

Systemic Therapy in Men with Metastatic Castration-Resistant Prostate Cancer

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Clinical Tools and Resources

Clinical Practice Guideline

Introduction

- This guideline pertains to men with CRPC and radiographically or pathologically demonstrated metastases
- In 2006, the CCO Genitourinary Cancer Disease Site Group developed a guideline on nonhormonal therapies for men with metastatic CRPC, endorsed by ASCO in 2007
- ASCO and CCO convened an expert panel to provide the current recommendations for systemic therapy in metastatic CRPC based on updated literature through June 2012

Guideline Development Process

- An Expert Panel with multidisciplinary representation in medical oncology, urologic oncology, radiation oncology, community oncology, patient advocacy, health services, implementation research, and guideline methodology was convened by ASCO and CCO
- ASCO guidelines are based on systematic review and are approved by the ASCO Clinical Practice Guideline Committee before publication
- All CCO guidelines are reviewed and approved by the CCO Report Approval Panel and a topic specific disease site group

Systematic Review Methods

- Articles were selected for inclusion in the CCO systematic review if they:
 - Were RCTs or evidence synthesis products based on RCTs
 - Included men with metastatic CRPC
 - Compared systemic therapy, alone or in combination with other agents, versus placebo or other drug regimens
 - Were published English-language reports
- Articles were excluded from the systematic review if they involved only androgen-deprivation therapy, bone targeted agents, or radionuclides

Guideline Question

Which systemic therapies improve outcomes in men with metastatic CRPC?

Recommendations

Androgen-Deprivation Therapy:

- Continuous androgen deprivation (pharmaceutical or surgical) should be continued indefinitely regardless of additional therapies

Therapies in Addition to Androgen-Deprivation Therapy: Therapies with demonstrated survival and quality-of-life benefits:

- Abiraterone acetate and prednisone should be offered
- Enzalutamide should be offered
- Radium-223 should be offered to men with bone metastases.
- Docetaxel and prednisone should be offered

Recommendations

Therapies with demonstrated survival benefit and unclear quality-of-life benefit:

- Sipuleucel-T may be offered to men who are asymptomatic or minimally symptomatic
- Cabazitaxel and prednisone may be offered to men who experience progression with docetaxel

Therapies with quality-of-life benefit without demonstrated survival benefit:

- Mitoxantrone plus prednisone may be offered

Therapies with biologic activity and unknown survival or quality-of-life benefit:

- Antiandrogens (eg, bicalutamide, flutamide, nilutamide) may be offered.
- Ketoconazole may be offered
- Low-dose corticosteroid monotherapy may be offered

Recommendations

Therapies without demonstrated survival or quality-of-life benefit:

- Bevacizumab should not be offered
- Estramustine should not be offered
- Sunitinib should not be offered

Palliative Care Services

- Palliative care should be offered to all patients, particularly to those exhibiting symptoms or quality-of-life (QOL) decrements, regardless of treatment type

Qualifying Statements

- Clinicians are advised to review the published regimens discussed in this guideline for their use in appropriate patient populations and for applicable dose selections/modifications, available from the product labels
- There is insufficient published evidence to recommend specific sequencing of these therapies or combinations of these therapies, except as otherwise noted

Qualifying Statements

- The distinction made in some clinical trials between pre- and post-docetaxel treatment contexts should not play a role in selecting therapies for individual patients, unless otherwise noted
- Patients may place a higher importance on QOL rather than length of life. It is essential to understand individual patient values and preferences for appropriate treatment decision making. Many patients with incurable metastatic disease misperceive the goals of care to be curative. Clear communication about goals as well as potential benefits and harms of care should be prioritized.

Qualifying Statements

- Cost and availability considerations may reasonably influence treatment decisions. There is wide variation in the financial burden individual patients face for various therapies, and this potential barrier or hardship should be openly discussed with patients.
- Most phase III clinical trials have included patients with good baseline performance status. The choice of treatment for patients with diminished performance status is not clearly informed by existing evidence in most cases.

Multiple Chronic Conditions

- Presence of any comorbid conditions should be taken into account when deciding on an individual treatment plan
- Most common comorbid conditions are:
 - Hypertension
 - Hyperlipidemia
 - Diabetes
 - Ischemic Heart Disease
 - Anemia
 - Arthritis
 - Chronic Kidney Disease
 - Depression
 - Chronic Obstructive Pulmonary Disease
 - Heart Failure
 - Cataract

Limitations & Future Directions

There is limited available evidence in the following areas of needed research in metastatic CRPC:

- Optimum sequencing and combination of available therapies
- Efficacy of drugs in treatment sequences other than those tested in clinical trials
- Potential benefits and harms of combining therapies
- Comparative QOL and symptomatic benefits of therapy options
- Effectiveness of therapies in real-world populations
- Cost-benefit analysis in the US context
- Out-of-pocket costs faced by most patients
- Shared decision-making tools
- Clinical benefits of lower-cost therapies in low resource contexts
- Impact of early access to palliative care
- Alternative approaches to continuous androgen deprivation

Limitations & Future Directions

The panel recommends inclusion of rigorously designed symptom and QOL outcome measures in all phase III clinical trials in metastatic CRPC. ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care and that all patients should have the opportunity to participate.

Additional Resources

- This guideline is available at <http://jco.ascopubs.org>
- The guideline, data supplements, a patient guide, and other resources are available at <http://www.asco.org/guidelines/mCRPC>
- The patient guide is also available at <http://www.cancer.net>
- Summary is available at <http://jop.ascopubs.org/>

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