NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA101; Docetaxel for the treatment of hormone refractory prostate cancer

This guidance was issued in June 2006.

The review date for this guidance is April 2013 (following a previous review decision in August 2009). The review proposal has been brought forward as a precursor to a review proposal on clinical guideline CG58: prostate cancer.

1. Recommendation

The guidance should be transferred to the 'static guidance list' and incorporated into the on-going update of clinical guideline CG58 'Prostate cancer: diagnosis and management'. That we consult on this proposal.

2. Original remit

"To appraise the clinical and cost effectiveness of docetaxel for hormone-refractory prostate cancer".

3. Current guidance

1.1. Docetaxel is recommended, within its licensed indications, as a treatment option for men with hormone-refractory metastatic prostate cancer only if their Karnofsky performance-status score is 60% or more.

1.2. It is recommended that treatment with docetaxel should be stopped:

- at the completion of planned treatment of up to 10 cycles, or
- if severe adverse events occur, or
- in the presence of progression of disease as evidenced by clinical or laboratory criteria, or by imaging studies.

1.3. Repeat cycles of treatment with docetaxel are not recommended if the disease recurs after completion of the planned course of chemotherapy.

4. Rationale[1]

There is no new evidence that would be likely to affect the recommendations in TA101. Docetaxel is the standard of care for the treatment of metastatic hormone-refractory prostate cancer. Limited evidence from retrospective or observational studies suggests that docetaxel retreatment may be effective in a small number of highly selected patients and docetaxel is now available as a generic drug. This suggests that it may be beneficial to update recommendation 1.3 as part of the update of clinical guideline CG58 'Prostate cancer: diagnosis and management'. However, during the consultation on the scope the guideline update this was not identified as a priority.

5. Implications for other guidance producing programmes

Following discussion at the clinical guideline scoping stakeholder workshop and consultation with stakeholders for the update of NICE clinical guideline CG58 'Prostate cancer: diagnosis and management', updating TA 101 was not considered to be a high priority for the clinical guideline update. CCP and the GDG would therefore like to recommend that TA101 is incorporated into the clinical guideline.

6. New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from March 2005 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

Docetaxel's UK marketing authorisation for the treatment of prostate cancer has not changed since TA101 was published ("Docetaxel in combination with prednisone or prednisolone is indicated for the treatment of patients with hormone refractory metastatic prostate cancer").

However, the patent protection for Taxotere has expired and docetaxel is consequently available in cheaper generic forms (£153.47 for a 1-ml vial of 20 mg/ml Taxotere compared with £54.61 for the same non-proprietary formulation), thereby strengthening the positive recommendation made in TA101 (recommendation 1.1).

Hospital Pharmacy Audit Index cost and volume data for docetaxel show that uptake of docetaxel has notably increased since TA101 was published in 2006; however, it is not possible to draw any firm conclusions about the use in prostate cancer from these data because the audit encompasses docetaxel's multiple indications.

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

New data for docetaxel as a first-line treatment for metastatic hormone-refractory prostate cancer have primarily been retrospective analyses of the pivotal TAX327 study or investigated the effects of different regimens (continuous versus intermittent), and these new data do not impact on the recommendations made in TA101.

Recommendation 1.3 of TA101 states that "repeat cycles of treatment with docetaxel are not recommended if the disease recurs after completion of the planned course of chemotherapy". In 2006, the Committee considered that there was no evidence to support a recommendation for further cycles of docetaxel following disease progression (section 4.3.10 of TA101). Since then, a small number of studies have investigated retreatment with docetaxel in patients who initially responded to the drug and have demonstrated that this can produce sustained responses in some highly selected patients (Ansari et al, 2008; Eymard et al, 2010; Loriot et al 2010). It is recognised that there are significant limitations to the available data because most docetaxel re-treatment studies have been either retrospective or early phase non-randomised studies which have not formally assessed quality of life or survival gain with re-treatment (Ansari et al, 2011).

8. Implementation

No submission was received from Implementation.

9. Equality issues

The Committee noted that the patient's performance status predicts the likelihood of patient benefit, irrespective of age, and recommended that treatment should be limited to patients with a Karnofsky score of 60% or higher. This Karnofsky performance-status score requires that a person is able to carry out self-care. This criterion would therefore discriminate against people with certain disabilities, such as paralysis. The Committee concluded that the minimum Karnofsky score should be interpreted by the clinician on an individual basis when considering treatment for disabled men.

GE paper sign off: Elisabeth George, 15 Feb 2012

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Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A review of the guidance should be planned into the appraisal work programme.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred.	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	Yes. Guidelines prefer this to the option below as we believe that the guidance does not require updating at this time. Incorporation will also maintain the funding direction associated with docetaxel in this indication.

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No.
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes.

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment
- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed

- The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

Prostate cancer diagnosis and treatment. Clinical Guideline CG58. Issued February 2008. An update of this guideline is currently being scheduled into the NICE work programme.

In progress

Cabazitaxel for the second line treatment of hormone refractory, metastatic prostate cancer. Technology Appraisal. Expected issue date: February 2012

Abiraterone for the treatment of metastatic castration resistant prostate cancer following previous cytotoxic therapy. Technology Appraisal. Expected issue date: May 2012.

Abiraterone acetate in combination with prednisolone for the treatment of metastatic, castrate-resistant prostate cancer in people who have not been previously treated with chemotherapy. Technology Appraisal. Expected issue date: July 2013.

Suspended/terminated

Atrasentan for hormone refractory prostate cancer. Technology Appraisal. Suspended in January 2007. The manufacturer did not seek regulatory approval for this indication.

In topic selection[2]

Chemotherapy-naïve advanced metastatic castration refractory prostate cancer - Abiraterone in combination with corticosteroid. Proposed Technology Appraisal - currently at the scoping stage.

[redacted]

[2] Information held by the NICE Topic Selection Team is treated as being potentially commercially sensitive by default. Details of the topics considered by NICE's Consideration Panels may be available on the NICE website, providing the manufacturers of the technologies under discussion have consented to the release of this information.

Details of changes to the indications of the technology

Indication considered in original appraisal	Proposed indication (for this appraisal)
In combination with prednisone or prednisolone for the treatment of patients with hormone-refractory metastatic prostate cancer.	As before.

Details of new products

Drug (manufacturer)	Details (phase of development, expected launch date,)
Prostate cancer vaccine (Bavarian Nordic)	Phase III for asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer. Estimated trial completion date: 2015.
Sipuleucel-t (Dendreon)	Phase III trial in metastatic, castration-resistant prostate cancer completed. UK launch anticipated Q1 2013.
Abiraterone acetate (Janssen Cilag)	Launched in the UK for the second-line treatment of castration-resistant/hormone-refractory in September 2011. Phase II in chemotherapy-naïve patients with castration-resistant prostate cancer.
Aflibercept (Sanofi)	Phase III as add-on to docetaxel/prednisone in first-line treatment of metastatic, androgen-independent prostate cancer. UK launch anticipated Q4 2012.
Bafetinib (CytRx)	Phase II as second-line treatment for metastatic, hormone refractory prostate cancer.
Bevacizumab (Roche)	Did not achieve its primary outcome outcome (improvement in overall survival) in phase III trial as add-on docetaxel/prednisone in hormone-refractory, metastatic prostate cancer (trial CALGB 90401) – March 2010.
Custirsen (OncoGenex)	Phase III in people with metastatic, castration-resistant prostate cancer

Drug (manufacturer)	Details (phase of development, expected launch date,)
	whose disease has progressed after receiving docetaxel/prednisone therapy. UK launch anticipated ~2014.
Dasatinib (Bristol-Myers Squibb)	Phase III as add-on to docetaxel/prednisone in people with hormone-refractory, metastatic prostate cancer. UK launch anticipated Q2, 2013.
Ipilimumab (Bristol-Myers Squibb)	Phase III add-on to radiotherapy in second-line treatment of metastatic, hormone refractory prostate cancer following previous docetaxel therapy.
MDV3100 (Astellas)	Phase III in progressive, castration-resistant prostate cancer previously treated with docetaxel.
Orteronel (Millennium Pharmaceuticals)	Phase III add-on to prednisone in people with hormone refractory, metastatic prostate cancer which has progressed following previous docetaxel therapy. UK launch anticipated ~2014.
Radium 223 (Bayer)	Phase III for the treatment of hormone refractory prostate cancer with bone metastases. UK launch anticipated ~2013.

Registered and unpublished trials

Trial name and registration number	Details
Docetaxel and Prednisone in Treating Patients With Hormone-Refractory Metastatic Prostate Cancer NCT00255606, CDR0000442891, AVENTIS-FIN-1-2003, FINNISH-URO-OGS-1-2003, PROSTY-FIN-1-2003, ICORG-06-14-Prosty, EU-20891.	RCT comparing two different docetaxel + prednisone dosing regimes n = 360 Completed ~2009

Trial name and registration number	Details
Cabazitaxel Versus Docetaxel Both With Prednisone in Patients With Metastatic Castration Resistant Prostate Cancer NCT01308567, EFC11784, 2010-022064-12, U1111-1117-8356	n = 1170 Currently recruiting Estimated completion date: January 2016
Prostate Cancer, Androgen Deprivation Withdrawal and Intermittent Chemotherapy NCT01224405, EudraCT 2010-019004-24, PON-PC-02.	Participants randomised to receive docetaxel + prednisolone ± maintenance of androgen deprivation therapy. Participants in each arm are further randomised into either continuous (10 cycle) docetaxel regimen, or an intermittent docetaxel regimen n = 600 Ongoing Estimated primary completion date: August 2010 Estimated study completion date: April 2016
Taxotere Prostate Cancer New Indication Registration Trial in China NCT00436839; DOCET_L_01833.	Docetaxel + prednisone vs. mitoxantrone + prednisone. Stated as “ongoing”. n = 240 Estimated completion date: December 2011
Phase III clinical trial comparing treatments of hormone-refractory prostate cancer (HRPC) with docetaxel: continuous treatment vs. intermittent repetition of treatment after progression EudraCT 2005-001602-76, AP 40/04, PRINCE	Completed ~2010 n = 424

Trial name and registration number	Details
A Phase III Randomized, Open-Label Study of CG1940 and CG8711 Versus Docetaxel and Prednisone in Patients with Metastatic Hormone-Refractory Prostate Cancer who are Chemotherapy-Naïve EudraCT 2005-002738-36, G-0029.	Prematurely ended in 2008 – reason not stated. n = 600
Androgen Suppression Alone or Combined With Zoledronate, Docetaxel, Prednisolone, and/or Celecoxib in Treating Patients With Locally Advanced or Metastatic Prostate Cancer (STAMPEDE trial) NCT00268476, CDR0000455008, EU-205102, MRC-PR08, ISRCTN78818544, EUDRACT-2004-000193-31.	STAMPEDE is a multi-centre randomised controlled trial for patients with locally advanced or metastatic prostate cancer who are about to commence hormone therapy (i.e. not hormone-refractory disease). The trial will assess the effects of adding different agents, both as single agents and in combinations, to hormone therapy. The investigational agents are (i) zoledronic acid, (ii) docetaxel, (iii) celecoxib. (iv) abiraterone. Recruitment to the celecoxib arms is now closed. Currently recruiting n = 2800 - 3600 Estimation completion date: October 2013

References

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