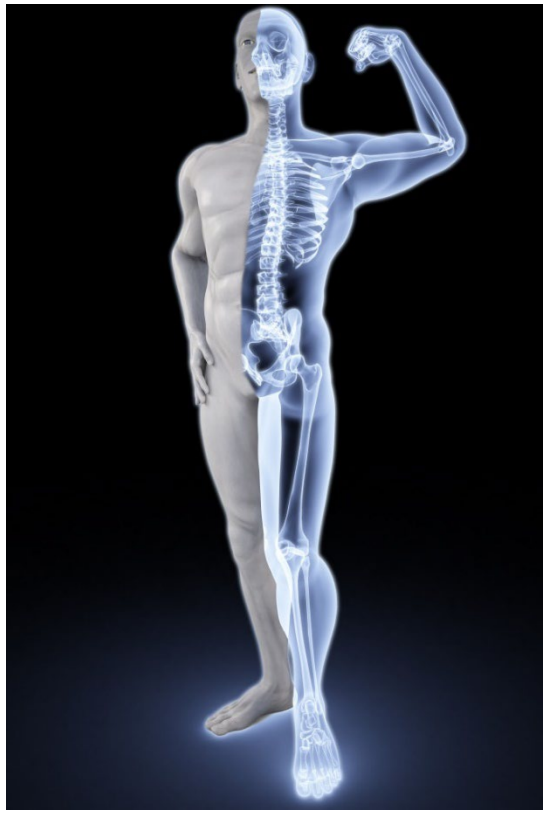
Optimizing Bone Health in Cancer Patients



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Disclosures

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  - **Others:** n/a

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Learning Objectives

- Describe the implications of cancer treatment-induced bone loss and bone mets on overall bone health
- Review treatment algorithms from Bone Health in Cancer: ESMO Clinical Practice Guidelines
- Discuss new updates for coverage of anti resorptive therapy in BC

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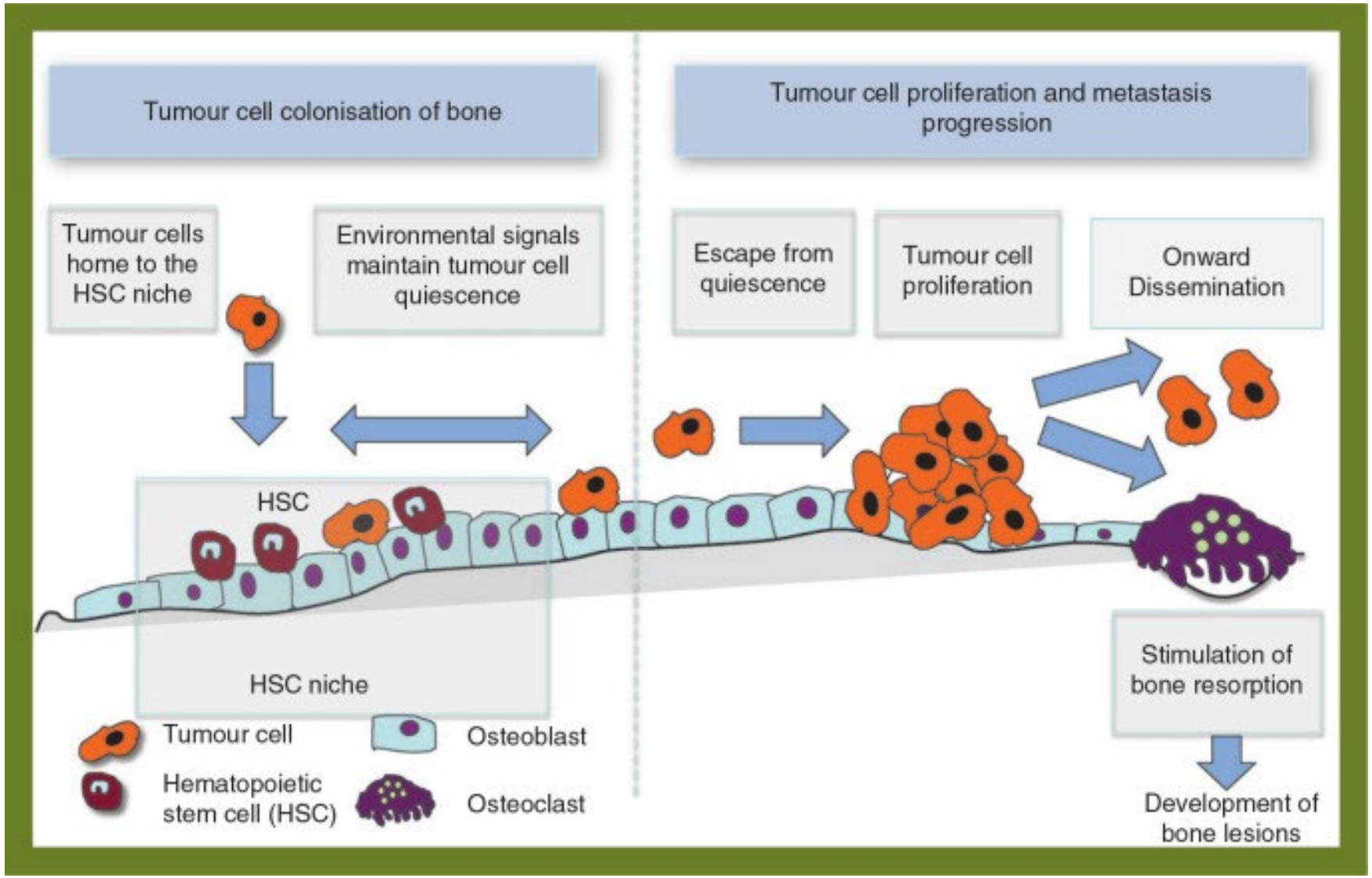
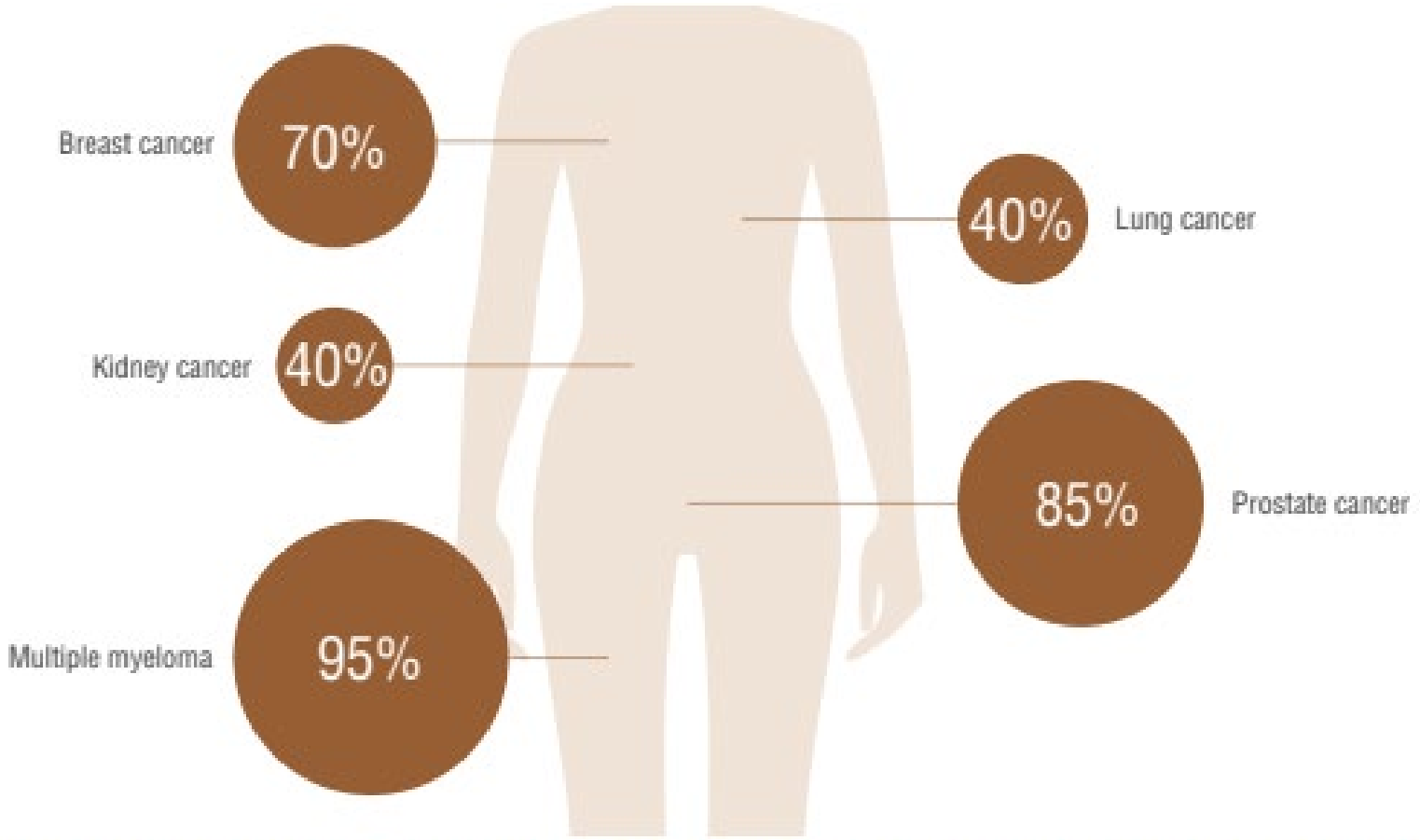
Development of bone metastases



R. Coleman, et al Bone health in cancer patients: ESMO Clinical Practice Guidelines†,Annals of Oncology,Volume 25, Supplement 3,2014,Pages iii124-iii137,

Probability of bone mets



*Estimated incidence (measure of the probability of development) of bone **metastases** in different types of **metastatic** cancer (Coleman et al., 2020).*

Effects of Breast Cancer Treatment on Bone Health

- Chemotherapy
  - Agents such as taxanes and anthracyclines lead to
    - Increased bone resorption
    - Bone loss
    - Reduction in bone architecture
  - Secondary amenorrhea in premenopausal women, resulting in increased osteoclastic bone resorption
  - Increased rates of fractures observed in women treated with chemotherapy for breast cancer

Effects of Breast Cancer Treatment on Bone Health

- Endocrine Treatment
  - Tamoxifen in post-menopausal women can result in a stabilization/increase of the BMD
  - Aromatase inhibitors, due to the induced estrogen deficiency, cause increased bone resorption, decreased BMD and increased fracture risk
    - Associated a with a 2-3 fold higher rate of bone loss compared to women not on AI's
- Breast cancer has highest mean rate of SRE (between 2-4/yr)

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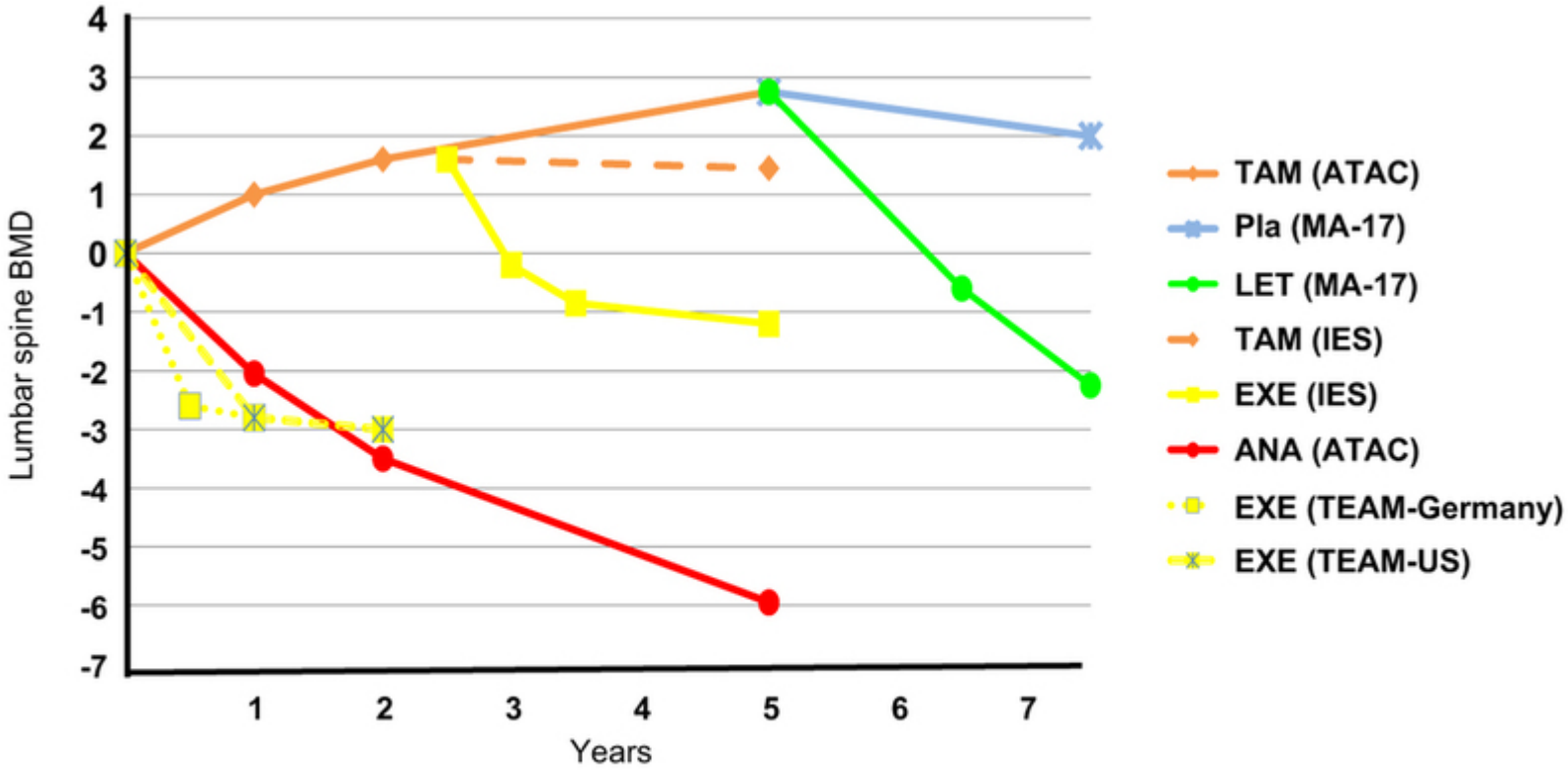
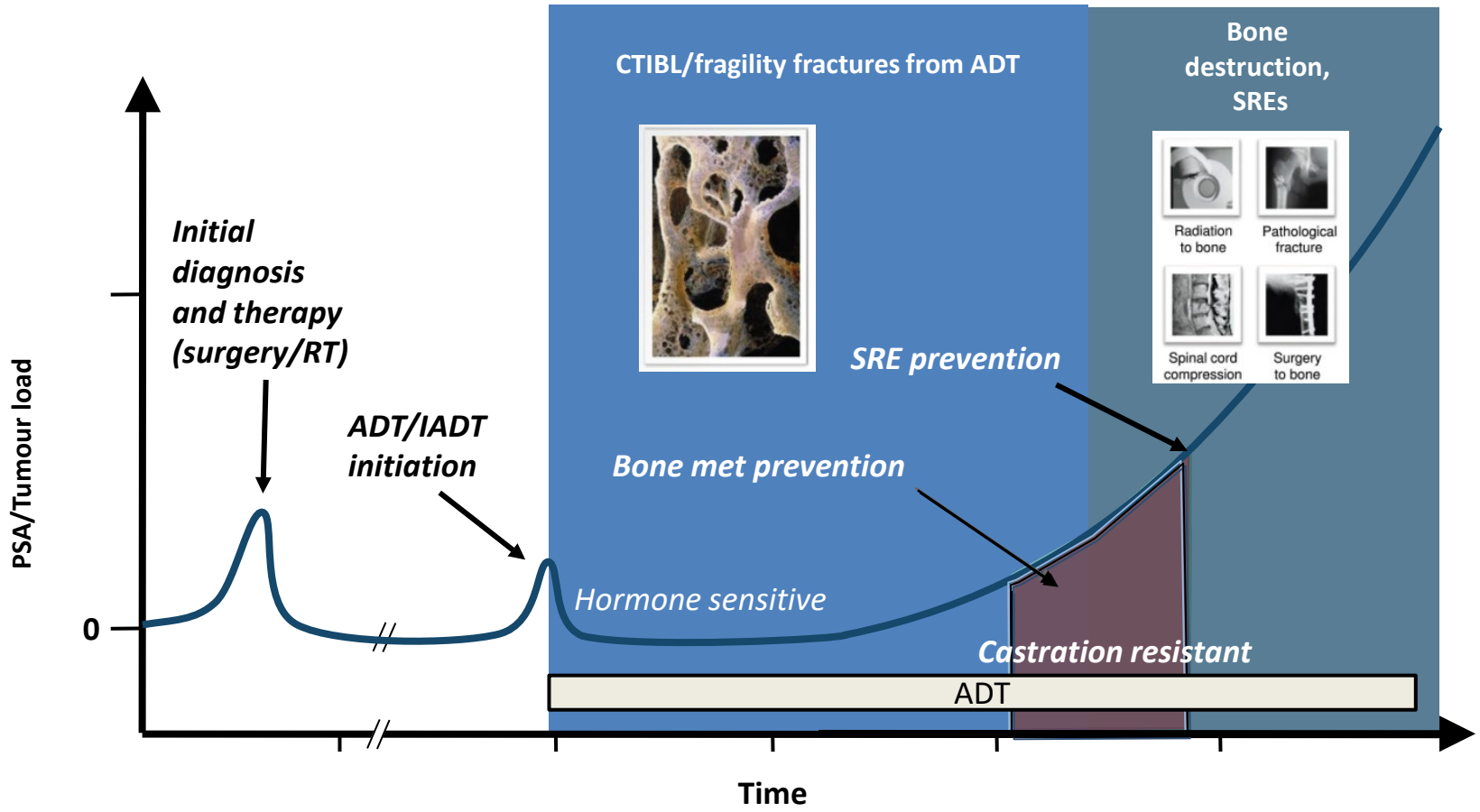


ATAC[1] Anastrozole vs tamoxifen upfront,; IES[2] Exemestane vs tamoxifen following switch after 2-3 years tamoxifen; MA-17[3] Letrozole vs placebo following switch after 5 years on tamoxifen,; TEAM[4] Exemestane vs tamoxifen for 2-3 years (before switching from TAM to EXE vs. EXE for 5 years)

1. Howell A, et al.*Lancet* 2005;365:60-62; 2. Coleman RE, et al. *Lancet Oncol.* 2007;8:119-127; 3. Goss PE, et al. *J Natl Cancer inst.* 2005;97:1262-1271; 4.Hadji P, et al. Presented at 31st Annual San Antonio Breast Cancer Symposium, San Antonio, TX, USA; December 10-14, 2008; Abstract 1143.

Bone Morbidity Across the Continuum of Prostate Cancer



Saad F, et al. J Natl Cancer Inst 2004;96:879-82.
Saad F, et al. Eur Urol 2004;46:731-40.

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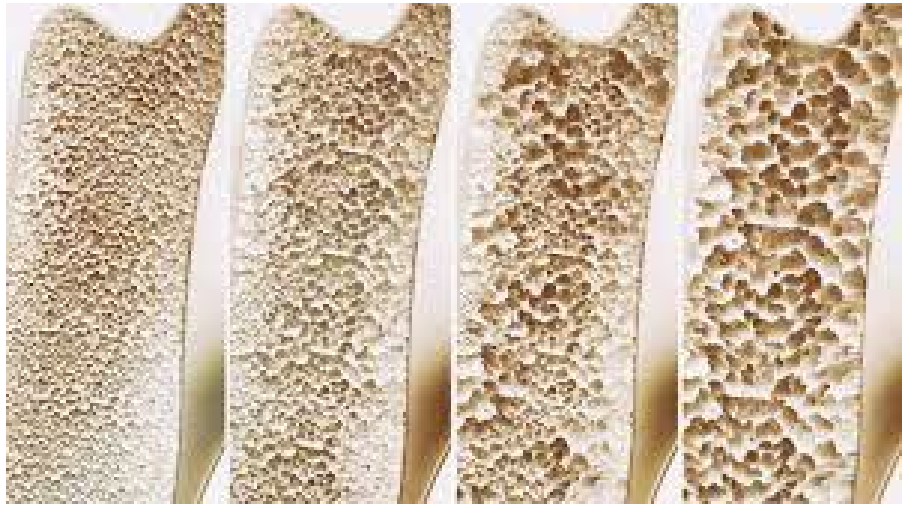
Cancer Treatment–induced Bone Loss (CTIBL) in Prostate Cancer



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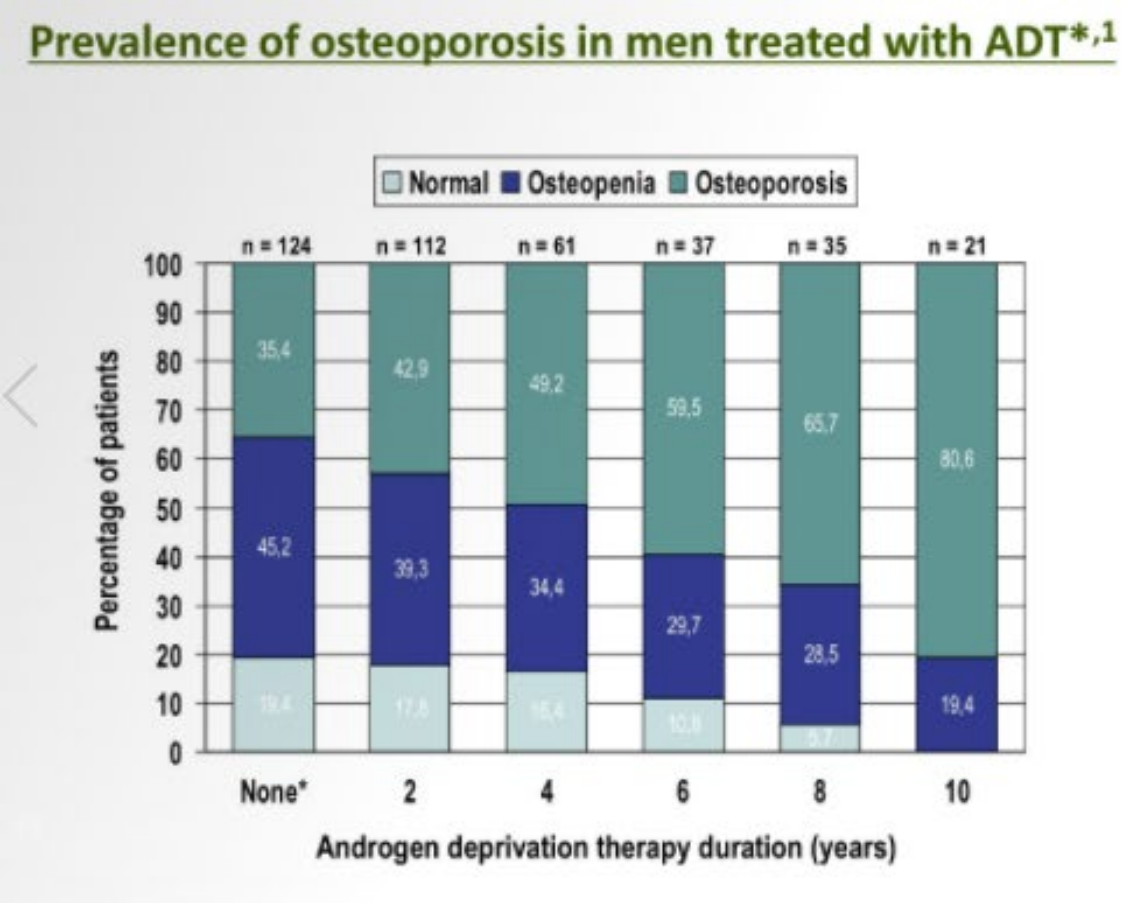
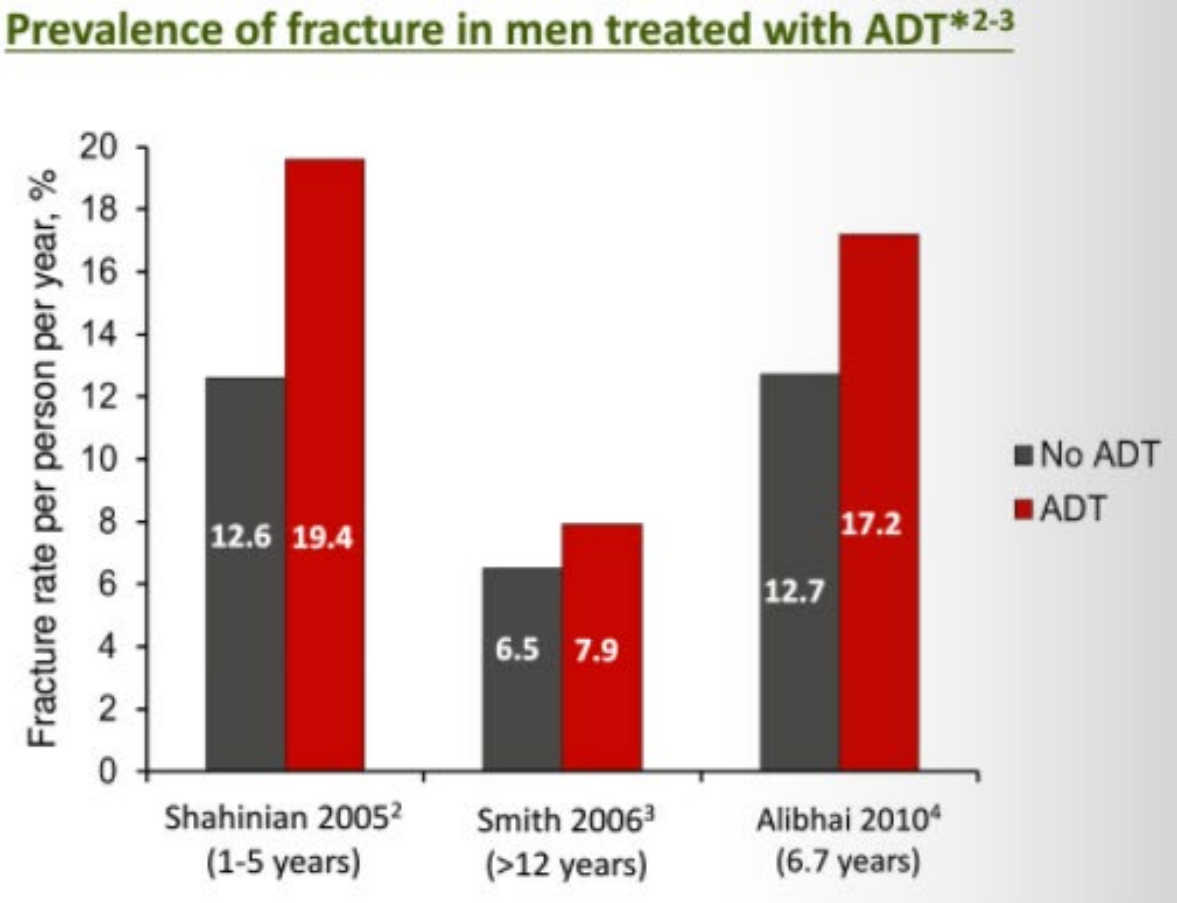
Pca Patients are at an Elevated Risk of Osteoporosis and Osteoporotic fractures due to ADT





ADT, androgen deprivation therapy; CI, confidence interval;

1. Morote J et al. Urology 2007;69:500–504; 2. Shahinian, et al. NEJM 2005;352:154–64; 3. Smith, et al. J Clin Oncol 2006;24:4448–56; 4. Alibhai, et al. J Urol 2010;184;918–24.

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ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Bone health in cancer: ESMO Clinical Practice Guidelines†

R. Coleman[1], P. Hadji[2,3], J.-J. Body[4], D. Santini[5], E. Chow[6], E. Terpos[7], S. Oudard[8], Ø. Bruland[9,10], P. Flamen[11], A. Kurth[12,13], C. Van Poznak[14], M. Aapro[15] & K. Jordan[16], on behalf of the ESMO Guidelines Committee*

[1]Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK; [2]Frankfurt Centre of Bone Health, Frankfurt; [3]Philipps University of Marburg, Marburg, Germany; [4]CHU Brugmann, Université Libre de Bruxelles, Brussels, Belgium; [5]Medical Oncology Department, University Campus Bio-Medico, Rome, Italy; [6]Department of Radiation Oncology, University of Toronto, Toronto, Canada; [7]National and Kapodistrian University of Athens, School of Medicine, Athens, Greece; [8]Department of Medical Oncology, Georges Pompidou Hospital, Paris Descartes University, Paris, France; [9]Institute of Clinical Medicine, University of Oslo, Oslo; [10]Department of Oncology, Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway; [11]Department of Nuclear Medicine, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium; [12]Department of Orthopaedic and Trauma Surgery, Campus Kemperhof, Community Clinics Middle Rhine, Koblenz; [13]Major Teaching Hospital of the University Medicine Mainz, Mainz, Germany; [14]University of Michigan, Ann Arbor, USA; [15]Genolier Cancer Centre, Genolier, Switzerland; [16]Department of Medicine V, Hematology, Oncology and Rheumatology, University of Heidelberg, Heidelberg, Germany

Available online 12 August 2020

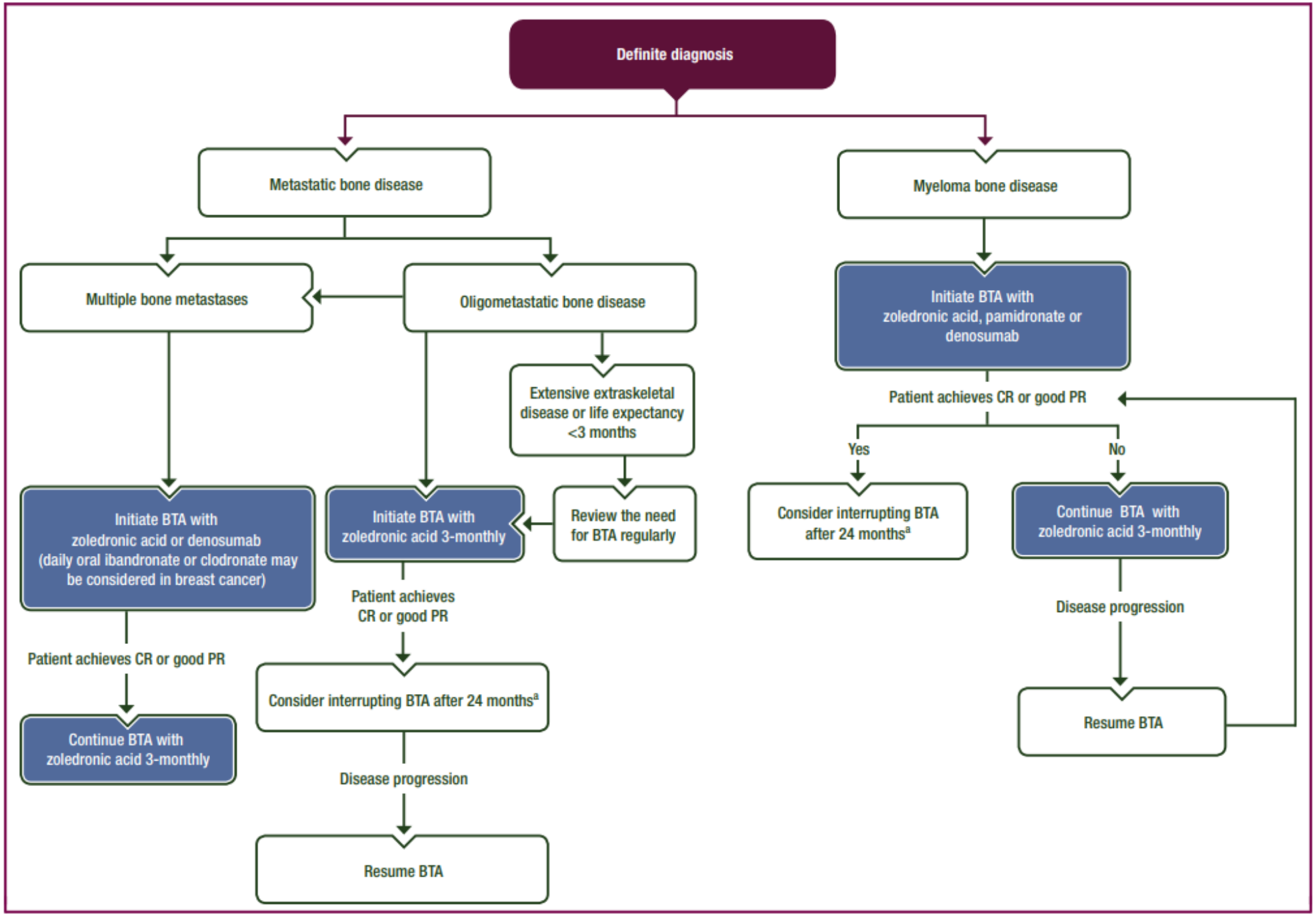
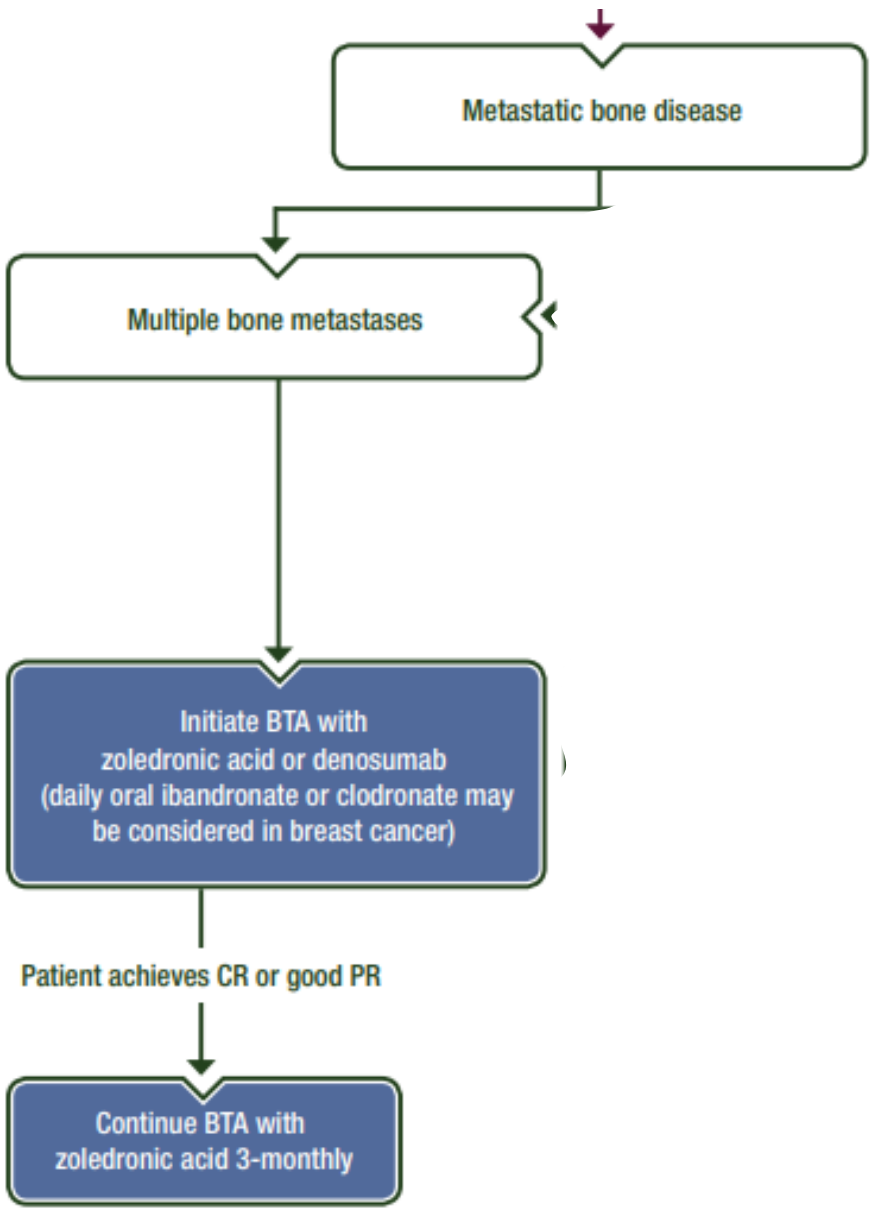


Figure 1. **Algorithm for use of bone-targeted treatments for bone metastases and myeloma bone disease.**


Metastatic bone disease
Multiple bone metastases
Initiate BTA with
zoledronic acid or denosumab
(daily oral ibandronate or clodronate may
be considered in breast cancer)
Patient achieves CR or good PR
Continue BTA with
zoledronic acid 3-monthly

Recommendations: Bone Targeted Therapy

- The investigation and management of patients with bone metastases/bone lesions should be discussed within a multidisciplinary team with links to all therapeutic modalities of relevance [V, A]

- Zoledronate or denosumab is recommended in patients with CRPC and bone metastases, whether they are symptomatic or not [I, A].

- Bone treatment, other than to prevent/treat cancer treatment-induced bone loss (CTIBL) or pre-existing osteoporosis is not recommended for ESPC [I, B].

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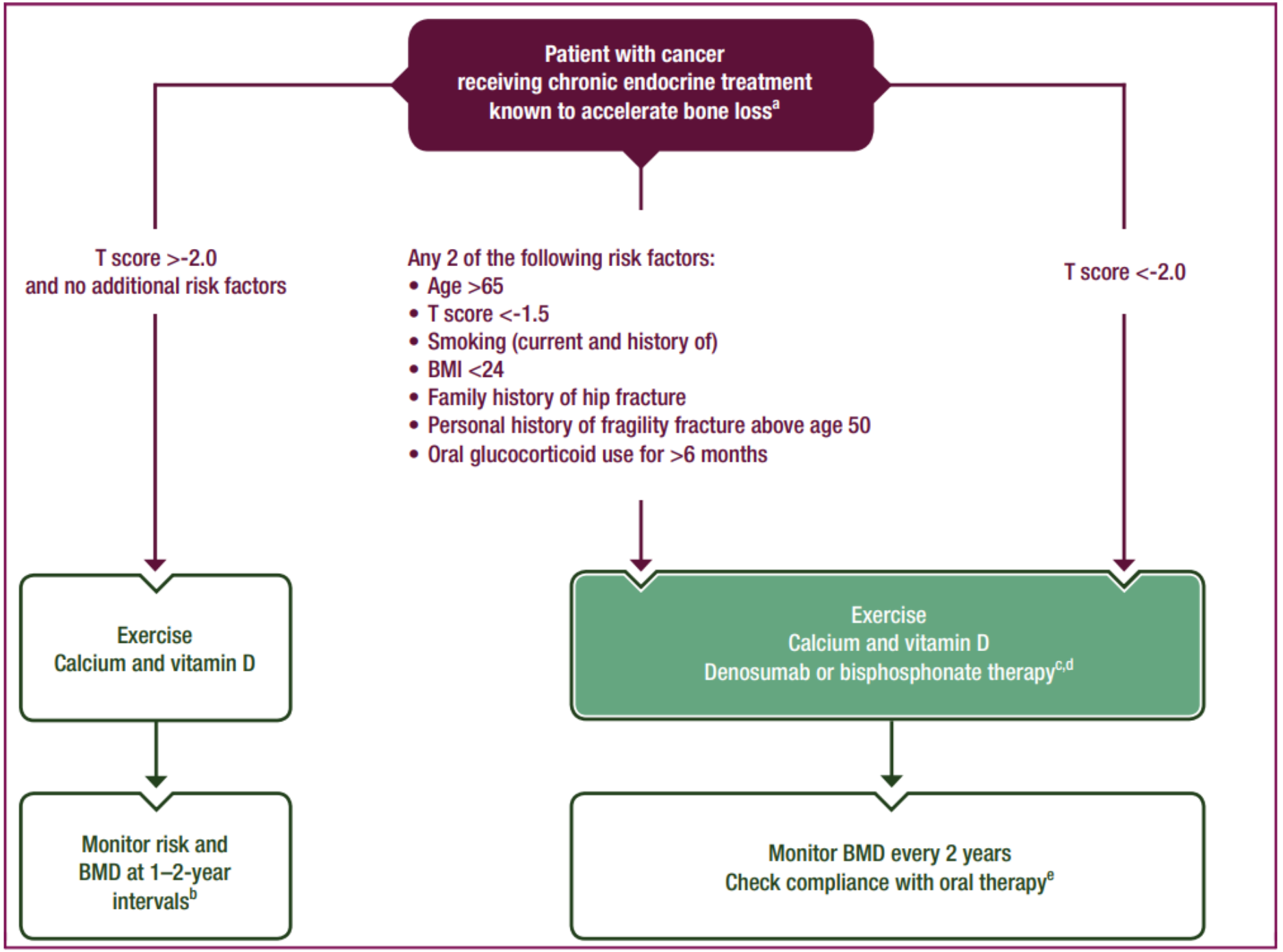


Figure 3. Recommended algorithm for managing bone health during cancer treatment.

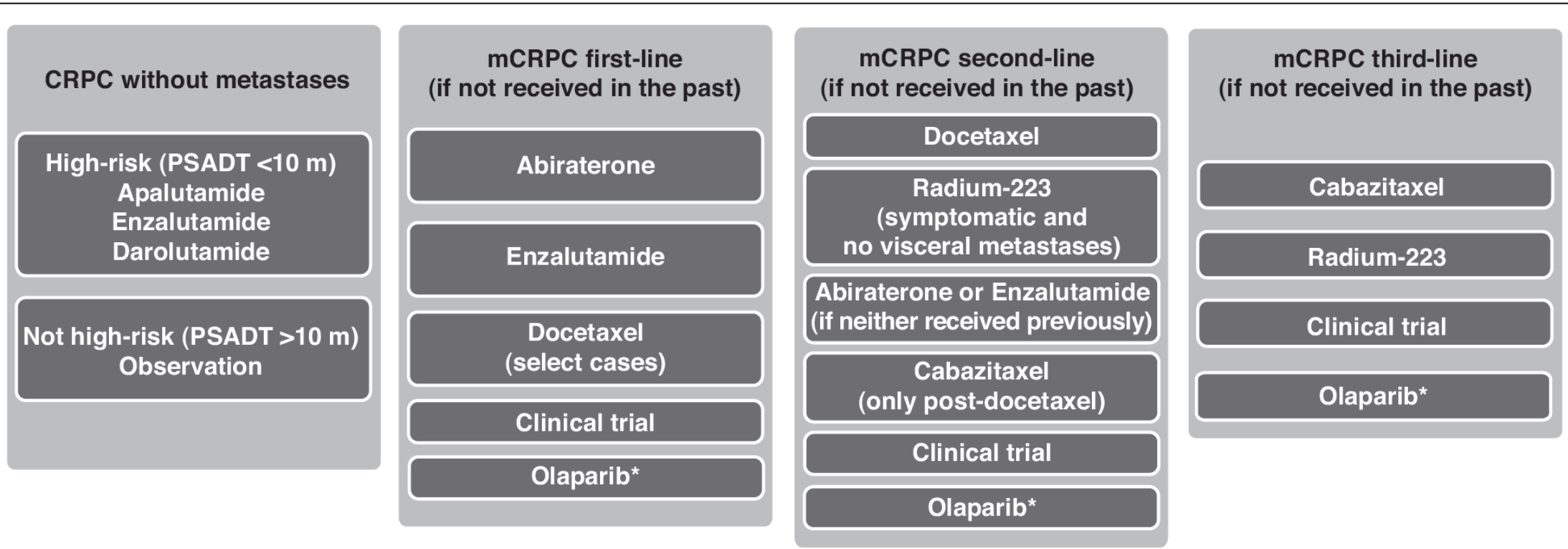
Recommendations

- In at-risk patients, an assessment of clinical risk factors and measurement of BMD by dual X-ray absorptiometry is recommended [V, A].
- Weight-bearing exercise, smoking cessation, reduced alcohol intake and vitamin D supplements (and calcium) should be encouraged [I, B].
- Antiresorptive therapy is recommended in women receiving either an AI or OFS and men on ADT for >6 months with either a BMD T score of <-2 or with ≥ 2 risk factors for fracture [I, A].
- Denosumab 60 mg every 6 months is the treatment of choice to prevent fractures in men on ADT and postmenopausal women with early breast cancer at low risk for disease recurrence [I, B].

2021 Canadian Urological Association (CUA)-Canadian Uro Oncology Group (CUOG) guideline: Management of castration-resistant prostate cancer (CRPC)

Fred Saad, MD[1]; Armen Aprikian, MD[2]; Antonio Finelli, MD[3]; Neil E. Fleshner, MD[3]; Martin Gleave, MD[4]; Anil Kapoor, MD[5]; Tamim Niazi, MD[6]; Scott A. North, MD[7]; Frederic Pouliot, MD[8]; Ricardo A. Rendon, MD[9]; Bobby Shayegan, MD[5]; Srikala S. Sridhar, MD[10]; Alan So, MD[4]; Nawaid Usmani, MD[11]; Eric Vigneault, MD[12]; Kim N. Chi, MD[13]

Management of CRPC



*For patients with HRR mutation and having progressed on an NHT

In the presence of bone metastases:

Denosumab or zoledronic acid are recommended to reduce the risk of skeletal complications

Palliative radiation therapy should be considered in patients with pain

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Bone Targeted Therapy

Life Prolonging Therapy

- Radium-223 every four weeks for six cycles is recommended in patients with pain due to bone metastases and who do not have visceral metastases *(Level 1, Strong recommendation)*.

- Radium-223 should not be combined with abiraterone. A bone-supportive agent (denosumab or zoledronic acid) should always be used when using radium-223 *(Level 1, Strong recommendation)*.

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Supportive agents: Denosumab and Zoledronic Acid

- In men with CRPC and bone metastases, denosumab (120 mg subcutaneous [SC]) or zoledronic acid (4 mg IV) every four weeks are recommended to prevent disease-related SREs, including pathological fractures, spinal cord compression, surgery, or radiation therapy to bone *(Level 1, Strong recommendation).*
  - In the setting of mCRPC, denosumab compared to zoledronic acid has shown significant improvement in the time to the first SRE (20.7 vs. 17.1 months; p=0.008 for superiority), while OS and PFS were not different
  - Good oral hygiene, baseline dental evaluation for high-risk individuals, and avoidance of invasive dental surgery during therapy are recommended to reduce risk of osteonecrosis of the jaw (ONJ) for patients treated with bone-targeted therapies *(Expert opinion)*.
  - The risk of ONJ appears to be related to time on bone-targeted therapy, therefore, caution should be taken in using these agents beyond two years *(Level 3, Weak recommendation).*
- Denosumab and zoledronic acid are not approved and not indicated for SRE prevention in the treatment of metastatic castration-sensitive prostate cancer or for bone metastases prevention.

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Additional considerations

- Calcium and vitamin D supplementation
  - Prostate cancer patients should supplement their diet with 1200–1500 mg calcium (preferably with calcium citrate) and 2000 IU Vitamin D[1]

  -Studies show only 50% of Canadian urologists and radiation oncologists recommend calcium supplementation to men starting ADT

  - Calcium citrate is recommended over calcium carbonate if the patient is taking PPI as carbonate is not adequately absorbed when the stomach pH is elevated
  - Vitamin D3 (cholecalciferol) is recommended over Vitamin D2 (ergocalciferol)
  - Vitamin D supplements should ideally be taken after the biggest meal of the day to maximize absorption

1. http://www.prostate-cancer.org/pcricms/node/226
2. Alibhai SM.Urology. 2006 Jul;68(1):126-31. doi: 10.1016/j.urology.2006.01.054. PMID: 16844454.

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Additional considerations

- Exercise
  - Evidence of the effectiveness of physical exercise to prevent the risk of accidental falls and fractures and BMD loss is lacking
  - Impact + resistance training is a safe and acceptable form of exercise for older Prostate Cancer survivors on ADT

Winters-Stone KM, Med Sci Sports Exerc. 2014 Aug;46(8):1482-8.
Bressi B Support Care Cancer. 2021 Apr;29(4):1811-1824.

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Bone Health Referral Pathway

- Initiated with BCCA Surrey in 2018
- Planned with the intention to disburden bone health management from BCCA doctors in high risk patients
- Model works well in virtual or in-person setting
- Referral pathway takes care of multiple aspects of bone health including calcium/vit. D counseling, bone-targeted therapy initiation, special auth paperwork, home injection assistance program

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When is referral indicated for bone health in PCa?

- Patient with multiple bone mets
- Patients >65 years on ADT >6 mos
- Patient on steroid therapy for >6 mos
- Patient with known history of osteoporosis/ fragility fractures

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When is referral indicated for bone health in BrCa?

- Patient with multiple bone mets
- Patients on AI with BMD <-1.5
- Patient on steroid therapy for >6 mos
- Patient with known history of osteoporosis/ fragility fractures

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Baseline investigations

- Consider ordering Serum Calcium, PTH, 25 OH vitamin D and TSH if not done in the past 3 months prior to referral
- BMD not indicated for mCRPC/mHSPC with bone mets or Breast cancer with bone mets
- BMD should be done if referral for CTIBL evaluation in patients on ADT or AI
- For patients with skeletal mets, indicate if patient on Palliative Care Benefits (denosumab covered if patient has PCB)

Clinical Pearl: It is absolutely essential that surveillance BMD/ DXA studies be performed at the same centre as previous studies, for reliable comparison

Bone Health Referral Form

BC CANCER
Provincial Health Services Authority

Today's date: _____

Dear Dr. Akshay Jain:

I would like to refer this oncology patient to you for:

☐ Longitudinal management of bone health/osteoporosis/fragility fracture
therapy)
☐ Prostate cancer with bone metastases with Castrate Sensitive prostate
☐ Prostate cancer with bone metastases with Castrate Resistant prostate
☐ Breast Cancer on aromatase inhibitor
☐ Other: _____

I would be grateful if this patient could be seen within 3 / 12 / _____ week
number of weeks) from date of referral.

I have requested or will send you a copy of a bone mineral density scan (i
blood tests as per checklist below and recent BC Cancer progress notes.
additional assessments such as dentistry as you see fit.

Checklist:
☐ Referral to dentistry for examination
☐ Requisition given to patient for chemistries
(calcium, phosphate, magnesium, TSH, Creatinine 25 hydroxyvitamin
☐ ask patient to initiate 1200 mg calcium from diet and supplement, 2000

Payment options:
☐ enrolled for palliative care benefits (if applicable)
☐ has private insurance
☐ no extended benefits

I will make arrangements for palliative care benefits if applicable.

Please have your MOA contact the patient directly for an appointment. I v
of your evaluations to be sent to my attention at BC Cancer – Surrey and
coordinate with his family doctor if you would like GP to participate in this

If you have any questions, please contact me.

Sincerely,

_____ _____
Print and Sign your name here

Today's date: _____

Dear Dr. Akshay Jain:

I would like to refer this oncology patient to you for:

☐ Longitudinal management of bone health/osteoporosis/fragility fractures (e.g. while on hormone therapy)
☐ Prostate cancer with bone metastases with Castrate Sensitive prostate cancer
☐ Prostate cancer with bone metastases with Castrate Resistant prostate cancer
☐ Breast Cancer on aromatase inhibitor
☐ Other: _____

I would be grateful if this patient could be seen within 3 / 12 / _____ weeks (circle one or insert number of weeks) from date of referral.

I have requested or will send you a copy of a bone mineral density scan (if applicable) and baseline blood tests as per checklist below and recent BC Cancer progress notes. Please arrange any additional assessments such as dentistry as you see fit.

Checklist:
☐ Referral to dentistry for examination
☐ Requisition given to patient for chemistries
(calcium, phosphate, magnesium, TSH, Creatinine 25 hydroxyvitamin D, intact PTH)
☐ ask patient to initiate 1200 mg calcium from diet and supplement, 2000 IU vitamin D per day

Payment options:
☐ enrolled for palliative care benefits (if applicable)
☐ has private insurance
☐ no extended benefits

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What happens following referral

Referral options for Abbotsford

- Initial consultation appointment can be done via telehealth
- Home injection services/ zoledronic acid infusions available via Wellness Pharmacy in Abbotsford
- Ongoing monitoring to ensure S. Calcium is >2.10 with monthly monitoring for patients on Xgeva/ Zoledronic acid. Renal function monitoring for Zoledronic acid

What’s on the horizon with denosumab?

- In 2023, Pharmacare approved coverage for treatment with Prolia version for women with breast cancer on AI therapy, for a duration of 5 years
- It remains to be seen what the coverage situation will be after 5 years, as likely benefits achieved with denosumab could be lost once treatment is discontinued
- Health Canada has recently approved biosimilar versions of denosumab. These are expected to launch in the near future

Thank You!

- Email: oxyjain@gmail.com

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