



Complete Summary

GUIDELINE TITLE

Initial hormonal management of androgen-sensitive metastatic, recurrent, or progressive prostate cancer: 2006 update of an American Society of Clinical Oncology practice guideline.

BIBLIOGRAPHIC SOURCE(S)

Loblaw DA, Virgo KS, Nam R, Somerfield MR, Ben-Josef E, Mendelson DS, Middleton R, Sharp SA, Smith TJ, Talcott J, Taplin M, Vogelzang NJ, Wade JL 3rd, Bennett CL, Scher HI, American Society of Clinical Oncology. Initial hormonal management of androgen-sensitive metastatic, recurrent, or progressive prostate cancer: 2006 update of an American Society of Clinical Oncology practice guideline. *J Clin Oncol* 2007 Apr 20;25(12):1596-605. [29 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Loblaw DA, Mendelson DS, Talcott JA, Virgo KS, Somerfield MR, Ben-Josef E, Middleton R, Porterfield H, Sharp SA, Smith TJ, Taplin ME, Vogelzang NJ, Wade JL Jr, Bennett CL, Scher HI. American Society of Clinical Oncology recommendations for the initial hormonal management of androgen-sensitive metastatic, recurrent, or progressive prostate cancer. *J Clin Oncol* 2004 Jul 15;22(14):2927-41.

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SCOPE

DISEASE/CONDITION(S)

Metastatic, recurrent, or progressive androgen-sensitive prostate cancer

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Oncology
Radiation Oncology
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To update the 2004 American Society of Clinical Oncology (ASCO) guideline on initial hormonal management of androgen-sensitive, metastatic, recurrent, or progressive prostate cancer (PCa)

TARGET POPULATION

Men with metastatic, recurrent, or progressive androgen-sensitive prostate cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Standard Initial Treatment Options

1. Bilateral orchiectomy
2. Medical castration with luteinizing hormone releasing hormone (LHRH) agonists
3. Diethylstilbestrol (DES) (no longer commercially available in North America and is not recommended as a standard first-line treatment option)
4. Patient education/counseling

Castration Alternatives

1. Nonsteroidal antiandrogen monotherapy (e.g., flutamide, nilutamide, and bicalutamide)
2. Steroidal antiandrogen (not recommended as monotherapy)

Combination Therapy

Medical or surgical castration plus a nonsteroidal antiandrogen

Early Androgen Deprivation Therapy versus Deferred Therapy (early therapy not strongly recommended)

MAJOR OUTCOMES CONSIDERED

- Overall survival
- Progression-free survival
- Toxicity of treatment
- Time to treatment failure
- Disease progression
- Complications due to progression
- Cost-effectiveness
- Time off therapy
- Time to hormone resistance
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
 Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature Review and Data Collection

For the 2006 update, the MEDLINE database (January 2003 through March 2006; National Library of Medicine, Bethesda, MD) was searched to identify relevant information from the published literature. A series of searches was conducted using the medical subject headings "prostatic neoplasms" and "androgen antagonists," and the text words "intermittent," "combined androgen," and "metastatic." These terms were combined with the following study design-related subject headings or text words: "meta-analysis," "systematic," "trial," and "randomized." Search results were limited to human studies and English-language articles.

In addition, the Cochrane Database of Systematic Reviews was searched using the phrase "prostate cancer," and directed searches were made of the reference lists from primary articles. Authors were contacted for clarification where needed. The Physician Data Query clinical trials database (http://www.cancer.gov/search/clinical_trials/) was searched for ongoing clinical trials in the identified subject areas.

Inclusion and Exclusion Criteria

Table 1 in the original guideline document describes the details of the inclusion criteria and outcome variables for each question addressed in this guideline. For each guideline question, letters, editorials, and articles published in a language other than English were not considered. In addition, for questions 4 (early vs. deferred androgen deprivation therapy [ADT]) and 5 (intermittent versus continuous ADT), the following were excluded:

1. Participants previously treated with hormonal therapy
2. Randomized clinical trials targeting men undergoing radiation as primary therapy

3. Nonrandomized prospective studies
4. Retrospective studies
5. Trials or trial arms that used diethylstilbestrol

NUMBER OF SOURCE DOCUMENTS

Seven randomized controlled trials (four new), one systematic review, one meta-analysis (new), one Markov model, and one delta-method 95% confidence interval (CI) procedure for active controlled trials (new) informed the guideline update.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

An evidence-based approach incorporating consensus by experts was the model used to create the recommendations. To this end, a subset of the original writing committee met via teleconference in February and March 2006 to consider the evidence for each of the 2004 recommendations. The guideline update was circulated in draft form to the full Expert Panel for review and approval. Suggestions from the Expert Panel were incorporated into the document, yielding a final set of recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

One article was reviewed that showed early therapy is associated with higher costs and greater frequency of treatment-related adverse effects.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The draft guideline was submitted to the American Society of Clinical Oncology (ASCO) Health Services Committee (HSC) for review and was endorsed in July 2006. The ASCO Board reviewed and approved the document in November 2006. Final text editing was performed by two of the guideline authors.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

1. What are the standard initial treatment options?

2006 Recommendation: Bilateral orchiectomy or medical castration with luteinizing hormone-releasing hormone (LHRH) agonists are the recommended initial treatments for metastatic prostate cancer. A full discussion between practitioner and patient should occur to determine which is best for the patient. Diethylstilbestrol (DES) should not be considered as a standard first-line treatment option and is no longer commercially available in North America.

2. Are antiandrogens as effective as other castration therapies?

2006 Recommendation: Nonsteroidal antiandrogen (NSAA) monotherapy may be discussed as an alternative, but steroidal antiandrogen (AA) monotherapy should not be offered.

3. Is combined androgen blockade better than castration alone?

2006 Recommendation: Combined androgen blockade (CAB) should be considered.

4. Does early androgen-deprivation treatment (ADT) improve outcomes over deferred therapy?

2006 Recommendation: For patients with metastatic or progressive prostate cancer, there is a moderate decrease (17%) in relative risk (RR) for prostate cancer-specific mortality, a moderate increase (15%) in RR for non-prostate cancer-specific mortality, and no overall survival advantage for immediate institution of androgen-deprivation treatment (ADT) versus waiting until symptom onset for patients. Therefore, the Panel cannot make a strong recommendation for the early use of ADT. Prostate-specific antigen (PSA) kinetics and other metrics allow the identification of populations at high risk

for prostate cancer-specific and overall mortality. Further studies must be completed to assess whether patients with adverse prognostic factors gain a survival advantage from immediate ADT. If a patient decides to wait until symptoms for ADT, he should have regular visits for monitoring. For patients with recurrent disease, clinical trials should be considered if available.

5. **What is the role of intermittent androgen blockade?**

2006 Recommendation: Currently, data are insufficient to support the use of intermittent androgen blockade outside of clinical trials.

CLINICAL ALGORITHM(S)

A clinical algorithm is provided for the initial hormonal management of androgen-sensitive advanced cancer (see "Availability of Companion Documents" field in this summary).

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by randomized controlled trials, a systematic review, a meta-analysis, one Markov model, and one delta-method 95% confidence interval (CI) procedure for active controlled trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of androgen-sensitive, metastatic, recurrent, or progressive prostate cancer

POTENTIAL HARMS

- Table 3 in the original guideline document provides a full list of adverse drug reactions seen in a randomized controlled trial of patients receiving an LHRH agonist and then either bicalutamide or placebo.
- Early therapy is associated with higher costs and greater frequency of treatment-related adverse effects. Deferred treatment risks the development of hormone independence in the tumor as well as serious complications such as spinal cord complications. The effects of these complications occurring during the treatment deferral period might not be completely reversible.

QUALIFYING STATEMENTS

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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, the American Society of Clinical Oncology (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.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Patient Resources
Personal Digital Assistant (PDA) Downloads
Slide Presentation

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Jun 7 (revised 2007 Apr)

GUIDELINE DEVELOPER(S)

American Society of Clinical Oncology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Society of Clinical Oncology (ASCO)

GUIDELINE COMMITTEE

American Society of Clinical Oncology (ASCO) Metastatic Prostate Cancer Expert Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Although all authors completed the disclosure declaration, the following authors or their immediate family members indicated a financial interest.

No conflict exists for drugs or devices used in a study if they are not being evaluated as part of the investigation. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

Employment: N/A **Leadership:** N/A **Consultant:** D. Andrew Loblaw, Astra Zeneca; Nicholas J. Vogelzang, Sanofi Aventis; Charles L. Bennett, Sanofi, Millenium **Stock:** N/A **Honoraria:** D. Andrew Loblaw, Astra Zeneca; James Talcott, Dendreon; Maryellen Taplin, Astra Zeneca; Nicholas J. Vogelzang, Astra Zeneca **Research Funds:** D. Andrew Loblaw, Astra Zeneca; Nicholas J. Vogelzang, Astra Zeneca; Charles L. Bennett, Amgen, Sanofi **Testimony:** N/A **Other:** D. Andrew Loblaw, Astra Zeneca, Sanofi-Aventis

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [American Society of Clinical Oncology \(ASCO\) Web site](#).

Print copies: Available from American Society of Clinical Oncology, Cancer Policy and Clinical Affairs, 1900 Duke Street, Suite 200, Alexandria, VA 22314; E-mail: guidelines@asco.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- American Society of Clinical Oncology (ASCO) treatment algorithm for the initial hormonal management of androgen-sensitive advanced cancer: 2007 update. Available from the [ASCO Web site](#). See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#).
- Initial hormonal management of androgen-sensitive metastatic, recurrent, or progressive prostate cancer: 2007 update. Slide set. Available from the [ASCO Web site](#). See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#).
- ASCO 2007 guideline update: recommendations for the initial hormonal management of androgen-sensitive metastatic, recurrent, or progressive

prostate cancer. Revisions Table. Available from the [ASCO Web site](#). See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#).

Guidelines are available for Personal Digital Assistant (PDA) download from the [ASCO Web site](#).

PATIENT RESOURCES

The following is available:

- American Society of Clinical Oncology (ASCO) patient guide: hormone therapy for advanced prostate cancer. Available from the [Cancer.Net Web site](#). See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

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