

Prostate cancer: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

A. Horwich¹, C. Parker² & V. Kataja³

On behalf of the ESMO Guidelines Working Group*

^{1,2}Department of Clinical Oncology, Royal Marsden Hospital, Sutton, UK; ³Department of Oncology, Kuopio University Hospital, Kuopio, Finland

incidence and mortality

- The crude incidence of prostate cancer in the European Union is 78.9/100 000 men/year. It is the most common cancer in men.
- The mortality in the EU is 30.6/100 000 men/year.
- Subclinical prostate cancer is present in the majority of men.
- Screening of healthy men using prostate-specific antigen (PSA) testing increases the incidence (overdiagnosis). The effect of screening and early intervention on mortality is not known.

diagnosis

- Serum PSA should be measured and digital rectal examination (DRE) carried out in patients presenting with urinary symptoms.
- Prostate biopsy should be offered to men suspected to have a clinically significant prostate cancer, such as those with an abnormal DRE and elevated serum PSA.
- Prostate biopsy should be performed under transrectal ultrasound (TRUS) guidance, and a minimum of eight cores obtained.
- The extent of involvement of each core, and the Gleason score should be reported.

staging and risk assessment

- General health and co-morbidities should be assessed.
- Clinical T stage should be evaluated by DRE.
- Pelvic imaging using MRI or CT should be performed before radical treatment when Partin tables indicate >15% risk of nodal involvement.

- Bone scintigraphy should be performed if bone metastases are suspected clinically, if the Gleason score is >4 + 3 or serum PSA is >15 mg/l [III, B].

treatment

localized disease (T1–2 N0/X M0/X)

- There is no general consensus as to what constitutes best treatment.

Patients should be informed of the potential benefits and harms of the various options.

- In the only randomized trial reported to date, radical prostatectomy improved overall survival at 10 years by 5% in comparison with watchful waiting (73% versus 68%, $P = 0.04$), but these results may not be generalizable to screen-detected cancers.
- In the only randomized trial to date, radical prostatectomy increased the rate of erectile dysfunction by 35% (80% versus 45%), and urinary leakage by 28% (49% versus 21%), in surgical centers.
- For low-risk disease (T1–2a, Gleason <6, PSA <10 mg/l), active surveillance with selected delayed intervention has given 99% disease-specific survival at 8 years.
- External beam radiotherapy should be delivered using conformal techniques, to a minimum target dose of 70 Gy given in 2.0 Gy fractions or the equivalent [II, B]. In non-randomized prospective series brachytherapy with permanent implants results in similar long-term survival to radical prostatectomy with less chronic urinary symptoms and erectile dysfunction.
- Following radical prostatectomy patients should be monitored with a sensitive PSA assay, with salvage radiotherapy to the prostate bed given in the event of PSA failure.

locally advanced disease (T3–4 N0/X M0/X)

- Long-term hormone therapy (androgen suppression or bicalutamide monotherapy) is a standard treatment.

*Correspondence to: ESMO Guidelines Working Group, ESMO Head Office, Via L. Taddei 4, CH-6962 Viganello-Lugano, Switzerland

Approved by the ESMO Guidelines Working Group: February 2002, last update October 2007. This publication supercedes the previously published version—Ann Oncol 2007; 18 (Suppl 2): ii36–ii37.

Conflict of interest: Prof. Horwich has reported no conflicts of interest; Dr Parker has not reported any conflicts of interest.

- Patients receiving external beam radiotherapy should receive androgen suppression before, during and after radiotherapy [II, A], for a minimum of 6 months duration.
- Patients receiving long-term bicalutamide monotherapy should be given breast bud irradiation (8–10 Gy in one fraction) to prevent painful gynaecomastia [I, A].

metastatic disease

- Androgen suppression using bilateral orchidectomy or an luteinizing hormone-releasing hormone (LHRH) agonist should be first-line treatment.
 - Short-course antiandrogen should be used to prevent disease flare on starting an LHRH agonist.
 - Patients with castration-refractory disease should have continued androgen suppression
 - Docetaxel using a 3-weekly schedule should be considered for symptomatic, castration-refractory disease [II, A].
 - External beam radiotherapy should be offered for patients with painful bone metastases from castration-refractory disease. Fractioning 1×8 Gy or 10×3 Gy may be used with equal pain-reducing efficacy [II, A].
 - Radioisotope therapy (e.g. strontium-89 or samarium-153-EDTMP) should be considered for patients with painful bone metastases from castration-refractory disease [II, A].
 - Patients with castration-refractory disease should receive second-line hormonal therapy (e.g. antiandrogen, corticosteroid) and be considered for third-line (e.g. oestrogen).
 - Intravenous bisphosphonates (e.g. pamidronate) should be considered for patients with bone pain resistant to palliative radiotherapy and conventional analgesics [II, A].
 - Patients with castration-refractory disease should be managed in collaboration with dedicated palliative care services.
3. Gleave ME, Coupland D, Drachenberg D et al. Ability of serum prostate-specific antigen levels to predict normal bone scans in patients with newly diagnosed prostate cancer. *Urology* 1996; 47: 708–712.
 4. Partin AW, Mangold LA, Lamm DM et al. Contemporary update of prostate cancer staging nomograms (Partin Tables) for the new millennium. *Urology* 2001; 58: 843–848.
 5. Lu Yao GL, Yao S-L. Population based study of long-term survival in patients with clinically localised prostate cancer. *Lancet* 1997; 349: 906–910.
 6. Bill-Axelsson, Holmberg L, Ruutu M et al. Radical prostatectomy versus watchful waiting in early prostate cancer. *N Engl J Med* 2005; 352: 1977–1984.
 7. Klotz L. Active surveillance with selective delayed intervention: using natural history to guide treatment in good risk prostate cancer. *J Urol* 2004; 172: S48–S51.
 8. Dearnaley DP, Khoo VS, Norman AR et al. Comparison of radiation side-effects of conformal and conventional radiotherapy in prostate cancer: a randomised trial. *Lancet* 1999; 353: 267–272.
 9. Bolla M, van Poppel H, Collette L et al. Postoperative radiotherapy after radical prostatectomy: a randomised controlled trial (EORTC trial 22911). *Lancet* 2005; 366: 572–578.
 10. Lawton CA, Winter K, Murray K et al. Updated results of the phase III Radiation Therapy Oncology Group (RTOG) trial 85-31 evaluating the potential benefit of androgen suppression following standard radiation therapy for unfavourable prognosis carcinoma of the prostate. *Int J Radiat Oncol Biol Phys* 2001; 49: 937–946.
 11. Pilepich MV, Winter K, John MJ et al. Phase III radiation Therapy Oncology Group (RTOG) trial 86-10 of androgen deprivation adjunct to definitive radiotherapy in locally advanced carcinoma of the prostate. *Int J Radiat Oncol Biol Phys* 2001; 50: 1243–1252.
 12. D'Amico AV, Manda J, Loffredo M et al. 6-month androgen suppression plus radiation therapy versus radiation therapy alone for patients with clinically localized prostate cancer: a randomized controlled trial. *JAMA* 2004; 292: 821–827.
 13. Denham JW, Steigler A, Lamb DS et al. Short-term androgen deprivation and radiotherapy for locally advanced prostate cancer: results from the Trans-Tasman Radiation Oncology Group 96.01 randomised controlled trial. *Lancet Oncol* 2005; 6: 841–850.
 14. Widmark A, Fosså SD, Lund MP et al. Does prophylactic breast irradiation prevent antiandrogen-induced gynaecomastia? Evaluation of 253 patients in the randomized Scandinavian trial SPCG-7/SFUO-3. *Urology* 2003; 61: 145–151.
 15. Tannock IF, de Witt R, Berry WR et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med* 2004; 351: 1502–1512.
 16. Petrylak DP, Tangen C, Hussain M et al. Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer. *N Engl J Med* 2004; 351: 1513–1520.
 17. Porter AT, McEwan AJ, Powe JE et al. Results of a randomized phase-III trial to evaluate the efficacy of strontium-89 adjuvant to local field external beam irradiation in the management of endocrine resistant metastatic prostate cancer. *Int J Radiat Oncol Biol Phys* 1993; 25: 805–813.
 18. Quilty P, Kirk D, Bolger JJ et al. A comparison of the palliative effects of strontium-89 and external beam radiotherapy in metastatic prostate cancer. *Radiother Oncol* 1994; 31: 33–40.
 19. Saad F, Gleason DM, Murray R et al. Long-term efficacy of zoledronic acid for the prevention of skeletal complications in patients with metastatic hormone-refractory prostate cancer. *J Natl Cancer Inst* 2004; 96: 879–882.

note

Levels of evidence [I–V] and grades of recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts and the ESMO faculty.

literature

1. Draisma G, Boer R, Otto SJ et al. Lead times and overdetection due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer. *J Natl Cancer Inst* 2003; 95: 868–878.
2. Thompson IM, Ankerst DP, Chi C et al. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. *J Natl Cancer Inst* 2006; 98: 529–534.