

Bone Health and Bone-Targeted Therapies for Prostate Cancer: ASCO Endorsement of a Cancer Care Ontario Guideline

Saylor et al.

Introduction

- Cancer Care Ontario (CCO) recently published recommendation on bone health and bone-targeted therapies for prostate cancer.
- An ASCO Expert Panel reviewed the guideline according to ASCO endorsement processes.
- Relevant clinical risks for men with prostate cancer range from osteoporotic fractures associated with androgen deprivation therapy (ADT) to morbidity and death due to progression of bone-metastatic castration-resistant disease
- The ASCO Expert Panel endorses the CCO guidelines and provides additional discussion to guide clinicians toward optimal use of bone-targeted therapies.

ASCO Endorsement Methodology

The ASCO Clinical Practice Guidelines Committee endorsement review process includes:

- a methodological review by ASCO guidelines staff
- a content review by an Expert Panel
- final endorsement approval by ASCO CPGC.

The full ASCO methodology manual can be found at:

www.asco.org/guideline-methodology

CCO Guideline Methodology can be found at:

<https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/31716>

Clinical Questions

1. Can therapeutic interventions reduce osteoporosis related outcomes in men with prostate cancer receiving androgen deprivation therapy (ADT)?
2. Can therapeutic interventions prevent bone metastases in men with prostate cancer?
3. Can bone-targeted therapies reduce the incidence of skeletal-related events (SREs), reduce pain, or improve quality of life (QoL) in men with prostate cancer metastatic to bone?
4. Can bone-targeted therapies improve overall survival in men with established prostate cancer and bone metastases?

Target Population and Audience

Target Population

Men with prostate cancer.

Target Audience

Health care professionals, health care administrators, medical or radiation oncologists who treat genitourinary cancer, urologists, radiologists, nuclear medicine physicians, endocrinologists, geriatricians, primary care physicians, osteoporosis experts, patients, and their caregivers.

Summary of Recommendations

CLINICAL QUESTION 1

Can therapeutic interventions reduce osteoporosis related outcomes in men with prostate cancer receiving androgen deprivation therapy (ADT)?

CCO Recommendation 1

For men with non-metastatic prostate cancer at high risk of fracture receiving ADT, denosumab at the osteoporosis-indicated dosage should be considered to reduce the risk of fracture. In situations or jurisdictions where denosumab is contraindicated or not available, a bisphosphonate is a reasonable option.

ASCO Discussion Point

The Expert Panel's opinion is that oral and intravenous bisphosphonates are also reasonable options for risk modification in this setting even though they have not been studied for fracture prevention.

Summary of Recommendations

CLINICAL QUESTION 2

Can therapeutic interventions prevent bone metastases in men with prostate cancer?

CCO Recommendation 2a

In men with high-risk localized prostate cancer, bisphosphonates are not recommended to reduce the risk of first bone metastasis.

CCO Recommendation 2b

In men with non-metastatic (castration-resistant prostate cancer; CRPC), denosumab at the bone metastasis-indicated dosage is not recommended to reduce the risk of first bone metastasis.

ASCO Discussion Point

No bone-targeted drug (denosumab, zoledronic acid, or any other bisphosphonate) has been approved for the prevention of the first prostate cancer bone metastasis in any clinical setting

Summary of Recommendations

CLINICAL QUESTION 3

Can bone-targeted therapies reduce the incidence of skeletal-related events (SREs), reduce pain, or improve quality of life (QoL) in men with prostate cancer metastatic to bone?

CCO Recommendation 3a

In men with metastatic CRPC (mCRPC), either zoledronic acid (minimally symptomatic or asymptomatic disease) or denosumab (disease independent of symptoms) (both at bone metastasis-indicated dosages) is recommended for preventing or delaying SREs. Insufficient evidence exists to make a recommendation with respect to men with CSPC and bone metastasis.

CCO Recommendation 3b

In men with symptomatic mCRPC and bone pain, radium-223 (Ra-223) should be considered for reducing symptomatic skeletal events and improving health-related QoL.

Summary of Recommendations

CCO Recommendation 3c

In men with mCRPC and bone pain, radiopharmaceuticals or intravenous bisphosphonates may be considered for pain palliation.

ASCO Discussion Points

- Optimal safe duration of monthly therapy for prevention of SREs is not well established. Pivotal trials treated for a maximum of 24 months. Incidence of osteonecrosis of the jaw (ONJ) has been higher with longer duration of exposure.
- Dental evaluation prior to start of zoledronic acid or denosumab is recommended as invasive dental procedures or ill-fitting dental appliances during therapy are a common predisposing factor in cases of ONJ.
- Calcium and vitamin D supplementation (e.g. calcium ≥ 500 mg and vitamin D ≥ 400 IU daily) has been prescribed or strongly recommended within clinical trials of zoledronic acid or denosumab and is recommended within the package inserts of both drugs.
- Multiple studies in the metastatic castration sensitive prostate cancer setting utilizing zoledronic acid monthly did not show a benefit for SRE risk reduction.

Summary of Recommendations

CLINICAL QUESTION 4

Can bone-targeted therapies improve overall survival in men with established prostate cancer and bone metastases?

CCO Recommendation 4

In men with symptomatic mCRPC, Ra-223 is recommended to extend overall survival.

ASCO Discussion Point

There is evidence to suggest harm in the form of increased fracture risk with the combination of Ra-223 when administered with abiraterone and prednisone initiation; that combination should be avoided. There is insufficient evidence to support concurrent use of Ra-223 with other secondary therapies known to prolong survival for mCRPC.

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Endorsement Statement

ASCO endorses the Bone Health and Bone-targeted Therapies for Prostate Cancer: CCO Clinical Practice Guideline with ASCO Expert Panel discussion points being offered.

Additional Resources

More information, including a Data Supplement with a reprint of all (ORG) recommendations, slide sets, and clinical tools and resources, is available at www.asco.org/gag-guidelines

Link to original guideline:

<https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/31716>

Patient information is available at www.cancer.net

ASCO Guideline Panel Members

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