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Prostate Cancer

Docetaxel Treatment for Metastatic Hormone-sensitive Prostate Cancer in Daily Practice

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Article info

Abstract

Background: Currently, metastatic hormone-sensitive prostate cancer (mHSPC) patients are often treated with docetaxel chemotherapy at the initiation of hormonal therapy. This treatment is based on the results of two pivotal trials. However, trial populations are not a representative of real-world patient populations.
Objective: We aimed to analyze whether survival rates in our daily practice cohort is comparable with those in clinical trials and to characterize the tolerability of docetaxel chemotherapy in daily practice.
Design, setting, and participants: In this retrospective cohort analysis, we studied 159 mHSPC patients treated with early docetaxel from April 2014 up to June 2020 in a top clinical hospital in The Netherlands. Patients were selected using hospital pharmacy records.
Outcome measurements and statistical analysis: We compared the results of our cohort with the results of the cohorts of the two pivotal trials. We aimed to analyze the survival rates in our cohort and characterize the tolerability of docetaxel chemotherapy in daily practice.
Results and limitations: Despite the relatively high number of comorbidities in our daily practice cohort, overall survival of our cohort showed great similarity with that of the two pivotal trials: 60.2 mo compared with 57.6 and 59.1 mo. Furthermore, early docetaxel was well tolerated in daily practice. Nearly 90% of the patients completed the full six cycles, and polyneuropathy led to relatively few dose reductions (6.9%).
Conclusions: Early docetaxel is well tolerated in daily practice. Our daily practice cohort showed great similarity in overall survival to the clinical trials. Our results might be of interest in the developing landscape of mHSPC treatment.

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Patient summary: We studied docetaxel chemotherapy for metastatic prostate cancer in daily practice. These patients have the same survival as selected patients participating in clinical trials. Docetaxel was well tolerated in daily practice.

1. Introduction

Prostate cancer is the second most common cancer in men worldwide, and the incidence is still rising [1]. For men diagnosed with metastatic disease, 5-yr survival rates are 31% [2].

For decades, androgen deprivation therapy (ADT) has been the cornerstone of treatment of metastatic hormone-sensitive prostate cancer (mHSPC). This treatment is based on eliminating the growth-stimulatory effect of testosterone by surgical or chemical castration. Ultimately, however, resistance occurs, leading to castration-resistant prostate cance (CRPC) [3,4].

In 2015 and 2016, two landmark studies, Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer (CHAARTED) and Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy (STAMPEDE), demonstrated that addition of docetaxel to ADT when initiating treatment for mHSPC prolongs survival. This so-called "early docetaxel" improved overall survival in these study populations by 13.6 and 10.0 mo, respectively. Secondary endpoints, including time to CRPC, also favored the addition of docetaxel [5,6].

However, when patients with metastatic disease are divided into subgroups based on their burden of disease, these pivotal studies show conflicting results. Patients can be divided into groups with high- or low-volume disease, with high-volume disease defined as four or more bone metastases, with at least one outside the pelvis and the vertebral column, or the presence of a visceral metastatic lesion [5]. Based on this definition, the benefits on survival endpoints are clear for early docetaxel in patients with high-volume disease. However, the addition of early docetaxel in patients with low-volume disease is debated. The most recent publication with results from the STAMPEDE group showed a significant benefit for early docetaxel in low-volume patients [7]. In contrast, the most recent results with long-term follow-up from the CHAARTED group did not show a survival benefit for the addition of early docetaxel in patients with low-volume disease [8].

The results of these landmark studies have changed daily practice dramatically. The beneficiary effects of early docetaxel have been reported only in selected study populations. Study patients typically do not fully reflect real-world patients. Real-world patients are often older, and have poorer performance status and worse disease prognosis [9]. This may limit the external validity of these randomized controlled trials.

The aim of this study is to describe patient, treatment, and survival characteristics in a population-based cohort of patients with mHSPC treated with early docetaxel. We aim to analyze whether our daily practice cohort shows similarity in survival to the clinical trial cohorts and describe the tolerability of early docetaxel in daily practice.

2. Patients and methods

Owing to the retrospective and descriptive nature of this study, patient consent was not necessary. The Dutch Central Committee on Human-Related Research (CCMO [Centrale Commissie Mensgebonden Onderzoek]) allows the use of anonymous data without prior approval of an institutional review board provided that the data are acquired for routine patient care. All patient data were anonymized by the removal of individually identifiable health information and identifiers. This study was approved by the Ethics Committee of the Martini Hospital, Groningen, The Netherlands.

2.1. Study population

Patients diagnosed with metastatic prostate cancer and treated with early docetaxel in the Martini Hospital at Groningen, a top clinical hospital in the northern part of The Netherlands, were selected retrospectively. Patients were treated between June 2014 and April 2020. Identification of patients occurred through the registries of the hospital pharmacy. The diagnosis of mHSPC was confirmed by a medical chart review. Patients were eligible for treatment if they had an Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2. Patients with a performance score of 2 were eligible only if the decrement in functioning was due to prostate cancer.

2.2. Patient characteristics

Patient, treatment, and survival characteristics were collected. Follow-up was completed up to April 2020. We reviewed the medical charts of all patients at the start of chemotherapy for pulmonary, vascular, and cardiac comorbidities. Pulmonary comorbidity was defined as known chronic pulmonary disease. Vascular disease was defined as any known ischemic arterial event in the past, with exclusion of cardiac events. Cardiac comorbidities were defined as known chronic heart failure, or any known cardiac ischemic event, for which either medical or interventional treatment had been initiated. Lymph nodes were

classified as regional or nonregional lymph nodes, based on their pattern of spread [10].

Patients were divided into subgroups based on their burden of disease at the start of treatment, as described previously. In the clinical trials, burden of disease was measured using conventional radiologic imaging (ie, bone scintigraphy or computed tomography [CT] scan). In our daily practice, some patients were staged with positron emission tomography (PET) scans only and no conventional radiologic imaging was performed. For the allocation of these patients to the subgroups based on the volume of disease, a blinded radiologist checked the number and localization of bone metastases on the low-dose CT scan that was performed for attenuation of the PET scan. Hereby, we were able to divide these patients into subgroups of burden of disease based on conventional imaging.

2.3. Treatment procedure

Patients received docetaxel as part of the standard of care (SOC) at the initiation of ADT (medical or surgical): six cycles on a 3-weekly regimen at a dose of 75 mg/m². Docetaxel was combined with oral prednisolone 5 mg twice daily. Dose modifications were made according to the protocol of the CHAARTED trial [5]. During the period of docetaxel administration, patients were evaluated for toxicity prior to administration of every cycle by their treating physician or a specialized nurse. After finishing treatment with docetaxel, patients were seen regularly by their treating physicians, approximately on a 3-monthly schedule. Prostate-specific antigen (PSA) levels were measured at each scheduled visit. Radiologic imaging was not performed routinely during follow-up.

2.4. Primary outcome measure

All patients who were diagnosed with mHSPC and who received early docetaxel for this indication were included in the analysis. Overall survival was compared with that in both clinical trials. To compare results with the CHAARTED trial, time to CRPC and time to clinical progression were determined. For comparison with the STAMPEDE trial, progression-free survival and failure-free survival (FFS) were determined. An overview of the exact definitions of these endpoints can be found in Supplementary Table 1.

Furthermore, time to second-line treatment (SLT) was measured. Time to SLT was defined as the time until the date of starting an SLT or death from prostate cancer. An SLT was defined as a treatment shown to be life prolonging in patients with metastatic CRPC (ie, docetaxel rechallenge, cabazitaxel, abiraterone-prednisolone, enzalutamide, or radium-223) [11].

2.5. Statistical analysis

Data were analyzed using IBM SPSS statistics software version 20 (IBM Corp., Armonk, NY, USA). Continuous and discrete variables are presented as median (range and interquartile range [IQR]) and counts (percentages), respectively. Age was calculated on the day of diagnosis. Time to event was analyzed by the Kaplan-Meier method. Median survival times for secondary endpoints of the STAMPEDE trial were extracted from the figures in the manuscript using WebPlotDigitzer [12]. Survival endpoints in the two trials were evaluated from the date of randomization, which was approximately 6 wk after starting hormonal therapy [5,6]. For the purpose of comparing our results with those of the clinical trials, we determined a surrogate randomization date 6 wk after starting hormonal therapy.

3. Results

3.1. Inclusion

Between July 2014 and February 2020, a total of 174 patients received early docetaxel in our clinic. Of these 174 prostate cancer patients, 15 were excluded. Eleven patients still underwent chemotherapy or recently finished the chemotherapy cycles and therefore were not yet available for analysis, two were lost to follow-up, and two did not receive therapy conforming to the SOC (Supplementary Fig. 1). This report represents data with a cutoff date for survival data of April 16, 2020.

3.2. Patient characteristics

Table 1 shows the baseline characteristics of patients in our cohort. The median follow-up was 20 mo (IQR 11–36). A total of 134 patients (84%) were newly diagnosed, 22 of 25 patients (88%) who were previously diagnosed with nonmetastatic prostate cancer underwent prior local therapy, and 86 patients (54%) were diagnosed with high-volume disease.

The median age was 71 yr (range 49–85); 43% of the patients had an ECOG performance status of 0 at baseline and 65% had a Gleason sum score of ≥8. The median PSA level at baseline was 129 μg/l (IQR 25–425). Nearly 60% of all patients had at least one comorbidity, with hypertension being the most frequently reported comorbidity (28.3%).

3.3. Survival and daily practice endpoints

The median overall survival in our cohort was 60.2 mo. The median survival at the time of analysis had not been reached in the subgroup with low-volume disease. In the subgroup of patients with high-volume disease, the median overall survival was 45.6 mo (Table 2 and Fig. 1). The median time to SLT was 44.4 mo. Time to SLT was longer for patients with low-volume disease than for patients with high-volume disease: 47.6 versus 27.0 mo. Of the patients who were radiologic staged at the time of progression, approximately 50% had only known bone metastasis (Table 3). Visceral metastases were diagnosed only in 7%. An SLT consisted most often of abiraterone-prednisolone or enzalutamide (Table 3).

3.4. Toxicity and safety

Nearly 90% of the 159 patients who started chemotherapy finished all six cycles. One patient did not complete one cycle due to severe infusion reactions. Of the 16 patients who stopped chemotherapy, nearly two-thirds stopped due to toxicity (Table 4).

Our cohort of patients underwent a total of 901 cycles of docetaxel; 23 cycles were postponed in 21 different patients, of which six cycles were postponed based on patient request. Dose reductions were applied in 22 patients; 11 were made due to polyneuropathy and

Table 1 – Baseline characteristics

	All patients (n = 159), n (%)	High volume (n = 86 [54.1%]), n (%)	Low volume (n = 73 [45.9%]), n (%)
Age			
Median	71	71.5	71
Range	49–85	49–85	56–85
IQR	66–76	66–76	66–76
ECOG performance status			
0	69 (43.4)	29 (33.7)	40 (54.8)
1	54 (34)	33 (38.4)	21 (28.8)
2	1 (0.6)	1 (1.2)	0
Unknown	35 (22)	23 (26.7)	12 (16.4)
T stage			
T1	13 (8.2)	3 (3.5)	10 (13.7)
T2	34 (21.4)	14 (16.3)	20 (27.4)
T3	62 (39)	35 (40.7)	27 (37)
T4	42 (26.4)	27 (31.4)	15 (20.5)
Tx	8 (5)	7 (8.1)	1 (1.4)
Nodal status			
N0	22 (13.8)	9 (10.5)	13 (17.8)
N+	76 (47.8)	28 (32.6)	48 (65.8)
Nx	61 (38.4)	49 (57)	12 (16.4)
Site of metastases [a]			
Bone	117 (73.6)	84 (97.7)	33 (45.2)
Lung	7 (4.4)	7 (8.1)	0
Nodes[b]	48 (30.2)	19 (22.1)	29 (39.7)
Other	1 (0.6)	0	1 (1.4)
Gleason sum score			
≤7	54 (34)	24 (27.9)	30 (41.1)
8–10	103 (64.8)	60 (69.8)	43 (58.9)
Unknown	2 (1.3)	2 (2.3)	
PSA level at start of ADT			
Median	129	280.5	28
Range	0.19–9584	7.2–9584	0.19–737
IQR	25–425	102.25–1184.5	8.5–136
Previous treatment			
No	137 (86.2)	82 (95.3)	55 (75.3)
Yes	22 (13.8)	4 (4.7)	18 (24.7)
Smoking			
Yes	14 (8.8)	11 (12.8)	3 (4.1)
No	48 (30.2)	23 (26.7)	25 (34.2)
Quitted	28 (17.6)	19 (22.1)	9 (12.3)
Unknown	69 (43.4)	33 (38.4)	36 (49.3)
Number of comorbidities			
0	69 (43.4)	36 (41.()	33 (45.2)
1	62 (39)	31 (36)	31 (42.5)
2	16 (10.1)	9 (10.5)	7 (9.6)
≥3	12 (7.5)	10 (11.6)	2 (2.7)
Subgroups comorbidities			
Hypertension			
Yes	45 (28.3)	30 (34.9)	15 (20.5)
No	114 (71.7)	56 (65.1)	58 (79.5)
Other malignancy			
Yes	25 (15.7)	12 (14)	13 (17.8)
No	134 (84.3)	74 (86)	60 (82.2)
Diabetes mellitus			
Yes	17 (10.7)	8 (9.3)	9 (12.3)
No	142 (89.3)	78 (90.7)	64 (87.7)
Pulmonary comorbidity			
Yes	16 (10.1)	8 (9.3)	8 (11)
No	143 (89.9)	78 (90.7)	65 (89)
Vascular disease			
Yes	13 (8.2)	8 (9.3)	5 (6.8)
No	146 (91.8)	78 (90.7)	68 (93.2)
Cardiac comorbidity			
Yes	17 (10.7)	15 (17.4)	2 (2.7)
No	142 (89.3)	71 (82.6)	71 (97.3)

ADT = androgen deprivation therapy; ECOG = European Cooperative Oncology Group; IQR = interquartile range; PSA = prostate-specific antigen.
[a] Patients were able to have more than one site of metastases. Percentages shown are for per individual site for total patients in the subgroups.
[b] Nodal metastases: nonregional lymph node.

Table 2 – Overview of survival endpoint data of our cohort compared with the two clinical trials [a]

|		Our cohort	CHAARTED	STAMPEDE
Overall survival	All	60.2	57.6	59.1
	High	45.6	51.2	39.3
	Low	MNR	63.5	93.2
Time to CRPC	All	26.2	19.4	
	High	17.4	14.9	
	Low	33.3	31.0	
Time to clinical progression	All	36.8	33.0	
	High	26.1	27.3	
	Low	47.1	42.5	
Failure-free survival	All	30.3		19.3
	High	19.6		14.0
	Low	33.8		38.8
Progression-free survival	All	36.8		36.3
	High	26.1		NA
	Low	47.1		NA

CHAARTED = Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer; CRPC = castration-resistant prostate cancer; MNR = median not reached; NA = not available; STAMPEDE = Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy.
[a] Numbers are shown as median overall survival in months.

eight due to neutropenia or neutropenic fever. During chemotherapy, a total of 50 hospitalizations occurred, of which 40% were due to the toxicity of chemotherapy (Table 4). Two patients died during treatment, which was possibly related to docetaxel treatment. One year after the completion of docetaxel treatment, grade II or higher polyneuropathy toxicity was described in the medical charts of 6.9% of patients.
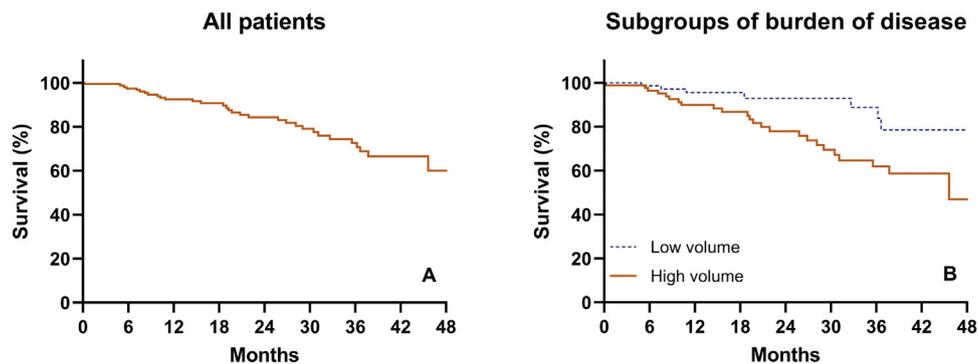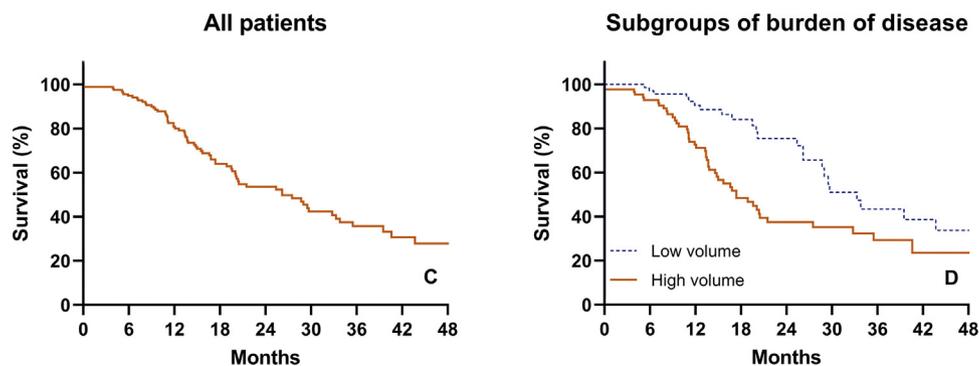

Fig. 1 – Kaplan-Meier estimates of overall survival for (A) all patients and (B) subgroups of patients based on their burden of disease, and for time to castration-resistant prostate cancer (CRPC) for (C) all patients and (D) subgroups of patients based on their burden of disease.

Table 3 – Overview of the type of radiologic progression and next line of treatment

	n (%)
Total of patients with radiologic progression	28
Radiologic site of progression	
Bone only	15 (53.6)
Bone and lymph nodes	8 (28.6)
Bone and visceral metastases	2 (7.1)
Lymph nodes only	2 (7.1)
Regional	1 (3.6)
Patients who started next line of therapy	44
Treatment at time of progression	
Enzalutamide	17 (38.6)
Abiraterone-prednisolone	16 (36.4)
Docetaxel rechallenge	4 (9.1)
Radium-223	3 (6.8)
Cabazitaxel	3 (6.8)
Cabazitaxel + carboplatin	1 (2.3)

Table 4 – Overview of toxicity and safety analysis

	n (%)
Number of patients	159
Number of cycles completed	
0	1 (0.6)
1	4 (2.5)
2	4 (2.5)
3	1 (0.6)
4	2 (1.3)
5	4 (2.5)
6	143 (89.9)
Reasons for stopping	
Toxicity	10 (62.5)
Treatment refusal	1 (6.3)
Intercurrent illness	3 (18.8)
Death	2 (12.5)
Cycles postponed	
Number of patients	21 (13.2)
Total cycles postponed	23
Reason for postponing cycle	
Toxicity	13 (56.5)
Intercurrent illness	4 (17.4)
Patient choice	6 (26.1)
Dose reductions	
Number of patients	22 (13.9)
Total dose reductions	23
Reason for dose reduction	
Polyneuropathy	11 (47.8)
Neutropenic fever	6 (26.1)
Neutropenia	2 (8.7)
Other	4 (17.4)
Emergency department visits	
Number of patients	47 (29.6)
Total number of visits	74
Hospitalization	
Number of patients	40 (25.2)
Total number of hospitalizations	50
Reason for hospitalization	
Toxicity related	22 (40.7)
Cancer related	9 (16.7)
Intercurrent illness	19 (35.2)

Table 5 – Baseline characteristics of patients of our cohort and the two clinical trials

	This analysis	CHAARTED trial	STAMPEDE trial
	n (%)	n (%)	n (%)
Patients included	159	397	272
Age			
Median	71	64	65
Range	49–85	36–88	–
IQR	66–76	–	62–70
Performance score			
0	69 (43.4)	277 (69.8)	204 (75)
1–2	55 (34.6)	120 (30.2)	68 (25)
Unknown	35 (22)	0	0
Volume of metastasis			
Low	73 (45.9)	134 (33.8)	124 (45.6)
High	86 (54.1)	263 (66.2)	148 (54.4)
Gleason sum score			
≤ 7	54 (34)	117 (29.5)	51 (18.8)
8–10	104 (64.8)	241 (60.7)	188 (69.1)
Unknown	2 (1.3)	39 (9.8)	33 (12.1)
Baseline PSA levels			
Median	129	50.9	96.8
Range	0.19–9584	0.2–8540.1	–
IQR	25–425	–	37.8–348.1
Prior treatment			
No	137 (86.2)	289 (72.8)	261 (96)
Yes	22 (13.8)	108 (27.2)	11 (4)

CHAARTED = Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer; IQR = interquartile range; PSA = prostate-specific antigen; STAMPEDE = Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy.

4. Discussion

To our knowledge, this is the first analysis to study early docetaxel in daily practice for mHSPC patients. Overall survival in our daily practice cohort was comparable with that in the selected trial populations. Second, early docetaxel is well tolerated in our daily practice cohort of patients.

Our cohort has a median overall survival time of 60.2 mo, while the two pivotal clinical trials had median overall survival times of 57.6 and 59.1 mo (Table 2). Current literature suggests that particularly high-volume mHSPC patients gain from early docetaxel treatment [13]. This subgroup of patients in our cohort especially shows great similarity in overall survival to the clinical trial cohorts (45.6 vs 51.2 and 39.3 mo; Table 2).

Besides overall survival, we compared other survival endpoints of the clinical trials with the data in our cohort. For the CHAARTED trial, the survival endpoints show great similarity. The time to CRPC and time to clinical progression are slightly longer for our cohort than for the cohort in the CHAARTED trial. The latter might be due to the fact that in our cohort antiandrogens were added to ADT when two consecutive rises in PSA levels had occurred. To illustrate, in our cohort, 60% of the patients started antiandrogen therapy before having either clinical symptoms or radiologic progression. This antiandrogen therapy could therefore have delayed the time to clinical progression as defined by the CHAARTED investigators. As the use of antiandrogen therapy in this setting is currently debated, it probably has not been used widely in the clinical trials [11].

The STAMPEDE trial showed longer time to survival endpoints for low-volume patients than for our cohort (38.8 vs 33.8 mo for FFS), while our cohort showed longer time to survival endpoints for high-volume patients (14.0 vs 19.1 mo for FFS and 39.3 vs 45.6 mo for overall survival; Table 2). This comparison, however, is hampered by the fact that the STAMPEDE investigators retrospectively divided their patients into subgroups of burden of disease, which might cause heterogeneity in the subgroups, possibly influencing survival data. Most importantly, as mentioned earlier, overall survival for all patients of our cohort is comparable with the overall survival for all patients of the STAMPEDE trial (Table 2).

We expected that our patients might not represent the cohorts of clinical trials. Our cohort has a higher median age and more patients have an ECOG performance score of >0. Interestingly, however, tumor characteristics, that is, Gleason sum score and PSA levels, are similar (Table 5). This similarity persists when we divide the patients in subgroups based on their volume of disease (Supplementary Table 2).

Despite the relatively high number of comorbidities in our daily practice cohort, more patients completed the full six cycles than the study population of the STAMPEDE trial [6]. Second, polyneuropathy or neutropenic fever led to a relatively low number of dose reductions (Table 4). This indicates that docetaxel is well tolerated in daily practice. Polyneuropathy is a feared complication that may impact quality of life [14,15]. This may, in daily practice, be a reason to refrain from docetaxel treatment. It is often hypothesized that polyneuropathy may occur more frequently in patients with comorbidities such as diabetes and therefore might occur more easily in daily practice [16]. However, 1 yr after completing docetaxel treatment, grade II or higher polyneuropathy was reported only in 6.9% of patients. This is less frequent than in the STAMPEDE trial (11%) [6]. Our results suggest that the incidence of polyneuropathy in real-world patients with comorbidities is not higher than that in the selected study populations.

The toxicity findings are of particular interest as in the current treatment landscape, several new treatment options become available for mHSPC. Recently, abiraterone with prednisolone proved to prolong overall survival when added to ADT at the initiation of treatment compared with ADT alone [17]. In current practice, the indication of docetaxel versus abiraterone in MHSPC is not clarified fully. Most recent literature does not suggest one particular therapy as being superior in efficacy [18,19]. Abiraterone is usually well tolerated, but increases cardiovascular toxicities significantly and is much more expensive than docetaxel [20,21]. The toxicity of abiraterone in daily practice in mHSPC patients is not yet described. Our findings suggest that, in daily practice, docetaxel is a well-tolerated and effective treatment option.

We acknowledge the limitations of our analysis. As in all retrospective analyses, data collection was hampered by the lack of detailed patient or survival characteristics. Furthermore, this is a single-center observation study that could hamper external validity. With the use of hospital pharmacy records for patient selection, we were able to minimize selection bias. In contrast with the pivotal trials, radiologic imaging was not performed routinely. This might favor slightly our time to event data, as we were not able to measure radiologic progression in cases it had occurred prior to serologic or clinical progression. However, in contrast, this delay in diagnosis and thus delay in initiating second-line therapy might have a negative influence on overall survival in those patients.

5. Conclusions

Early docetaxel is well tolerated in daily practice patients with mHSPC. The overall survival in our daily practice population is comparable with that in the clinical trial population. Our findings might be of interest in the current developing treatment landscape for mHSPC.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.euros.2021.08.008.

References

[1] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394–424.

[2] American Cancer Society. Cancer facts & figures 2020. Atlanta, GA: American Cancer Society; 2020. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2020/cancer-facts-and-figures-2020.pdf

[3] Huggins C, Hodges CV. Studies on prostate cancer. I. The effect of castration, of estrogen and of androgen injection on serum phosphatases in metastatic carcinoma of the prostate. Am Assoc Cancer Res 1941;1:293.

[4] Perlmutter MA, Lepor H. Androgen deprivation therapy in the treatment of advanced prostate cancer. Rev Urol 2007;9(Suppl 1):S3–8.

[5] Sweeney CJ, Chen Y-H, Carducci M, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. N Engl J Med 2015;373:737–46.

[6] James ND, Sydes MR, Clarke NW, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. Lancet 2016;387:1163–77.

[7] Clarke NW, Ali A, Ingleby FC, et al. Addition of docetaxel to hormonal therapy in low- and high-burden metastatic hormone sensitive prostate cancer: long-term survival results from the STAMPEDE trial. Ann Oncol 2019;30:1992–2003.

[8] 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;36:1080–7.

[9] Kennedy-Martin T, Curtis S, Faries D, Robinson S, Johnston J. A literature review on the representativeness of randomized controlled trial samples and implications for the external validity of trial results. Trials 2015;16:495.

[10] O'Shea A, Kilcoyne A, Hedgire SS, Harisinghani MG. Pelvic lymph nodes and pathways of disease spread in male pelvic malignancies. Abdom Radiol (NY) 2020;45:2198–212.

[11] Heidenreich A, Bastian PJ, Bellmunt J, et al. EAU guidelines on prostate cancer. Part II: treatment of advanced, relapsing, and castration-resistant prostate cancer. Eur Urol 2014;65:467–79.

[12] Moeyart M, Maggin D, Verkuilen J. Reliability, validity, and usability of data extraction programs for single-case research designs. Behav Modif 2016;40:874–900.

[13] Parker C, Castro E, Fizazi K, et al. Prostate cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2020;31:1119–34.

[14] Ventzel L, Madsen CS, Karlsson P, et al. Chronic pain and neuropathy following adjuvant chemotherapy. Pain Med 2018;19:1813–24.

[15] Eckhoff L, Knoop A, Jensen MB, Ewertz M. Persistence of docetaxel-induced neuropathy and impact on quality of life among breast cancer survivors. Eur J Cancer 2015;51:292–300.

[16] Ewertz M, Qvortrup C, Eckhoff L. Chemotherapy-induced peripheral neuropathy in patients treated with taxanes and platinum derivatives. Acta Oncol 2015;54:587–91.

[17] Fizazi K, Tran N, Fein L, et al. Abiraterone plus prednisone in metastatic, castration-sensitive prostate cancer. N Engl J Med 2017;377:352–60.

[18] McNamara M, Sweeney C, Antonarakis ES, Armstrong AJ. The evolving landscape of metastatic hormone-sensitive prostate cancer: a critical review of the evidence for adding docetaxel or abiraterone to androgen deprivation. Prostate Cancer Prostatic Dis 2018;21:306–18.

[19] Wallis CJD, Klaassen Z, Bhindi B, et al. Comparison of abiraterone acetate and docetaxel with androgen deprivation therapy in high-risk and metastatic hormone-naïve prostate cancer: a systematic review and network meta-analysis. Eur Urol 2018;73:834–44.

[20] Iacovelli R, Ciccarese C, Bria E, et al. The cardiovascular toxicity of abiraterone and enzalutamide in prostate cancer. Clin Genitourin Cancer 2018;16:e645–53.

[21] Rydzewska LHM, Burdett S, Vale CL, et al. Adding abiraterone to androgen deprivation therapy in men with metastatic hormone-sensitive prostate cancer: a systematic review and meta-analysis. Eur J Cancer 2017;84:88–101.