**Management of Newly-diagnosed Metastatic Hormone-sensitive Prostate Cancer: a Survey of UK Uro-oncologists**

**Running title:** management ofmetastatic hormone-sensitive prostate cancer

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**Authorship**

The authors led the design of the questionnaire, which was approved by the BUG Executive Committee; Right Angle (BUG Secretariat) collated the data for analysis by the Authors. All authors reviewed and commented on the manuscript.

**Acknowledgements**

The authors would like to thank Right Angle (BUG Secretariat) for their editorial assistance in the preparation of this manuscript. Heather Payne’s work was supported by the UCLH/UCL Comprehensive Biomedical Research Centre.

**Conflict of interests**

None of the authors have received any financial compensation for writing this publication.

**Funding**

This is a BUG initiative, supported by an educational grant from Sanofi. The educational grant financed the implementation of the survey and editorial assistance. Sanofi had no influence over the design of the survey, analysis of the data or resulting publication.

**ABSTRACT**

**Aim:** To explore the practice and views of uro-oncologists in the UK regarding their use of chemotherapy and androgen receptor-targeted agents (ARTAs) in patients with newly-diagnosed metastatic hormone-sensitive prostate cancer (mHSPC).

**Methods:** An expert-devised paper or online questionnaire was completed by members of the British Uro-oncology Group.

**Results:** All respondents stated that they would offer patients with newly-diagnosed mHSPC docetaxel and androgen deprivation therapy (ADT) if they were sufficiently fit to receive chemotherapy (this was the only option available at the time of the survey); 64% would strongly recommend docetaxel for those with high-volume metastatic disease and 31% for those with low-volume disease. Hypothetically, if both docetaxel and ARTAs were available in the UK for mHSPC, almost 65% of respondents would recommend an ARTA with ADT to these patients in at least one-half of all cases, with the strongest recommendations to patients with high-risk disease. Imaging for response was conducted according to suspicion of disease progression, regardless of treatment, with the minority of clinicians recommending routine imaging. If a choice of therapy was available, docetaxel would be more likely to be offered to patients with liver or lung metastases, and ARTAs to patients with bone or lymph node only metastases. Almost all respondents would offer local radiotherapy to the primary tumour in patients with low-volume disease.

**Conclusion:** All the UK uro-oncologists surveyed stated that they would offer docetaxel in combination with ADT to all newly-diagnosed patients with mHSPC if fit enough for chemotherapy. ARTAs would be offered to many patients if available, especially those with high-risk disease or those unfit to receive chemotherapy. Scanning was typically conducted following treatment only at suspicion of disease progression.

**Key words:** metastatic hormone-sensitive prostate cancer, abiraterone, apalutamide, docetaxel, enzalutamide

**What’s known?**

* Several high-quality randomised controlled trials have demonstrated survival benefits in patients with metastatic hormone-sensitive prostate cancer (mHSPC) with docetaxel and androgen receptor-targeted agents (ARTAs)
* It has been suggested that the greatest benefit of docetaxel added to androgen deprivation therapy (ADT) is in patients with a high metastatic burden, although post-hoc data challenge this
* Post-hoc analyses have suggested that ARTAs are beneficial in patients with either high- or low-volume disease

**What’s new?**

* All UK uro-oncologists surveyed would currently offer patients with newly-diagnosed mHSPC docetaxel and ADT if they were fit to receive chemotherapy
* If ARTAs were available in UK for mHSPC, almost two-thirds of respondents would recommend an ARTA with ADT in preference to chemotherapy with ADT in at least one-half of all cases suitable for either treatment, with the strongest recommendations to patients with high-risk disease
* Scanning following treatment is conducted according to suspicion of disease progression, regardless of treatment

**1 INTRODUCTION**

Survival outcomes for men with metastatic hormone-sensitive prostate cancer (mHSPC) remain poor, but particularly so in men with a high metastatic burden at diagnosis.1 In the CHAARTED study, of the 393 patients who received androgen deprivation therapy (ADT) alone, median overall survival was 34.4 months in those with high-volume disease (defined as the presence of visceral metastases or ≥4 bone lesions with ≥1 beyond the vertebral bodies and pelvis), but not reached in those with low-volume disease.2 Furthermore, worse outcomes were observed for those patients with *de novo* high-volume mHSPC relative to those with high-volume disease who had failed prior local therapy. Similarly, in the GETUG-AF15 trial median overall survival was 83.4 months in the 202 patients with low-volume disease receiving ADT alone compared with 35.1 months in the 183 patients with high-volume disease (CHAARTED definition).3 Again, patients with *de novo* metastatic prostate cancer had poorer overall survival. A single-centre study conducted at the Dana Farber Cancer Institute involving 436 patients with mHSPC treated with ADT showed that the worst prognosis was for patients with *de novo* metastatic disease and high-volume disease (n=148; defined as above) relative to those who had received prior local treatment and had low-volume disease (n=125; median overall survival of 43.2 months vs 92.4 months).1

Addition of docetaxel to ADT offers a survival advantage relative to ADT alone in men with mHSPC. Of the studies reporting data for these patients, STAMPEDE is the largest randomised trial conducted to investigate treatment outcomes in men with high-risk localised or metastatic prostate cancer.4 Its multi-arm, multi-stage (MAMS) design permits the assessment of different treatments, in terms of overall survival, when added to long-term hormone therapy. The primary analysis from the study was the evaluation of docetaxel added to long-term ADT (592 patients) and in the overall population, a significant benefit was observed relative to the 1184 patients randomised to ADT alone (median overall survival, 71 vs 81 months; hazard ratio [HR], 0.78; 95% confidence interval [CI], 0.66-0.93; p=0.006). Similar findings were reported in the CHAARTED study.2, 5 However, in the GETUG-AF15 trial there was no difference between standard of care alone and the addition of docetaxel.3 A subsequent meta-analysis of data from STAMPEDE, CHAARTED and GETUG-AF15 has shown that risk of death in men with M1 mHSPC was reduced by 23% with the addition of docetaxel to ADT, when assuming a 4-year survival of 40% with ADT monotherapy (HR, 0.77; 95% CI, 0.68-0.97).6

The clinical trial data are also inconsistent with respect to outcomes according to volume of disease. In the CHAARTED study, for the 263 patients with high-volume disease (defined above) who received the combination of ADT and docetaxel, overall survival was significantly improved relative to ADT alone (HR, 0.63; 95% CI, 0.50-0.79; p<0.001).2 However, there was no apparent survival benefit with docetaxel in patients with low-volume mHSPC. Notably, improved survival was evident in the subgroup of patients with high-volume *de novo* disease but not for patients with high-volume mHSPC and prior local therapy, although the numbers of patients in the latter group were small. An analysis of data from STAMPEDE demonstrated that the observed survival benefit with docetaxel was apparent irrespective of disease volume (CHAARTED criteria; low-volume disease: HR, 0.76; 95% CI, 0.54-1.07; high-volume disease: HR, 0.81; 95% CI, 0.64-1.02).7 Conversely, in GETUG-AF15 there were no significant differences between treatment arms for the subgroups of patients with either high- or low-volume disease.3

Positive outcomes have also been widely reported for the combination of ADT and androgen receptor-targeted agents (ARTAs). LATITUDE compared abiraterone acetate (cytochrome P450 17A1 inhibitor) with prednisone (AAP) in combination with ADT vs ADT alone, in a pre-defined high-risk disease population: ‘at least two of the three of the following high-risk factors associated with poor prognosis’: a Gleason score of 8 or more, at least three bone lesions, and the presence of measurable visceral metastasis.8 The relative risk of death was reduced by 38% with ADT and AAP vs ADT alone (HR, 0.62; 95% CI, 0.51-0.76; p<0.001). Notably, in a post-hoc analysis of data from LATITUDE a subgroup of 955 patients with high-volume disease was defined according to CHAARTED criteria.9 In these patients, median overall survival was 49.7 months with ADT and AAP vs 33.3 months with ADT alone (HR, 0.62; 95% CI, 0.52-0.74; p<0.0001).

In the STAMPEDE trial, 3-year survival with ADT and AAP was 83% compared with 75% for ADT alone (HR, 0.63; 95% CI, 0.52-0.76; p<0.001) for the whole study population.10 Similar results were observed for the subgroup of 1002 men with metastatic disease (HR, 0.61; 95% CI, 0.49-0.75). When data from STAMPEDE were analysed according to the high-risk criteria used in LATITUDE study, a 46% reduction in mortality was observed with ADT and AAP vs ADT alone in patients with high-risk disease (HR, 0.54; 95% CI, 0.41-0.70; p<0.001), and a 34% reduction in patients with low-risk disease (HR, 0.66; 95% CI, 0.44-0.98; p=0.041).11 There was also a survival benefit of AAP when the data were analysed according to the CHAARTED criteria for high- and low-volume disease. A benefit of AAP was observed in both *de novo* and previously treated mHSPC, regardless of disease volume or risk stratification.

The addition of enzalutamide (a novel non-steroidal antiandrogen) to ADT in patients with mHSPC was compared with ADT monotherapy in the ARCHES trial.12 At a median follow-up of 14.4 months, median radiographic progression-free survival was not reached in the ADT and enzalutamide group vs 19.0 months in the ADT group (HR, 0.39; 95% CI, 0.30-0.50; p<0.001). However, overall survival data are yet to be reported. In the subgroup of patients with high-volume disease, there was a significant radiographic progression-free survival benefit with the addition of enzalutamide to ADT (HR, 0.43; 95% CI, 0.33-0.57), which was also observed in patients with low-volume disease (HR, 0.25; 95% CI, 0.14-0.46).

The combination of enzalutamide and ADT was compared with standard non-steroidal antiandrogen therapy in combination with ADT in ENZAMET and showed that it was associated with a significantly reduced risk of death (HR, 0.67; 95% CI, 0.52-0.86; p=0.002).13 At 3 years, clinical progression-free survival was 68% in the ADT and enzalutamide group vs 41% in the standard of care group (HR, 0.40; 95% CI, 0.33-0.49; p<0.001). Notably, the data do not support the concurrent use of docetaxel—in this subgroup there was no benefit of enzalutamide in terms of overall survival relative to ADT monotherapy (HR, 0.90; 95% CI, 0.62-1.31). Unsurprisingly, toxicities were more frequent in those patients who received both docetaxel and enzalutamide, including haematological toxicity, infections, sensory neuropathy and alopecia.13

Data supporting the use apalutamide (another novel non-steroidal antiandrogen) in combination with ADT in men with newly-diagnosed mHSPC are provided by the TITAN study.14 Like ARCHES, the primary endpoint was radiographic progression-free survival, and at a median follow-up of 22.7 months, a benefit was observed with apalutamide (HR, 0.48; 95% CI, 0.39-0.60; p<0.001). There was also a 33% lower risk of death with ADT and apalutamide vs ADT alone (HR, 0.67; 95% CI, 0.51-0.89; p=0.005). When the data from TITAN were analysed according to metastatic volume (CHAARTED criteria), there was a benefit of apalutamide in patients with high-volume disease (HR, 0.68; 95% CI, 0.50-0.92) but this was absent in patients with low-volume disease (HR, 0.67; 95% CI, 0.67-0.34-1.32).

Progression to metastatic castration-resistant prostate cancer (mCRPC) is associated with substantial reductions in quality of life due to an increase in disease-related symptoms such as fatigue and pain and a decline in vitality and mental health. In a UK-based survey of 132 men with mCRPC starting systemic therapy, quality of life had deteriorated significantly after 6 months of treatment and those who received ADT alone experienced worse outcomes than those on concomitant chemotherapy.15 For many of the patients, pain levels remained the same as before treatment initiation or increased. A systematic review of randomised controlled trials in men with mCRPC reported cancer-related fatigue in up to 21% of patients, and in 18% this was severe.16 Delaying progression to castration resistance is therefore a key treatment objective in managing men with mHSPC. In CHAARTED, progression to mCRPC in patients receiving ADT alone was 8.6 months for those with high-volume disease compared to 22.7 months for those with low-volume disease.2 However, outcomes were significantly improved in the high-volume group with the addition of docetaxel. The STAMPEDE trial showed that the benefits of adding docetaxel improved this outcome irrespective of disease volume at study entry.7

In the UK, the National Institute for Health and Care Excellence (NICE) guidance for prostate cancer makes a general recommendation that patients with newly-diagnosed metastatic prostate cancer should be offered docetaxel in combination with ADT;17 however, combined androgen blockade with ARTAs such as abiraterone acetate, enzalutamide or apalutamide has currently not been recommended as a first-line treatment option (note: after completion of the survey, enzalutamide was made available via the Cancer Drugs Fund during the Covid-19 pandemic). Indeed, at present it is unclear as to how such therapies should be used in patients with newly-diagnosed mHSPC, in terms of patient selection and treatment sequencing.

The purpose of this survey was therefore to explore the practice of uro-oncologists in the UK with respect to management of this group of patients in current practice to determine the use of docetaxel in patients fit to receive chemotherapy and also how practice would change if ARTAs were available.

**2 METHODS**

A survey of uro-oncologists from around the UK was conducted at the British Uro-oncology Group (BUG) Annual Meeting in September 2019, following presentations covering the latest results of studies evaluating all these agents. At the meeting, delegates completed a paper questionnaire and there was a subsequent opportunity to participate online via Survey Monkey. The questionnaire was devised by a steering group of BUG members. No formal statistical testing was performed on the data collected; the number of responses and percentages are presented.

**3 RESULTS**

The questionnaire was distributed to 150 members of BUG and 103 completed the survey (69%). The majority were either clinical oncologists (77%) or medical oncologists (12%). Of these, 96 respondents currently managed patients with advanced prostate cancer and 77 were recruiting patients into the STAMPEDE study.

The members were firstly asked about their use of ADT alone in patients with newly-diagnosed mHPSC; 56.8% used ADT monotherapy in fewer than 25% of these patients and an additional 39.0% in 25-50% of these patients. Multiple reasons were cited for use of ADT monotherapy (Table 1), most commonly poor performance status, comorbidities, frailty and patients’ preference not to receive chemotherapy even if they were sufficiently fit.

Two-thirds of the respondents said that they treated more than 50% of their newly-diagnosed mHSPC patients with ADT and docetaxel and all stated that they would offer docetaxel to such patients who are fit for chemotherapy. Almost all (97.9%) would highly or strongly recommend docetaxel to these patients who have high-volume disease but this decreased to 62.1% for patients with low-volume disease (Figure 1), and fewer than 5% would strongly recommend against docetaxel treatment for this group. Regarding the prescription of docetaxel, although more than 70% of respondents had access to a pharmacy or nurse prescriber, in 85% of cases these were used for fewer than 25% of patients.

There was a wide range of opinion regarding imaging after completion of docetaxel treatment: 47% highly or strongly recommended imaging at this point (estimated prostate-specific antigen [PSA] nadir); 28% rarely or did not at all routinely scan their patients. With respect to further imaging after completion of docetaxel treatment, the majority (82%) stated that this would be guided by clinical or biochemical progression rather than fixed points in time.

A total of 78.9% of respondents would highly or strongly recommend an ARTA in combination with ADT in patients with high-risk newly-diagnosed mHSPC if this option was available and 70.0% would highly or strongly recommend in patients with low-risk disease if there were no restrictions to their use (Figure 2). Abiraterone was the most frequent choice of ARTA (57%) followed by enzalutamide (34%). Approximately 59% of those surveyed scanned at PSA nadir during ARTA treatment and 77% would scan again only on suspicion of clinical or biochemical progression.

The uro-oncologists were then asked specific questions regarding treatment decisions if docetaxel and ARTAs were both available, in the context of the type and extent of metastases (Table 2). With regards to patients with liver metastases, 88.7% would be highly likely to recommend treatment with docetaxel, compared with ARTA recommendation in only 23.9% of such patients. Approximately three-quarters of respondents stated that for their patients with lung metastases they would highly recommend docetaxel but an ARTA in fewer than one-third. A higher proportion of those surveyed reported that they were highly likely to recommend treatment with an ARTA (74.4%) rather than docetaxel (50.0%) in patients with bone metastases only. Similarly, more were likely to highly recommend an ARTA (54.6%) than docetaxel (39.5%) for patients with only nodal disease, but the reverse was true for patients with both bone and nodal metastases (docetaxel, 64.4%; ARTA, 59.8%). For patients with BRCA-positive mHPSC, 60.5% and 29.7% of respondents were highly likely to recommend docetaxel or an ARTA, respectively.

In agreement with STAMPEDE (Parker et al, 2018), almost all of the uro-oncologists (96%) would offer local radiotherapy to their patients with low metastatic burden mHSPC but only 12% would offer it to patients with high-volume disease.

**4 DISCUSSION**

The survey reported here provides a snapshot of newly-diagnosed mHSPC management by uro-oncologists in the UK. Perhaps unsurprisingly, among respondents, treatment with ADT alone was uncommon in patients who are considered fit for docetaxel which is the only additional therapy available in the UK at the time of the survey. Indeed, the reasons for offering ADT alone were largely based on frailty and comorbidities. A key consideration is quality of life, in the context of that although the addition of docetaxel to ADT unquestionably prolongs survival,2, 4, 5, 7 the toxicity associated with chemotherapy may outweigh the benefits of treatment for these individual men. Consideration must also be given to the cost-effectiveness of chemotherapy in the mHSPC setting relative to patients with castration-resistant disease.

It should be remembered that the adverse effects of docetaxel that matter most to patients may not be obvious from clinical trial data; in a real-life survey of men with mHSPC the most troublesome effects associated with docetaxel treatment included fatigue, nausea, vomiting, anaemia, diarrhoea, mouth ulcers, rash and bone pain.18 Notably, an impact on daily activities was also reported, e.g. limits to ambulatory capacity and psychological effects. In an analysis of data from GETUG-AF15 all cumulative toxicity measures (i.e., all grades/severity of adverse events) were associated with reduced quality of life.19 However, the negative impact of docetaxel on quality of life is associated with treatment toxicity within the first 3 months but typically recovers after cessation of treatment. Indeed, function was reduced in patients on ADT and docetaxel in CHAARTED relative to ADT alone at 3 months; at 12 months this had returned to baseline values in patients receiving chemotherapy but had deteriorated in those on ADT.20 In the GETUG-AF15 trial, only appetite loss and constipation remained an issue after docetaxel treatment cessation when compared with patients receiving ADT monotherapy.21

Without exception, the respondents surveyed agreed that they would offer docetaxel in addition to ADT to their patients with newly-diagnosed mHSPC who were considered fit enough for chemotherapy. However, this does not reflect real life clinical practice—in the latest National Prostate Cancer Audit, only 27% of men within this group received ADT and docetaxel between 2017 and 2018 in England and Wales.22 The results of the survey therefore likely reflect intent rather than practice.

However, there were differences with respect to metastatic burden—a strong recommendation in 64% of patients with high-volume disease compared with only 31% of patients with low-volume disease. This reflects the findings from CHAARTED, where overall survival in patients with high-volume disease was superior with docetaxel, but no benefit was observed in patients with low-volume disease.2 However, a recent analysis of data from the STAMPEDE study demonstrated benefit from docetaxel, irrespective of disease burden when applying the same criteria for disease volume that were used in CHAARTED. These conflicting results concerning patients with low-volume metastatic disease cannot be fully explained, although the number of patients in this group included in CHAARTED was small and the study was statistically underpowered for such an analysis. Such inconsistency may impact clinical practice.

Approximately one-third of respondents stated that they would treat more than one-half of their patients with newly-diagnosed mHSPC with an ARTA if there were no restrictions on prescribing and these were available in the UK, and that the most frequent option would be AAP. When considering the high-risk definition employed in LATITUDE, 46% would recommend ARTA use in such patients but only 36% in low-risk patients. In this study, the relative risk of death in this population was significantly reduced with ADT and AAP relative to ADT alone and risk of radiographic progression or death was also significantly reduced.8 Additionally, a post-hoc analysis of data from LATITUDE has shown that in the subgroup with high-volume disease (CHAARTED criteria) there was also a significant overall survival benefit,9 and similar outcomes with AAP have been reported from STAMPEDE.11 In ARCHES, enzalutamide treatment was associated with improved radiographic progression-free survival in both high- and low-volume disease,12 but there was no apparent benefit with apalutamide in patients with low-volume mHSPC in TITAN.14

ARTAs may be suitable for patients not sufficiently fit for chemotherapy due to frailty, comorbidities, a high risk of infection with chemotherapy or pre-existing neuropathy that could be exacerbated by docetaxel. However, these agents are not without side effects themselves that can influence selection of a particular agent.12, 14

Treatment with abiraterone is associated with an increased frequency of hypertension, hypokalaemia and fluid retention,8 likely due to increased mineralocorticoid levels resulting from CYP17 inhibition. Therefore, caution is recommended when considering treatment in men at risk of, or with established cardiovascular disease, and intensive monitoring of blood pressure, serum potassium and fluid retention is required.23 The combination with prednisone also necessitates frequent blood sugar monitoring in patients with diabetes. Hypertension also occurs with both enzalutamide and apalutamide12-14 and monitoring is advised, especially in those with known cardiovascular risk factors.24, 25

An increased percentage of patients receiving ADT and enzalutamide in clinical trials experienced cognitive impairment relative to ADT alone12, 13 and this must be taken into consideration when selecting treatment. Apalutamide treatment is associated with an increased frequency of falls and fractures, skin rash and thyroid function abnormalities, all impacting patient selection.14 There is also a need to monitor metabolic parameters in patients due to an increased risk of ischaemic heart disease.25

Fatigue is a key concern with all ARTAs, and as a small number of seizures were observed in the clinical trials, caution is needed when considering treatment in men at increased risk or those with existing seizure disorder.8, 12, 14

The majority of uro-oncologists would select abiraterone as their first choice ARTA, followed by enzalutamide. Although there was no specific question regarding reasons for this choice, it may be reasonable to argue that as these two agents have been approved for a number of years and are recommended by NICE as second-line options for the treatment of mCRPC following previous treatment with docetaxel,26, 27 this would suggest a longer period of clinical experience and established treatment pathways and monitoring regimens.

In patients receiving ADT and docetaxel, 47% of respondents stated that they would highly or strongly recommend scanning patients at the nadir of PSA, the same percentage would not. For patients receiving ARTAs, approximately 60% of respondents would scan their patients at the approximate PSA nadir and the remainder would not. In the opinion of the UK uro-oncologists, further scanning is generally conducted based on clinical or biochemical progression, rather than at pre-defined (routine) times, regardless of treatment type. This is in agreement with current European guidelines for advanced and metastatic prostate cancer, which recommend that asymptomatic patients with stable PSA levels require no further imaging.28 The guidelines recommend that in patients with new-onset symptoms or PSA progression, bone scans and other imaging modalities should be considered. However, there is an argument for baseline scanning so that that the nature of progression can be determined when it occurs.

Currently there are no strong, directly comparative clinical trial data to support differentiation between chemotherapy and ARTA therapy in terms of efficacy based on disease characteristics. However, two network meta-analyses have been published for the first-line treatment of newly-diagnosed mHSPC. The first included data from CHAARTED, LATITUDE and GETUG-AF15.29 When comparing AAP in combination with ADT vs ADT and docetaxel, the HR for overall survival in patients with high-risk/high-volume disease was 0.85 (95% CI, 0.63-1.14), and for radiographic progression-free survival was 0.71 (95% CI, 0.49-1.02), indicating no significant differences. A separate network meta-analysis included data from eight randomised phase 2 or 3 trials involving men with mHSPC. This estimated that the HR for death was 1.195 (95% CI, 0.980-1.456) when comparing ADT and docetaxel vs ADT and AAP, while the HR for progression-free survival was 1.653 (95% CI, 1.408-1.939). There was no significant difference for treatment-related mortality (HR, 1.438; 95% CI, 0.508-4.075).30 In STAMPEDE, both ADT with docetaxel and ADT with AAP were separately compared with standard of care in men starting long-term ADT. A post-hoc analysis of data from this trial has been conducted, including 342 patients with M1 disease. No differences between ADT and AAP and ADT and docetaxel were found in terms of overall survival (HR, 1.13; 95% CI, 0.77-1.66).31 However, progression-free survival (excluding rising PSA) was longer with ADT and AAP (HR, 0.69; 95% CI, 0.50-0.95; p=0.023). Failure-free survival was also significantly better with AAP, but the authors concluded that four in every five FFS events was driven by a rise in PSA only.

In the first network meta-analysis, when assessed at 3-12 months after treatment initiation, Brief Pain Index and Functional Assessment of Cancer Therapy-Prostate (FACT-P) scores were significantly improved with ADT and AAP vs ADT and docetaxel.29 A substudy of STAMPEDE has also assessed quality of life with docetaxel and abiraterone.32 Mean global quality of life scores were comparable for the two groups at baseline, but average global quality of life was higher with abiraterone than docetaxel over the 2-year period. However, although the difference was statistically significant (+3.9%; 95% CI, 0.6-0.710; p=0.021), it did not meet the predefined clinical parameter (a difference of 4%). Cross-sectional analyses showed clinically meaningful better quality of life with abiraterone vs docetaxel at 3 and 6 months but these differences were not apparent at 1 or 2 years. Indeed, mean quality of life scores decreased from the start of docetaxel therapy through 18 weeks, prior to subsequent recovery. In an exploratory analysis of 207 patients with metastatic disease, mean quality of life score was better in the abiraterone group relative to the docetaxel group (+4.44; 95% CI, 0.2-8.6; p=0.036). Over the 2-year period, docetaxel treatment was associated with greater fatigue scores and higher pain scores.

A key unanswered question is which sequence of treatments, i.e. docetaxel first and then an ARTA at progression, or vice-versa, is superior, but there is little information to provide guidance.

Almost all of the respondents stated that they would offer local radiotherapy to the primary tumour to their patients with low metastatic burden newly-diagnosed mHSPC. This is supported by findings from STAMPEDE, which showed an overall survival benefit only in patients with low-volume (HR, 0.68; 95% CI, 0.52-0.90) but not high-volume (CHAARTED criteria; HR, 1.07; 95% CI, 0.90-1.28) disease.33 Similar findings were reported for progression-free survival, with a significant 22% reduction in patients with low-volume disease (HR, 0.78; 95% CI, 0.63-0.98) but with no difference between treatment arms in high-volume disease (HR, 1.09; 95% CI, 0.94-1.26).

There is a key limitation of the study. With respect to ARTAs, the questions were posed with the hypothesis that all these agents would be approved available within the UK (currently in the UK ARTAs are not recommended by NICE and therefore unavailable though recent changes in the COVID-19 scenario has enabled use of enzalutamide, but this was not available at time of survey and still is not a NICE approved option). Furthermore, the uro-oncologists surveyed here were not asked about their use of ARTAs based on volume of disease or reasons why they would choose one specific ARTA over another.

**5 CONCLUSIONS**

From the perspective of UK uro-oncologists, in patients with newly-diagnosed M1 mHSPC the majority would offer docetaxel in combination with ADT to patients fit enough for chemotherapy in their current practice, although this is not borne out by the National Prostate Cancer Audit. However, patient-related factors would also determine choice between first-line chemotherapy and ARTA therapy if these were all available, including preference against the former. Scanning is typically conducted according to clinical judgement rather than routinely.

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**TABLES**

**TABLE 1** Reasons for treating patients with newly-diagnosed mHSPC with ADT alone (N=95)

|  |  |
| --- | --- |
| **Reason** | **Responses, n (%)** |
| Comorbidities | 95 (100.0) |
| Performance status | 94 (99.0) |
| Frailty | 88 (92.6) |
| Unwilling to undergo chemotherapy, despite fitness | 84 (88.4) |
| Older age | 54 (56.8) |
| Social factors (ability to travel, family support, cognitive status) | 54 (56.8) |
| Quality of life vs length of survival | 45 (47.4) |
| Concomitant medication | 30 (31.6) |
| Access to drugs | 14 (14.7) |
| Healthcare resource implications | 4 (4.2) |

**TABLE 2** Use of specific treatments according to type of metastases

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Not at all/rarely, %** | **Sometimes, %** | **Highly likely, %** |
| Liver metastases |  |  |  |
| Docetaxel | 1.1 | 10.2 | 88.7 |
| ARTA | 25.0 | 51.1 | 23.9 |
| Lung metastases |  |  |  |
| Docetaxel | 1.1 | 23.6 | 75.3 |
| ARTA | 19.5 | 48.3 | 32.2 |
| Bone only metastases |  |  |  |
| Docetaxel | 8.0 | 42.0 | 50.0 |
| ARTA | 3.5 | 22.1 | 74.4 |
| Lymph node only metastases |  |  |  |
| Docetaxel | 13.9 | 46.6 | 39.5 |
| ARTA | 6.8 | 38.6 | 54.6 |
| Mixed bone and lymph node metastases |  |  |  |
| Docetaxel | 4.6 | 31.0 | 64.4 |
| ARTA | 4.6 | 35.6 | 59.8 |
| BRCA-positive disease |  |  |  |
| Docetaxel | 3.7 | 35.8 | 60.5 |
| ARTA | 6.8 | 63.5 | 29.7 |

Questionnaire scale from 0 (not at all) to 10 (highly likely) Not at all/rarely: scores of 1-3; sometimes, scores of 4-7; highly likely: scores of 8-10. ARTA, androgen receptor-targeted agent.

**FIGURE LEGENDS**

**FIGURE 1** Strength of recommendation for docetaxel and ADT according to disease characteristics

Questionnaire scale from 0 (not at all) to 10 (strongly). Not at all/rarely: scores of 1-3; sometimes, scores of 4-7; highly/strongly: scores of 8-10.

ADT, androgen deprivation therapy; HSPC, hormone-sensitive prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; nmHSPC, non-metastatic hormone-sensitive prostate cancer.

**FIGURE 2** Strength of recommendation for androgen receptor-targeted agents and ADT according to disease characteristics

Questionnaire scale from 0 (not at all) to 10 (strongly). Not at all/rarely: scores of 1-3; sometimes, scores of 4-7; highly/strongly: scores of 8-10.

ADT, androgen deprivation therapy; HSPC, hormone-sensitive prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; nmHSPC, non-metastatic hormone-sensitive prostate cancer.