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ORIGINAL ARTICLE

Efficacy and safety of 4-weekly cabazitaxel for castration-resistant prostate cancer: a multi-institutional study

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Abstract

Objective This study aimed to reveal the efficacy and safety profiles of 4-weekly cabazitaxel in patients with castration-resistant prostate cancer (CRPC).

Methods The study included 62 Japanese patients who were treated for CRPC with ≥ 2 courses of cabazitaxel between 2014 and 2017. The oncological outcomes and adverse events were compared between 16 (25.8%) and 46 (74.2%) men who were treated with standard 3-weekly and alternative 4-weekly regimens, respectively.

Results The prostate-specific antigen (PSA) response was comparable between the 3-weekly and 4-weekly regimens (median [interquartile range]: − 9.9% [− 64.5 to 13.0%] and − 30.7% [− 52.8 to 10.9%], $P = 0.89$), respectively. For patients on the 4-weekly regimen, the risks of progression (hazard ratio [HR], 95% confidence interval [CI] 1.27, 0.71–2.43, $P = 0.44$), treatment failure (HR, 95% CI 0.84, 0.48–1.55, $P = 0.57$) and any-cause mortality (HR, 95% CI 1.09, 0.58–2.17, $P = 0.79$) were comparable to those for patients on the 3-weekly regimen. The incidences of severe adverse events were also similar between the 3-weekly and 4-weekly regimens.

Conclusions 3-weekly and 4-weekly regimens of cabazitaxel showed similar efficacy and safety profiles in a real-world clinical setting. These data suggest that a 4-weekly regimen may be acceptable for selected patients.

Keywords Castration-resistant prostate cancer · Cabazitaxel · Docetaxel · Prognostic factor · Adverse event

Introduction

Androgen-deprivation therapy, alone or in combination with docetaxel or abiraterone, is standard first-line therapy for recurrent or advanced prostate cancer [1–3]. However, most cases eventually relapse and progress to castration-resistant prostate cancer (CRPC) [1–3]. Drugs targeting the androgen receptor axis (abiraterone, apalutamide, and enzalutamide), chemotherapeutic agents (docetaxel and cabazitaxel), and a radioisotope (radium-223) are now available for the treatment of CRPC [4]. In the phase 3 TROPIC trial, the next-generation taxane cabazitaxel showed beneficial effects on survival and pain relief for patients with CRPC after docetaxel chemotherapy [5, 6]. In addition, cabazitaxel showed

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anticancer effects comparable to docetaxel as first-line therapy for CRPC in the phase 3 FIRSTANA trial [7].

Two recent studies reported that a reduction in cabazitaxel dose from 25 to 20 mg/m^2 did not change prognosis but did decrease hematological toxicity; however, the prostate-specific antigen (PSA) response was inferior at the lower dose, suggesting that it may have had a weaker antitumor effect [7, 8]. Although cabazitaxel is conventionally administered on a 3-weekly schedule based on the TROPIC trial [5], a 4-weekly regimen is sometimes utilized, which not only allows the patient a 1-week drug holiday but also may improve the adverse event (AE) profile due to the prolonged cycle. However, a 4-weekly regimen reduces the relative dose intensity and may have detrimental effects on oncological outcomes.

In this multi-institutional study, we investigated the efficacy and safety of a standard 3-weekly and an alternative 4-weekly regimen of cabazitaxel in Japanese patients with CRPC.

Materials and methods

Patients

We enrolled 62 patients with CRPC who were treated with ≥ 2 courses of cabazitaxel between 2014 and 2017 in the following institutions: Kyushu University Hospital (Fukuoka), National Hospital Organization Kyushu Cancer Center (Fukuoka), Harasanshin Hospital (Fukuoka), Oita Prefectural Hospital (Oita), National Hospital Organization Kyushu Medical Center (Fukuoka), Kyushu Central Hospital (Fukuoka), Kitakyushu Municipal Medical Center (Kitakyushu), Japanese Red Cross Fukuoka Hospital (Fukuoka), JCHO Kyushu Hospital (Kitakyushu), and Miyazaki Prefectural Miyazaki Hospital (Miyazaki). The study was approved by the institutional review board of each hospital. A waiver for informed consent was granted by the institutional review boards on the condition that the patient was provided an opt-out right. The eligibility criteria included: (1) histopathologically diagnosed carcinoma of the prostate, (2) confirmed failure of primary androgen-deprivation therapy, and (3) age ≥ 20 years. Patients who received a single administration of cabazitaxel were excluded.

Treatment

Cabazitaxel was administered in 3-weekly ($n = 16$) or 4-weekly ($n = 46$) regimens of 20–25 mg/m^2 based on the TROPIC [5] and PROSELICA [8] trials, and one patient was treated with 15 mg/m^2 cabazitaxel. Prednisolone 5 mg was administered twice daily concurrently with medical or surgical castration. The choice of 3- or 4-weekly administration was based on the physician's judgement and/or the patient's preference. The cabazitaxel dose was modified according to the severity of AEs, and treatment was discontinued according to the patient's wishes or physician's judgement based on disease progression and AEs.

Endpoints

Progressive disease was defined as an increase in serum PSA of > 2 ng/mL and a 50% increase over the nadir, and/or the appearance of a new lesion or progression of one or more known lesions classified according to the Response Evaluation Criteria in Solid Tumors version 1.1 [9]. Radiographic progression was defined as measurable disease or bone scan progression. Treatment failure was defined as discontinuation of cabazitaxel chemotherapy. AEs were assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0. Clinically significant pain was defined as pain derived from prostate cancer requiring daily consumption of narcotic or non-narcotic analgesics. Performance status was determined according to the Eastern Cooperative Oncology Group criteria.

Statistical analysis

All statistical analyses were performed using JMP version 13 software (SAS Institute, Cary, NC, USA). Progression-free survival (PFS), treatment failure-free survival (TFFS), and overall survival (OS) were determined by the Kaplan–Meier method, and the log-rank test was used to compare survival time between groups. Univariate and multivariate analyses were performed using the Cox proportional hazards regression model. All tests were two sided, and $P < 0.05$ was considered significant.

Results

Patient characteristics

We enrolled a total of 62 Japanese patients with a median age of 71 years (interquartile range [IQR], 67–76 years). Patients received a median of five cycles of cabazitaxel therapy (IQR 3–9) and had previously received a median of eight cycles of docetaxel therapy (IQR, 5–12). Fifty-five (88.7%) and 3 (4.8%) men were treated with abiraterone/enzalutamide and radium-223, respectively, for CRPC. Performance status was 0 in 38 (69.1%) patients, 1 in 11 (20.0%), and ≥ 2 in 6 (10.9%). The median pretreatment serum PSA level was 81.1 ng/mL (IQR, 24.0–281.6 ng/mL). Most patients had metastatic lesions in lymph nodes ($n = 36$, 58.1%), bone ($n = 55$, 88.7%), and viscera, including liver and lung ($n = 18$, 29.0%). The starting dose of

cabazitaxel was ≤ 20 mg/m^2 and > 20 mg/m^2 in 21 (33.9%) and 41 (66.1%) men, respectively (Table 1). In 56 (90.3%) men, pegfilgrastim was administered for primary prophylaxis against febrile neutropenia. Of the 62 patients, 16 (25.8%) and 46 (74.2%) were treated with the 3-weekly and 4-weekly regimens, respectively. The characteristics of the two patient groups were comparable, except

Table 1 Patient characteristics according to cabazitaxel treatment schedule

Variables	All ($n=62$)	Treatment schedule of cabazitaxel		*P* value
		3 weekly ($n=16$)	4 weekly ($n=46$)	
Median age, years (IQR)	71 (67–76)	70 (64–75)	72 (69–76)	0.52
Median PSA at diagnosis, ng/ml (IQR)	48.3 (18.4–414.6)	41.7 (15.2–178.5)	59.7 (19.4–432.8)	0.40
NA	2	0	2	
Biopsy Gleason score, *n* (%)				
≤ 7	11 (18.6%)	4 (25.0%)	7 (16.3%)	
8	11 (18.6%)	4 (25.0%)	7 (16.3%)	
≤ 9	37 (62.7%)	8 (50.0%)	29 (67.4%)	0.48
NA	3	0	3	
Prior local therapy, *n* (%)				
Absence	43 (69.4%)	11 (68.8%)	32 (69.6%)	
Presence	19 (30.6%)	5 (31.3%)	14 (30.4%)	0.95
Time to CRPC, years (IQR)	1.4 (0.8–2.5)	1.9 (0.8–4.8)	1.2 (0.6–2.4)	0.18
NA	6	0	6	
Cycle number of docetaxel (IQR)	8 (5–12)	7 (6–15)	8 (5–12)	0.90
Prior treatment for CRPC, *n* (%)				
Abiraterone/enzalutamide	55 (88.7%)	12 (75.0%)	43 (93.5%)	0.060
Radium-223	3 (4.8%)	0 (0.0%)	3 (6.5%)	0.17
ECOG PS at pretreatment, *n* (%)				
0	38 (69.1%)	10 (62.5%)	28 (71.8%)	
1	11 (20.0%)	3 (18.8%)	8 (20.5%)	
≥ 2	6 (10.9%)	3 (18.8%)	3 (7.7%)	0.52
NA	7	0	7	
Pain at pre-treatment, *n* (%)				
Absence	34 (54.8%)	9 (56.3%)	25 (54.3%)	
Presence	28 (45.2%)	7 (43.8%)	21 (45.7%)	0.90
Median PSA at pre-treatment, ng/ml (IQR)	81.1 (24.0–281.6)	48.9 (9.9–426.1)	90.8 (29.6–219.7)	0.55
Metastatic sites, *n* (%)				
Lymph node	36 (58.1%)	7 (43.8%)	29 (63.0%)	0.18
Bone	55 (88.7%)	14 (87.5%)	41 (89.1%)	0.86
Visceral	18 (29.0%)	3 (18.8%)	15 (32.6%)	0.28
Cycle number of cabazitaxel (IQR)	5 (3–9)	6 (3–11)	5 (3–9)	0.67
Cabazitaxel starting dose				
≤ 20 mg/m^2	21 (33.9%)	2 (12.5%)	19 (41.3%)	
> 20 mg/m^2	41 (66.1%)	14 (87.5%)	27 (58.7%)	0.026*
Use of pegfilgrastim				
Absence	6 (9.7%)	2 (12.5%)	4 (8.7%)	
Presence	56 (90.3%)	14 (87.5%)	42 (91.3%)	0.67

*Statistically significant

CRPC castration-resistant prostate cancer, *ECOG-PS* Eastern Cooperative Oncology Group-Performance Status, *IQR* interquartile range, *NA* not available, *PSA* prostate-specific antigen

that significantly more patients on the 4-weekly regimen received a reduced starting dose (Table 1).

Oncological outcomes of patients treated with 3- or 4-weekly cabazitaxel regimens

PSA response data were available for 54 men. A decrease in PSA was observed in 38 patients (70.4%), of whom 27 (50.0%) and 16 (29.6%) achieved > 30% and > 50% PSA decline from baseline, respectively. During the observation period (median 7.6 months; IQR 5.7–13.8 months), disease progression, treatment failure, and all-cause mortality were observed in 56 (90.3%), 54 (87.1%), and 42 patients (67.7%), respectively. Among the entire patient cohort, 44 (71.0%), 8 (12.9%), and 2 (3.2%) patients experienced treatment failure due to disease progression, AEs, and patient request, respectively, and cabazitaxel treatment was completed in the remaining 8 patients (10.8%). Among the 16 patients on the 3-weekly regimen, 12 (75.0%), 3 (18.8%), and 1 (6.3%) discontinued cabazitaxel chemotherapy due to disease progression, AEs, and patient request, respectively. For the 46 patients on the 4-weekly regimen, the corresponding numbers were 32 (69.6%), 5 (10.9%), and 1 (2.2%), respectively. The median PFS, TFFS, and OS for the 62 patients were 4.3 months (95% CI 2.8–5.5 months), 4.3 months (95% CI 3.0–6.0 months), and 9.3 months (95% CI 7.5–13.7 months), respectively.

Next, we compared the response to treatment and prognoses of patients on 3- and 4-weekly regimens. The PSA response was comparable between the two groups, with median reductions of −9.9% (IQR −64.5 to 13.0%) for the 3-weekly regimen and −30.7% (IQR −52.8 to 10.9%) for the 4-weekly regimen ($P = 0.89$, Fig. 1a). The risks of progression (hazard ratio [HR], 95% confidence interval [CI] 1.27, 0.71–2.43, $P = 0.44$), treatment failure (HR, 95% CI 0.84, 0.48–1.55, $P = 0.57$), and any-cause mortality (HR, 95% CI 1.09, 0.58–2.17, $P = 0.79$) for patients on the 4-weekly regimen were comparable to those on the 3-weekly regimen. After adjustment for the lower starting cabazitaxel dose of patients on the 4-weekly regimen, the risks of progression (HR, 95% CI 1.10, 0.59–2.17, $P = 0.77$), treatment failure (HR, 95% CI 0.76, 0.41–1.45, $P = 0.39$), and any-cause mortality (HR, 95% CI 1.01, 0.49–2.13, $P = 0.98$) remained comparable to those of patients on the 3-weekly regimen.

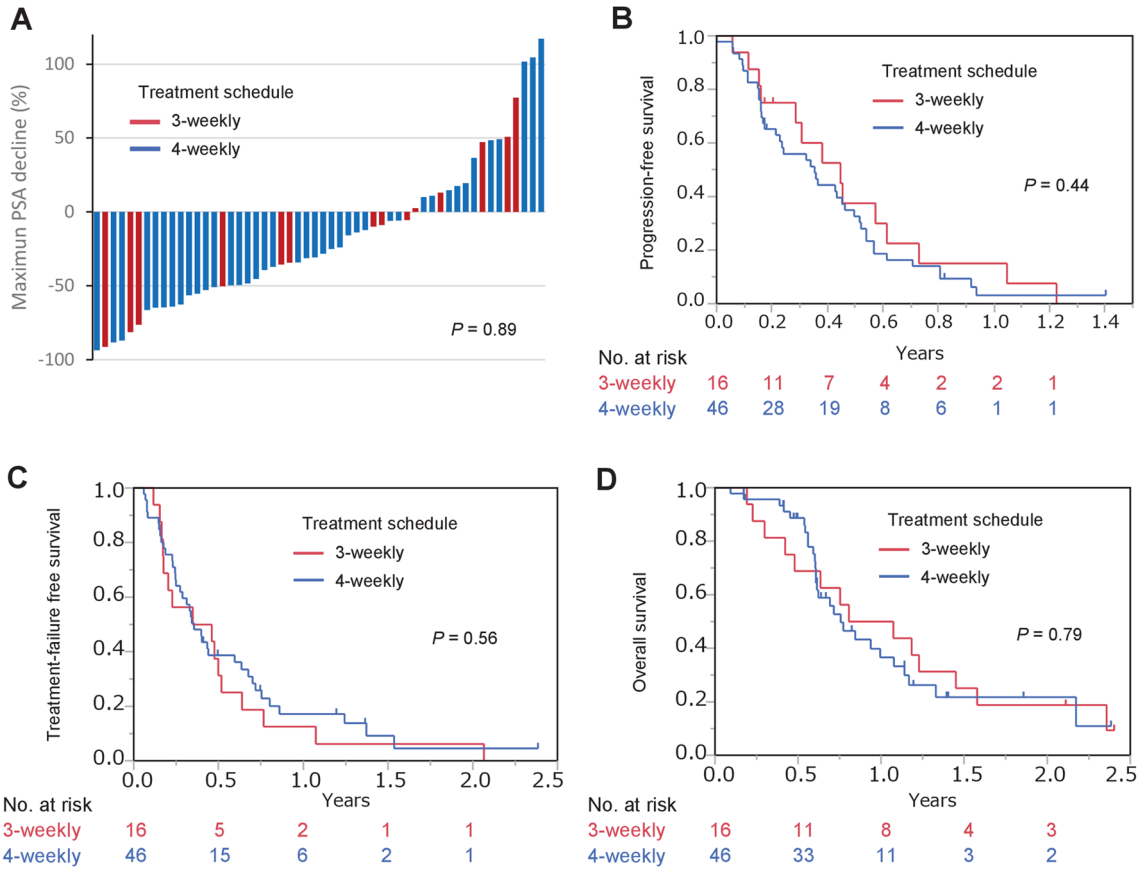

Fig. 1 Anticancer effects of 3-weekly and 4-weekly cabazitaxel chemotherapy. **a** Waterfall plot of the maximum decline in PSA from baseline for the 16 and 46 CRPC patients on the 3-weekly and 4-weekly treatment regimens, respectively. **b–d** Kaplan–Meier survival curves of PFS (**b**), TFFS (**c**), and OS (**d**) in CRPC patients stratified by treatment regimen

Consistent with this finding, Kaplan–Meier curves showed that PFS (Fig. 1b), TFFS (Fig. 1c) and OS (Fig. 1d) were comparable for the two groups.

Safety profiles of patients treated with 3- and 4-weekly cabazitaxel regimens

Grade ≥ 3 neutropenia and febrile neutropenia were observed in 47 (75.8%) and 19 (30.6%) patients, respectively. In addition to the hematological AEs, severe non-hematological AEs were observed in 12 (19.4%) men, with a similar incidence in patients on the 3- and 4-weekly regimens (Table 2).

Discussion

The standard schedule of 3-weekly cabazitaxel chemotherapy for CRPC is based on evidence from the phase 3 TROPIC trial. However, in an effort to obtain improved outcomes for both efficacy and safety, several trials have been conducted with alternative treatment regimens. The Spanish Oncology Genitourinary Group (SOGUG) trial obtained satisfactory antitumor effects with a weekly cabazitaxel regimen in patients who were unfit for the 3-weekly regimen (PSA responses of ≥ 50%, 34.8%; median PSA-PFS, 4.8 months) [10]. Similarly, in the phase 2 ConCab trial, a weekly regimen of 10 mg/m^2 cabazitaxel and the 3-weekly regimen of 25 mg/m^2 cabazitaxel showed comparable antitumor responses [11], and a 2-weekly regimen of 16 mg/m^2 also showed satisfactory antitumor effects (PSA responses of ≥ 50%, 40.5%; median PSA-PFS, 4.5 months) [12]. In addition to modifications of the treatment schedule, dose modifications have also been investigated [7, 8]. In the PROSELICA trial, 20 mg/m^2 cabazitaxel demonstrated a non-inferior OS compared with 25 mg/m^2 cabazitaxel, whereas the PSA response and time to PSA progression were both inferior [8]. Similarly, in the FIRSTANA trial, 20 mg/m^2 and 25 mg/m^2 cabazitaxel were comparable with respect to PSA-PFS and OS, but the PSA response trended towards inferiority in the 20 mg/m^2 group [7]. In the present study comparing 3- and 4- weekly cabazitaxel regimens, we found comparable efficacy in the PSA response, PFS, TFFS, and OS. After adjustment for a lower starting dose on the 4-weekly regimen, the median risks of progression, treatment failure, and any-cause mortality were 10%, − 24%, and 1% higher, respectively, on the 4-weekly compared with the 3-weekly regimen. These results indicate an acceptable difference in antitumor effects because the combination of a slightly higher risk of progression and lower risk of treatment failure resulted in comparable OS for the two regimens.

The reduced relative dose intensity of the 4-weekly regimen suggested that it may have a better safety profile than the 3-weekly regimen. The SOGUG trial found lower toxicities with the weekly regimen in patients deemed unfit for the standard cabazitaxel regimen (grade ≥ 3 neutropenia, 2.8%; febrile neutropenia, 0%) [10]. Similarly, the ConCab trial showed reduced hematological toxicity with weekly 10 mg/m^2 compared with 3-weekly 25 mg/m^2 cabazitaxel [11], and another trial found lower toxicity with 2-weekly 16 mg/m^2 cabazitaxel (grade ≥ 3 neutropenia, 11.6%; febrile neutropenia, 4.7%) [12]. In the FIRSTANA and PROSELICA trials, the incidence of AEs was lower in patients treated with 20 mg/m^2 compared with 25 mg/m^2 cabazitaxel [7, 8]. In the present study, we observed similar safety profiles among patients on the 3- and 4-weekly regimens. Taken together, these data suggest that the efficacy and safety profiles of the modified 4-weekly regimen are comparable to those of the standard 3-weekly regimen. The 4-weekly regimen is more convenient for practitioners, patients, and caregivers alike, provides patients with a drug holiday, and has economic benefits compared with the 3-weekly regimen. However, further studies on this alternative treatment schedule should be performed.

This study has some limitations. First, this was a retrospective study and included a small number of cases. Assignment of the treatment schedule was not randomized, which may have introduced unexpected biases. In addition, the study was conducted using data from multiple institutions, which may have resulted in diagnostic and therapeutic variations. Finally, quality-of life and patient-reported outcomes were not investigated in this study.

In conclusion, a 4-weekly regimen of cabazitaxel demonstrated similar efficacy and safety profiles compared with the standard 3-weekly regimen in a real-world clinical setting. The data suggest that the 4-weekly regimen will be acceptable for patients who desire less frequent treatment and are deemed eligible by their physicians. However, further investigation is required to confirm and extend these findings.

Table 2 Grade ≥ 3 adverse events according to cabazitaxel treatment regimen

	All (n = 62)	Treatment schedule of cabazitaxel		P value
		3 weekly (n = 16)	4 weekly (n = 46)	
Hematological				
Neutropenia (≥ G3)	47 (75.8%)	11 (68.8%)	36 (78.3%)	0.45
Febrile neutropenia (≥ G3)	19 (30.6%)	5 (31.3%)	14 (30.4%)	0.95
Non-hematological (≥ G3)	12 (19.4%)	3 (18.8%)	9 (19.6%)	0.94

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Compliance with ethical standards

Conflict of interest The authors have no conflict of interest to declare.

Ethical approval IRB approval from Kyushu University Hospital, National Hospital Organization Kyushu Cancer Center, Harasanshin Hospital, Oita Prefectural Hospital, National Hospital Organization Kyushu Medical Center, Kyushu Central Hospital, Kitakyushu Municipal Medical Center, Japanese Red Cross Fukuoka Hospital, JCHO Kyushu Hospital, and Miyazaki Prefectural Miyazaki Hospital.

References

1. Shiota M, Yokomizo A, Eto M (2016) Taxane chemotherapy for Hormone-Naïve prostate cancer with its expanding role as breakthrough strategy. Front Oncol 5:304
2. Shiota M, Eto M (2016) Current status of primary pharmacotherapy and future perspectives toward upfront therapy for metastatic hormone-sensitive prostate cancer. Int J Urol 23:360–369
3. Komura K, Sweeney CJ, Inamoto T, Ibuki N, Azuma H, Kantoff PW (2018) Current treatment strategies for advanced prostate cancer. Int J Urol 25:220–231
4. Fujimoto N (2016) Novel agents for castration-resistant prostate cancer: early experience and beyond. Int J Urol 23:114–121
5. de Bono JS, Oudard S, Ozguroglu M, Hansen S, Machiels JP, Kocak I, Gravis G, Bodrogi I, Mackenzie MJ, Shen L, Roessner M, Gupta S, Sartor AO, Investigators TROPIC (2010) Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. Lancet 376:1147–1154
6. Bahl A, Oudard S, Tombal B, Ozgüroglu M, Hansen S, Kocak I, Gravis G, Devin J, Shen L, de Bono JS, Sartor AO, Investigators TROPIC (2013) Impact of cabazitaxel on 2-year survival and palliation of tumour-related pain in men with metastatic castration-resistant prostate cancer treated in the TROPIC trial. Ann Oncol 24:2402–2408
7. Oudard S, Fizazi K, Sengeløv L, Daugaard G, Saad F, Hansen S, Hjälm-Eriksson M, Jassem J, Thiery-Vuillemin A, Caffo O, Castellano D, Mainwaring PN, Bernard J, Shen L, Chadjaa M, Sartor O (2017) Cabazitaxel versus docetaxel as first-line therapy for patients with metastatic castration-resistant prostate cancer: a randomized phase III trial-FIRSTANA. J Clin Oncol 35:3189–3197
8. Eisenberger M, Hardy-Bessard AC, Kim CS, Géczi L, Ford D, Mourey L, Carles J, Parente P, Font A, Kacso G, Chadjaa M, Zhang W, Bernard J, de Bono J (2017) Phase III study comparing a reduced dose of cabazitaxel (20 mg/m^2) and the currently approved dose (25 mg/m^2) in postdocetaxel patients with metastatic castration-resistant prostate cancer-PROSELICA. J Clin Oncol 35:3198–3206
9. Scher HI, Halabi S, Tannock I, Morris M, Sternberg CN, Carducci MA, Eisenberger MA, Higano C, Bubley GJ, Dreicer R, Petrylak D, Kantoff P, Basch E, Kelly WK, Figg WD, Small EJ, Beer TM, Wilding G, Martin A, Hussain M, Prostate Cancer Clinical Trials Working Group (2008) Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group. J Clin Oncol 26:1148–1159
10. Climent MÁ, Pérez-Valderrama B, Mellado B, Fernández Parra EM, Fernández Calvo O, Ochoa de Olza M, Muinelo Romay L, Anido U, Domenech M, Hernando Polo S, Arranz Arija JÁ, Caballero C, Juan Fita MJ, Castellano D (2017) Weekly cabazitaxel plus prednisone is effective and less toxic for 'unfit' metastatic castration-resistant prostate cancer: phase II Spanish Oncology Genitourinary Group (SOGUG) trial. Eur J Cancer 87:30–37
11. Yachnin J, Gilje B, Thon K, Johansson H, Brandberg Y, Panaretakis T, Ullén A (2018) Weekly versus 3-weekly cabazitaxel for the treatment of castration-resistant prostate cancer: a randomised phase II trial (ConCab). Eur J Cancer 97:33–40
12. Clément-Zhao A, Auvray M, Aboudagga H, Blanc-Durand F, Angelergues A, Vano YA, Mercier F, El Awadly N, Verret B, Thibault C, Oudard S (2018) Safety and efficacy of 2-weekly cabazitaxel in metastatic castration-resistant prostate cancer. BJU Int 121:203–208