



American Society of Clinical Oncology

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Initial Hormonal Management of  
Androgen-Sensitive Metastatic,  
Recurrent, or Progressive Prostate  
Cancer: 2007 Update  
Clinical Practice Guideline

# Introduction

- ASCO convened the Metastatic Prostate Cancer Expert Panel to review and update the 2004 recommendations for the initial hormonal management of androgen-sensitive, metastatic, recurrent, or progressive prostate cancer.
- The Expert Panel used an evidence-based strategy to form consensus on standard initial treatment options, anti-androgens as monotherapy, combined androgen blockade, androgen deprivation therapy (ADT), and intermittent androgen blockade.
- This Update addresses the palliation of prostate cancer using ADT when this form of therapy is considered the most appropriate initial treatment option.

# Guideline Methodology: Systematic Review

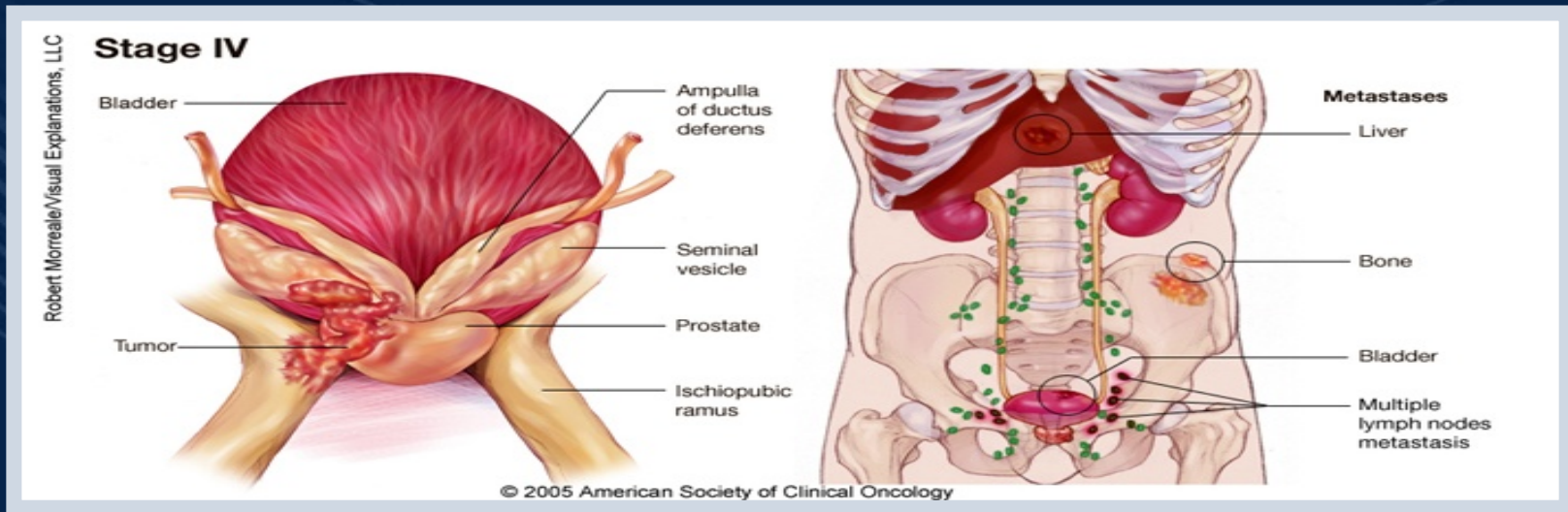
- The Expert Panel completed a review and analysis of data published since January 2003 to March 2006:
  - ✓ MEDLINE
  - ✓ Cochrane Database of Systematic Reviews
  - ✓ Physician Data Query Clinical Trials Database

# Guideline Methodology (cont 'd): Panel Members

- Howard I. Scher, MD, *Co-chair* Memorial Sloan-Kettering Cancer Center
- Charles L. Bennett, MD, PhD, *Co-chair* VA Chicago Health Care System-Lakeside & The Robert H Lurie Comprehensive Cancer Center of Northwestern University
- Edgar Ben-Josef, MD Wayne State University
- D. Andrew Loblaw, MD, MSc Sunnybrook Health Sciences Centre
- David S. Mendelson, MD Premiere Oncology of Arizona
- Richard Middleton, MD University of Utah Medical School
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- Thomas J. Smith, MD Massey Cancer Center, Medical College of Virginia
- Stewart A. Sharp, MD Danville Hematology & Oncology, Inc
- James Talcott, MD, MPH Massachusetts General Hospital
- Mary-Ellen Taplin, MD Dana-Farber Cancer Institute
- Katherine S. Virgo, PhD, MBA Saint Louis University & Department of Veterans Affairs Medical Center
- Nicholas J. Vogelzang, MD University of Chicago Cancer Research Center
- James L. Wade, III, MD Cancer Care Specialists of Central Illinois

# Background

- Prostate cancer (PCa) is the most common form of non-skin cancer in American men and the second leading cause of cancer death
- PCa can exist without death for up to a decade or more and many men with the disease die of other causes



# Background (cont ' d)

- Surveillance or watchful waiting may appeal to men who can tolerate the knowledge of untreated cancer
- ADT palliation is the standard first-line treatment for patients with metastatic, recurrent or progressive disease. ADT palliation includes:
  - Surgical or pharmacologic castration
  - Anti-androgen therapy
  - Combination of both
- Shared decision-making between patients and physicians is necessary for optimal use of ADT

# 2006 Update Recommendation Questions

- For men with metastatic or recurrent androgen-sensitive prostate cancer, in whom ADT is considered the most appropriate initial intervention:
  1. What are the standard initial treatment options?
  2. Are anti-androgens as effective as other castration therapies?
  3. Is combined androgen blockade better than castration alone?
  4. Does early androgen deprivation therapy improve outcomes over deferred therapy?
  5. Is intermittent androgen deprivation therapy better than continuous androgen deprivation therapy?

# What are the standard initial treatment options?

<p>✓ Recommended</p>	<ul style="list-style-type: none"><li>▪ Bilateral orchiectomy (surgical castration)</li><li>▪ Medical castration w/LHRH agonists</li></ul> <p>Toxicities of castration include hypotestosteronemia, weight gain, mood lability, gynecomastia, fatigue, lassitude, cognitive changes, loss of libido</p>
<p>✗ Not Recommended</p>	<ul style="list-style-type: none"><li>▪ DES</li></ul> <p>No longer commercially available in North America; associated with cardiovascular toxicities including myocardial infarction, stroke, and pulmonary embolism</p>

Note: Long-term castrate levels of testosterone can induce osteopenia and hypercholesterolemia

# Standard initial treatment options (cont ' d)

- Oncologists should discuss treatment options with their patients

Initial Tx Option	Benefits	Harms
<b>Bilateral Orchiectomy</b>	<ul style="list-style-type: none"> <li>•Rapid palliation</li> <li>•Patient compliance</li> <li>•Relative low costs</li> </ul>	<ul style="list-style-type: none"> <li>•Traumatic</li> <li>•Nonreversible</li> <li>•Toxicities</li> <li>•Minor risk of surgical complications</li> </ul>
<b>Medical Castration w/LHRH agonist*</b>	<ul style="list-style-type: none"> <li>•Less emotionally taxing</li> <li>•Potentially reversible</li> <li>•Some toxicity-related symptoms resolve after cessation of therapy</li> </ul>	<ul style="list-style-type: none"> <li>•More expensive than orchiectomy</li> <li>•Toxicities</li> <li>•Patients may experience flare phenomenon (initial worsening of signs/symptoms)</li> </ul>

\* Contraindicated as monotherapy in men with impending spinal cord compression, urinary obstruction, or pain due to the potential for exacerbating symptoms.

# Are anti-androgens as effective as other castration?

Anti-Androgen	Recommendation	Vs. Medical/Surgical Castration
<b>Nonsteroidal (NSAA)</b> [Agents: bicalutamide, flutamide, nilutamide]	NSAA monotherapy may be discussed as an alternative	Equivalent overall survival compared to orchiectomy with less toxicity regarding loss of libido and physical capacity
<b>Steroidal</b> [Agents: cyproterone acetate, goserelin acetate]	Steroidal anti-androgen monotherapy <b><u>should not</u></b> be offered	Inferior time to progression of disease compared to LHRH agonists

- Both forms of anti-androgens have been associated with hepatotoxicity
- Additional NSAA toxicities include gynecomastia and breast pain
- Cyproterone acetate is only available in Canada and Europe

# Is combined androgen blockade better than castration alone?

- Combined androgen blockade (CAB) should be considered
- Survival is greater with the addition of a non-steroidal anti-androgen to medical or surgical castration (increased side effects may occur)
- Though survival benefits are not yet available bicalutamide CAB should be considered
  - ✓ Commonly-used
  - ✓ Once-a-day dosing
  - ✓ Lowered gastrointestinal and ophthalmologic side effects than other NSAAs
  - ✗ More expensive than other NSAAs though cheaper than newer systemic therapies
  - ✗ May not be covered by health plans

# Does early ADT improve outcomes over deferred therapy?

- For patients with metastatic or progressive PCa:
  - 17% decrease in relative risk (RR) for PCa-specific mortality
  - 15% increase in RR for non-PCa-specific mortality
  - No overall survival advantage for immediate institution of ADT versus waiting until symptom onset for patients
- For patients with recurrent disease, clinical trials should be considered (if available)
- The Panel cannot make a strong recommendation for the early use of ADT
- Patients that decide to wait until symptoms develop before beginning ADT should have regular visits for monitoring

# Is intermittent ADT better than continuous ADT?

- Data are insufficient to support the use of intermittent androgen blockade outside of clinical trials

Ongoing Clinical Trials*		
Clinical Prospective	Trial Name	Status
Timing of androgen deprivation therapy after radical radiation	Timing of Androgen Deprivation (TOAD)	Opened in 2004
	Early vs. Late Androgen Ablation Trial (ELAAT)	Opened in 2006
Intermittent versus continuous androgen therapy	Southwest Oncology Group (SWOG 9346)	Open and accruing patients
	National Cancer Institute Canada (PR7)	Reached accrual goals; first analysis in 2013

\* All studies include quality of life as an outcome measure

# Summary

Treatment Option	✓ Recommended	✗ Not Recommended
<b>Initial Treatment Options</b>	Bilateral orchiectomy or Medical castration with LHRH agonists	DES
<b>Anti-Androgens</b>	NSAA monotherapy may be discussed	Steroidal anti-androgens as monotherapy
<b>Combined Androgen Blockade</b>	CAB should be considered	
<b>Early Use of ADT</b>	Panel cannot make a strong recommendation	
<b>Intermittent Androgen Blockade</b>		Data insufficient to support its use

# Additional ASCO Resources

- The full-text guideline as well as the following tools and resources are available at:  
<http://www.asco.org/guidelines/asprostate>
  - Summary Slide Set
  - Guideline Summary
  - [ASCO Patient Guide](#)
  - [Revisions Table](#)
  - [Treatment Algorithm](#)

# ASCO Guidelines

It is important to realize that many management questions have not been comprehensively addressed in randomized trials and guidelines cannot always account for individual variation among patients. A guideline is not intended to supplant physician judgment with respect to particular patients or special clinical situations and cannot be considered inclusive of all proper methods of care or exclusive of other treatments reasonably directed at obtaining the same results. Accordingly, ASCO considers adherence to this guideline to be voluntary, with the ultimate determination regarding its application to be made by the physician in light of each patient's individual circumstances. In addition, the guideline describes administration of therapies in clinical practice; it cannot be assumed to apply to interventions performed in the context of clinical trials, given that clinical studies are designed to test innovative and novel therapies in a disease and setting for which better therapy is needed. Because guideline development involves a review and synthesis of the latest literature, a practice guideline also serves to identify important questions for further research and those settings in which investigational therapy should be considered.