AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Docetaxel in combination with androgen deprivation therapy for the treatment of hormone-naive metastatic prostate cancer

ONE WALES INTERIM COMMISSIONING DECISION RETIRED NOVEMBER 2019 DOCETAXEL FOR THIS INDICATION IS RECOMMENDED IN NICE CLINICAL GUIDELINE (NG131) PUBLISHED MAY 2019

ONE WALES INTERIM COMMISSIONING DECISION

Docetaxel in combination with androgen deprivation therapy for the treatment of hormone-naive metastatic prostate cancer

Date of original advice: August 2016
Date of review: November 2018

The following Interim Pathways Commissioning Group (IPCG) recommendation has been endorsed by health board Chief Executives.

Using the agreed starting and stopping criteria, docetaxel, in combination with androgen deprivation therapy, can continue to be made available within NHS Wales for the treatment of men with hormone-naive metastatic prostate cancer.

Docetaxel is not licensed to treat this indication and is therefore 'off-label'. Each provider organisation must ensure all internal governance arrangements are completed before this medicine is prescribed.

The risks and benefits of the off-label use of docetaxel for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the General Medical Council Guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

One Wales advice assists consistency of access across NHS Wales and will be disseminated to the service following agreement of Health Board Chief Executives

Starting and stopping criteria for docetaxel in combination with androgen deprivation therapy for the treatment of hormone-naive metastatic prostate cancer.

These criteria are taken from the NHS England Clinical Commissioning policy document[1].

Starting and stopping criteria

Starting criteria:

Patients will be eligible for treatment under this policy who:

- have newly diagnosed metastatic, prostate cancer;
- are either commencing, or who have commenced within 12 weeks, long-term hormone therapy (Androgen Deprivation Therapy [ADT]) for metastatic disease for the first time; and
- have sufficient performance status to be treated with 6 cycles of docetaxel chemotherapy.

Stopping criteria:

Unlike most cancer chemotherapies, docetaxel in the hormone naive context is given while men are responding to their ADT. Most patients will thus stop docetaxel for reasons either for toxicity or from patient preference. Formal stopping rules are as follows:

- disease progression on treatment (this is likely to be rare);
- toxicity precluding safe administration of further therapy (e.g. severe sepsis, grade 3 neuropathy);
- patient request; and
- at the end of 6 cycles of treatment.

Docetaxel is a widely used drug in this patient population, hence clinicians are familiar with the safe use and stopping rules for the agent.

Following treatment with docetaxel, men will continue with ADT until the disease becomes resistant to this treatment. This policy statement does not impact on the current standard of care where prostate cancer has become resistant to ADT. The current standard of care includes abiraterone, enzalutamide and docetaxel (in accordance with NICE TA101).

1. NHS England. Clinical commissioning policy statement: Docetaxel in combination with androgen deprivation therapy for the treatment of hormone naive metastatic prostate cancer. 2016. Available at: https://www.england.nhs.uk/wp-content/uploads/2016/01/b15psa-docetaxel-policy-statement.pdf. Accessed March 2016.

This is a summary of new evidence available to inform the review.

Background
Clinicians in Wales consider there is a cohort of patients who could benefit from docetaxel in combination with androgen deprivation therapy (ADT) for the treatment of hormone-naïve metastatic prostate cancer. Docetaxel is available for this off-label indication from NHS England through clinical commissioning. Based on unmet need to treat a serious condition in a cohort of patients, this medicine was considered suitable for assessment via the One Wales process. Following 12 month review in August 2017 the One Wales decision was endorsed for a further year.

Current One Wales Interim Commissioning Decision
Using the agreed starting and stopping criteria, docetaxel, in combination with ADT can continue to be made available for the treatment of men with hormone-naïve metastatic prostate cancer. September 2017.

Licence status
Docetaxel in combination with ADT for the treatment of men with hormone-naïve metastatic prostate cancer is off-label.

Guidelines
There are no changes to current guidelines.

Licensed alternative medicines/Health Technology Appraisal advice for alternative medicines
NICE ID945: Abiraterone for treating newly diagnosed high risk metastatic hormone-naïve prostate cancer. Expected publication date: 03 October 2018[1].

Efficacy/Effectiveness
Further sub-group analysis of overall survival of patients with high-volume disease versus low-volume disease has been published for the CHAARTED and GETUG-AFU15 studies[2,3]. Quality of life data have also been published for the CHAARTED study[4].

Median follow up in the GETUG-AFU15 (n = 385) and CHAARTED (n = 790) studies was 83.2 and 48.2 months respectively in patients who survived[2]. High-volume disease was defined in the CHAARTED study as the presence of visceral metastases and/or at least four bone metastases with at least one outside the vertebral bodies and pelvis, low-volume disease was for other patients. For the GETUG-AFU15 study, post hoc analysis distinguished patients with high- and low-volume disease using the same criteria. For patients with high-volume disease the median overall survival in the ADT group were 34.4 and 35.1 months in CHAARTED and GETUG-AFU15 respectively and 51.2 and 39.8 months for the ADT plus docetaxel groups. Results of the two studies were pooled to compare ADT versus ADT plus docetaxel. In patients with high-volume disease median overall survival was improved with the addition of docetaxel (average hazard ratio [HR] 0.68; 95% confidence interval [CI] 0.56 to 0.82; $p < 0.001$). Pooled results showed no evidence of improved survival between treatment groups for patients with low-volume disease (HR 1.03; 95% CI 0.77 to 1.38; $p = 0.8$)[2].

Quality of life was compared for patients in the ADT plus docetaxel versus the ADT arms of the CHAARTED study[4]. Quality of life was assessed by Functional Assessment of Cancer Therapy-Prostate (FACT-P) at baseline, 3, 6, 9 and 12 months. Results in the ADT plus docetaxel group showed a significant decline in FACT-P score between baseline and 3 months (-2.7 points; $p < 0.001$) but no significant difference between baseline and 12 months ($p = 0.38$). For the ADT alone group there was no significant difference in FACT-P score between baseline and 3 months (-1.1 points; $p = 0.4$). When compared with the ADT group, FACT-P scores were significantly lower at 3 months for the ADT plus docetaxel group ($p = 0.02$) and significantly higher at 12 months ($p = 0.04$). Overall, treatment with ADT plus docetaxel was associated with a statistically worse quality of life at 3 months and better quality of life at 12 months compared to treatment with ADT alone. Although statistically significant, the differences between treatment arms did not meet the criteria for a clinically meaningful difference at any time point[4].

Safety
There are no new significant safety issues.

Cost effectiveness
Two cost-effectiveness studies from China and one from Brazil have been published[5-7]. The study conducted in Brazil explored the cost-effectiveness of ADT plus docetaxel versus ADT alone for patients with hormone-naïve high-risk non-metastatic prostate cancer, metastatic disease and high-volume metastatic disease[6]. Data from the GETUG-AFU12 and CHAARTED studies were used. For patients with metastatic disease, the addition of docetaxel to ADT gave an increase of 0.53 quality-adjusted life-years (QALY). For patients with high-volume metastatic disease, there was an increase of 0.70 QALY with the addition of docetaxel to ADT[6]. Using data from the CHAARTED study alone resulted in similar QALY gains in one Chinese study (0.69 for high-volume metastatic disease and 0.48 for all metastatic patients) when combining docetaxel with ADT versus ADT alone[5]. The second Chinese cost-effectiveness study using data from the STAMPEDE study estimated QALY gains of 0.2 for patients with advanced hormone-naïve cancer when comparing docetaxel plus standard of care to standard of care alone[7].

An abstract was presented at the 2018 American Society of Clinical Oncology Genitourinary Cancers Symposium exploring the cost effectiveness of ADT plus docetaxel for patients with metastatic prostate cancer and patients with non-metastatic prostate cancer (high-risk locally advanced disease or node positive disease)[8]. Outcome data, costs in the UK NHS and quality of life data were derived from the STAMPEDE clinical trial[9]. The addition of docetaxel to ADT was estimated to extend predicted survival by an average of 0.89 years for patients with metastatic disease and 0.78 years for patients with non-metastatic disease[8]. The addition of docetaxel was deemed cost-effective in metastatic (incremental cost-effectiveness ratio = £5,514 per QALY versus standard of care) and non-metastatic patients (higher QALYs, lower costs versus standard of care). Probabilistic sensitivity analysis indicated a high probability (> 99%) that docetaxel is cost-effective in both patient groups. Docetaxel remained cost-effective for non-metastatic patients when no survival advantage was assumed due to reductions and delays in relapse[8]. *Academic in confidence removed*[10].

Budget impact
No information on patient numbers has been received.

Welsh commercial access agreement
This medicine is currently not licensed for the indication under consideration (i.e. off-label) and therefore as the Pharmaceutical Industry's code of practice prevents a company from promoting an off-label use of a medicine, a commercial agreement cannot be offered by the company.

Impact on health and social care services
No new information has been provided.

Patient outcome data
No patient outcome data have been received.

Next review date: September 2019

References

1. National Institute for Health and Care Excellence. ID945 Abiraterone for treating newly diagnosed high risk metastatic hormone-naive prostate cancer. Expected publication date: 03 October 2018. Available at: https://www.nice.org.uk/Search?q=ID945. Accessed July 2017.
2. Gravis G, Boher J-M, Chen Y-H et al. Burden of Metastatic Castrate Naive Prostate Cancer Patients, to Identify Men More Likely to Benefit from Early Docetaxel: Further Analyses of CHAARTED and GETUG-AFU15 Studies. *Eur Urol.* 2018;73(6):847-855.
3. Kyriakopoulos CE, Chen Y-H, Carducci MA et al. Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer: Long-Term Survival Analysis of the Randomized Phase III E3805 CHAARTED Trial. *J Clin Oncol.* 2018;36(11):1080-1087.
4. Morgans AK, Chen Y-H, Sweeney CJ et al. Quality of Life During Treatment With Chemohormonal Therapy: Analysis of E3805 Chemohormonal Androgen Ablation Randomized Trial in Prostate Cancer. *J Clin Oncol.* 2018;36(11):1088-1095.
5. Zheng HR, Wen F, Wu YF et al. Cost-effectiveness analysis of additional docetaxel for metastatic hormone-sensitive prostate cancer treated with androgen-deprivation therapy from a Chinese perspective. *Eur J Cancer Care (Engl).* 2017;26(6).
6. Aguiar PN, Jr., Barreto CMN, Gutierres BdS et al. Cost effectiveness of chemohormonal therapy in patients with metastatic hormone-sensitive and non-metastatic high-risk prostate cancer. *Einstein.* 2017;15(3):349-354.

7. Zhang P, Wen F, Fu P et al. Addition of docetaxel and/or zoledronic acid to standard of care for hormone-naive prostate cancer: A cost-effectiveness analysis. *Tumori.* 2017;103(4):380-386.
8. James N, Woods B, Sideris E et al. Addition of docetaxel to first-line long-term hormone therapy in prostate cancer (STAMPEDE): Long-term survival, quality-adjusted survival, and cost-effectiveness analysis. Presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium 8-10 February 2018. *J Clin Oncol.* 36(Suppl 6) http://ascopubs.org/doi/abs/10.1200/JCO.2018.36.6_suppl.162. Accessed August 2018.
9. James N, Sydes M, Clarke N et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results for from an adaptive, multiarm, multistage, platform randomised controlled trial. *Lancet.* 2016;387:14.
10. Academic in confidence.