Journal of Geriatric Oncology xxx (2020) xxx

Contents lists available at ScienceDirect

Journal of Geriatric Oncology

Cabazitaxel in patients aged ≥80 years with castration-resistant prostate cancer: Results of a post-marketing surveillance study in Japan

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ARTICLE INFO

Article history:
Received 29 October 2019
Received in revised form 23 January 2020
Accepted 26 February 2020
Available online xxxx

Keywords:
Cabazitaxel
Castration-resistant prostate cancer
Post-marketing drug surveillance
Geriatric oncology

ABSTRACT

Objectives: Data on the safety and efficacy of cabazitaxel in patients aged ≥80 years with castration-resistant prostate cancer (CRPC) are limited. We report the safety (adverse drug reactions [ADRs]) and efficacy (overall survival [OS], time to treatment failure [TTF], and prostate-specific antigen [PSA] response rates) in patients aged <80 or ≥80 years treated with cabazitaxel for CRPC in clinical practice.
Materials and methods: We performed post-hoc subgroup analyses of a Japanese post-marketing surveillance study involving 662 patients with CRPC treated with cabazitaxel between September 2014 and June 2016.
Results: In patients aged <80 (n = 610) and ≥80 years (n = 49), median PSA at baseline was 168.7 and 109.0 ng/mL, and 86.7% and 83.7% of patients were previously treated with enzalutamide and/or abiraterone. ADRs (all grade) occurred in 77.2% and 79.6% of patients aged <80 and ≥80 years, with grade three/worse ADRs in 61.8% and 63.3% of patients. Hematologic toxicities were the most common grade three/worse ADRs, including neutropenia, febrile neutropenia, and anemia in both subgroups. No specific ADRs were observed in patients aged ≥80 years. The PSA response and median OS and TTF were 28.3%, 292 days, and 116 days in patients aged ≥80 years, and 29.7%, 319 days, and 125 days in patients aged <80 years.
Conclusion: Cabazitaxel could be a treatment option for CRPC in patients aged ≥80 years based on its safety and efficacy profiles. This is the first report to investigate the safety and efficacy of cabazitaxel in patients aged ≥80 years with CRPC.

1. Introduction

Prostate cancer (PC) is a major cancer with an estimated incidence of 445,000 cases and 107,000 deaths in Europe in 2018 based on data from the GLOBOCAN surveillance program [1]. Worldwide, PC is one of the most commonly diagnosed cancers, accounting for 7.1% of cases; for comparison, lung cancer and breast cancer were each reported to account for 11.6% of cases [2]. PC is also a significant cancer in Japan, with an age-standardized incidence rate of 30.4 per 100,000 person-years and a mortality rate of 5.0 per 100,000 person-years [3]. Between 2000–04 and 2010–14, the age-standardized 5-year survival rate increased from 85.9% to 93.0% in Japan [4], which may reflect continued improvements in treatment strategies.

Although androgen deprivation therapy is the mainstay treatment for patients with advanced PC, many patients experience castration-resistant prostate cancer (CRPC) [5]. Since 2008, chemotherapy with docetaxel was the main treatment option for patients with CRPC. More recently, several new treatment options were introduced, including the androgen signaling inhibitors enzalutamide and abiraterone, radium-223, and the new taxane, cabazitaxel [6,7]. These four drugs are now recommended for the treatment of CRPC in several guidelines for PC [8].

Cabazitaxel is a second generation taxane that was demonstrated to be effective in combination with prednisone in men with metastatic CRPC in the international TROPIC study [9], which led to its approval in the US in 2010 and Europe in 2011.

Older patients with PC or CRPC are typically frailer and less able to tolerate taxane-based chemotherapy than are younger patients. Indeed, subgroup analyses of the TAX327 study suggested that docetaxel was associated with trends towards worse tolerability with advancing age [10]. As a consequence, in 2013, the International Society of Geriatric Oncology established a working group to update recommendations on the management of older patients with PC. The working group proposed that the treatment approach should be modified according to the

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https://doi.org/10.1016/j.jgo.2020.02.014

patient's health status, not based on chronological age, such that healthy/fit patients should receive the same regimen as younger patients [11]. By contrast, vulnerable patients with reversible impairments should receive standard treatment after medical interventions and frail patients with non-reversible impairments should receive adapted treatment [11].

Contrary to these guidelines, an international registry of 333 patients aged ≥70 years old suggested that first-line taxane therapy may be more beneficial than alternative, non-taxane-based therapies in older patients with metastatic CRPC [12]. Moreover, cabazitaxel showed more favorable efficacy than mitoxantrone in patients aged ≥65 years (hazard ratio [HR] 0.62, 95% confidence interval [CI] 0.50–0.78) than in younger patients (<65 years; HR 0.81; 95% CI 0.61–1.08) in the TROPIC study; however, the authors did not compare the safety between these two groups of patients [9]. Considering this background, it is important to evaluate the safety and efficacy of treatments for PC in older patients.

Preliminary results of compassionate-use programs in Europe involving 746 patients (<70 years, 421 patients; 70–74 years, 180 patients; ≥75 years, 145 patients) suggested that the tolerability of cabazitaxel was similar in all three age-groups [13]. The analysis also revealed that prophylactic use of granulocyte colony-stimulating factor (G-CSF) was associated with a reduced risk of grade three/worse neutropenia and/or neutropenic complications [13]. However, there are limited efficacy and safety data for older patients treated with cabazitaxel in real-world daily practice.

Following its approval in Japan in 2014, a post-marketing surveillance study (PMS) of cabazitaxel was started to monitor its safety and tolerability in real-world clinical practice [14]. The PMS registered 662 patients who were newly treated with cabazitaxel, regardless of age, and confirmed the efficacy and safety of cabazitaxel in real-world daily practice.

A recent retrospective observational study of 47 patients treated with cabazitaxel in Japan found no significant difference in OS between patients aged <75 (39 patients) or ≥75 (eight patients) years old [15]. However, the study was relatively small and did not compare tolerability between the two age-groups. Therefore, we used data from the Japanese PMS to characterize the safety and outcomes of cabazitaxel in older patients. To achieve this, we performed post-hoc analyses of the PMS in which we divided the patients into two age-groups: <80 and ≥80 years old.

2. Materials and Methods

2.1. Ethics

This survey was designed by Sanofi, reviewed by the Japanese Pharmaceutical and Medical Devices Agency (PMDA), and conducted in compliance with the Ministerial Ordinance on Good Postmarketing Study Practice for Drugs (GPSP) in Japan. Because this survey was conducted in accordance with Japanese regulations and all data were collected using anonymized forms that could not be linked to individual patients, informed consent was not necessary.

2.2. Survey Objectives

As previously described [14], this PMS was designed in order to collect information on cabazitaxel in real-world clinical settings in Japan, with a focus on unexpected ADRs, occurrence of ADRs, factors that may affect safety, and factors that may affect efficacy. In the present report, we describe the safety and efficacy of cabazitaxel in two age-groups of patients (<80 and ≥80 years old). We chose 80 years as a cutoff because there are no published data on the treatment outcomes in patients ≥80 years old.

2.3. Patients and PMS Design

The design of this PMS is described in more detail in a prior report [14]. Briefly, patients with CRPC who started treatment with cabazitaxel during a four-year registration period from September 2014 were registered in this all-patient PMS. Registration was to stop once ~500 patients were registered or at the end of the four-year period, whichever came first.

The physicians completed case-report forms to record patient demographics, Eastern Cooperative Oncology Group performance status (ECOG PS), disease characteristics, treatment history and concomitant therapies for PC, and prostate-specific antigen (PSA) levels before the start of cabazitaxel, and additional forms to record exposure to cabazitaxel and prednisolone in each cycle, premedications, use of concomitant drugs, prophylactic use of G-CSF, PSA, and adverse events (AEs)/adverse drug reactions (ADRs). The grade of AEs/ADRs was reported by the physician according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

This was a non-interventional survey, and all treatments, including the use of cabazitaxel, prophylaxis, and concomitant drugs, were at the attending physician's discretion and in accordance with routine clinical practice.

2.4. Statistical Analyses

ADRs and efficacy outcomes (OS, TTF, and PSA response) were assessed for the overall population and in the two groups separately. All data were analyzed descriptively by calculating the number (percent) of patients and mean ± standard deviation or median (range) as appropriate. No formal statistical testing or between-group comparisons were done in these post-hoc analyses. For OS and TTF, we calculated the median (95% CI). SAS 9.2 or 9.4 (SAS Institute, Cary, NC, USA) was used for data analysis.

3. Results

3.1. Patient Characteristics and Prior Treatments

A total of 662 patients had been registered as of June 2015, at which time further registration was stopped, although it was planned to complete patient registration once 500 patients had been enrolled (or upon reaching the end of the four-year registration period). Of these 662 patients, two were excluded from the full analysis population; the case-report form was unavailable for the first patient and was completed by unauthorized personnel (and deemed ineligible) for the second patient. Another patient was excluded from the present analyses because the patient's age was unknown. Therefore, we analyzed data for 659 patients, of which 610 were <80 years old and 49 were ≥80 years old (Fig. 1).

The characteristics of patients in the <80 and ≥80 year-old groups are shown in Table 1. The median (range) ages were 70.0 (43–79) and 81.0 (80–91) years, respectively. About half of the patients in the <80 year-old group were ≥65 to <75 years old. ECOG PS scores were 0, 1, and ≥2 in 57.1%, 28.6%, and 14.3% of patients aged ≥80 years. The median (range) PSA at baseline was 168.7 (0.01–16,697) ng/mL in the <80 year-old group and 109.0 (1.06–2060) ng/mL in the ≥80 year-old group.

About 57% of patients in each group died during the observation period (57.2% of patients aged <80 years and 57.1% of patients aged ≥80 years). The causes of death were mainly due to primary disease, followed by AEs (Fig. 1). Details of ADRs resulting in death are given in the prior report [14]. The treatment-related AE that resulted in death in the ≥80 year-old group was interstitial lung disease in one patient (2.0%). Fourteen patients (2.3%) in the <80 year-old group died from ADRs, which included febrile neutropenia in seven patients, interstitial lung disease in two patients, and a combination of febrile

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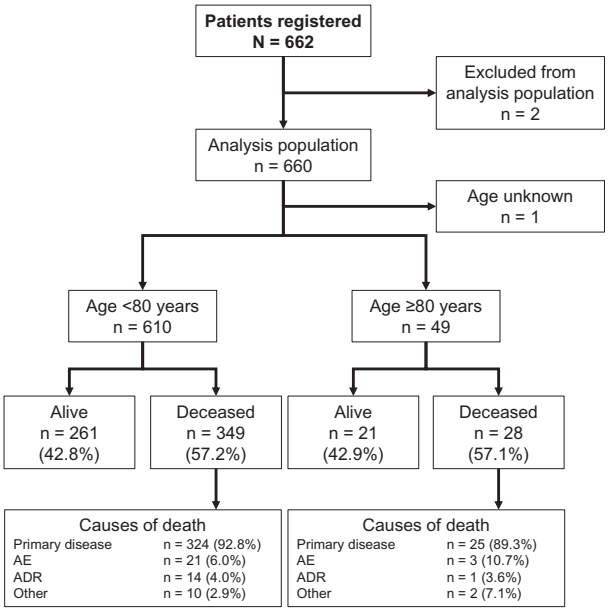

Fig. 1. Patient disposition and treatment outcomes. The other causes of death were as follows: <80 year-old group: aspiration pneumonia (two patients), cerebral hemorrhage following a fall (one patient), nosebleed (one patient), choking (one patient), drowning (one patient), and not otherwise specified (four patients); ≥80 year-old group: brain trauma following a fall (one patient) and cancerous DIC trauma (one patient). AE, adverse event.

neutropenia, interstitial lung disease, and pneumonia in one patient. The other four deaths were related to disseminated intravascular coagulation, multiple organ dysfunction syndrome, subdural hematoma, and thrombocytopenia.

The patients' treatment history is also shown in Table 1. About one-third of patients in both groups had received local treatment as a curative intent. The majority of patients had been treated with enzalutamide and/or abiraterone. Nearly all of the patients in both groups (98% [597/610] and 98% [48/49]) had previously received docetaxel, with a median of nine cycles in both groups.

3.2. Cabazitaxel Exposure

Cabazitaxel exposure is shown in Table 2. The median initial dose of cabazitaxel was 20.0 mg/m^2 and the median average dose was 20.0 mg/m^2/cycle in both groups. The percentages of patients who received an initial dose of <15 mg and an average dose of <15 mg/m^2 were 6.1% and 8.2%, respectively, in the ≥80 year-old group. The corresponding values in the <80 year-old group were 2.3% and 1.8%. Overall, 8.2% of patients in the ≥80 year-old group and 18.7% in the <80 year-old group received an average dose of ≥25 mg/m^2. In the ≥80 year-old group, the median cumulative dose, actual dose intensity, and relative dose intensity were 80.0 mg/m^2, 5.16 mg/m^2/week, and 61.9%, respectively. The corresponding values in the <80 year-old group were 85.0 mg/m^2, 5.63 mg/m^2/week, and 67.5%, respectively. Patients in both groups received a median of four cycles of cabazitaxel. About 81% of patients in both groups received prophylactic G-CSF in any cycle.

3.3. Safety

The rate of ADRs, including events related to laboratory abnormalities, is summarized in Table 3, broken down by all-grade and CTCAE grade three/worse. For non-hematologic and hematologic ADRs, all of the events occurring in the ≥80 year-old group are shown together with the corresponding rates in the <80 year-old group. ADRs were observed in 39 patients (79.6%) in the ≥80 year-old group, including grade three/worse ADRs in 31 patients (63.3%). In the <80 year-old group, ADRs were observed in 471 patients (77.2%), including grade three/worse ADRs in 377 patients (61.8%).

Table 1
Patient characteristics and treatment history.

	<80 years old (n = 610)	≥80 years old (n = 49)
Age, years		
Mean ± SD	69.0 ± 6.3	81.9 ± 2.5
Median (range)	70.0 (43–79)	81.0 (80–91)
Age-group, years		
<65	133 (21.8)	0
≥65 to <75	346 (56.7)	0
≥75	131 (21.5)	49 (100.0)
ECOG PS		
0	384 (63.0)	28 (57.1)
1	179 (29.3)	14 (28.6)
≥2	46 (7.5)	7 (14.3)
Unknown	1 (0.2)	0
PSA at baseline, ng/mL	n = 604	n = 49
Mean ± SD	519.0 ± 1241.0	290.3 ± 431.8
Median (range)	168.7 (0.01–16,697)	109.0 (1.06–2060)
Prior curative focal therapy	197 (32.3)	15 (30.6)
Prior palliative radiotherapy	184 (30.2)	13 (26.5)
Treatment with new-generation anti-AR agents	529 (86.7)	41 (83.7)
Enzalutamide	487 (79.8)	39 (79.6)
Abiraterone	336 (55.1)	26 (53.1)
Both	294 (48.2)	24 (49.0)
Not previously treated with docetaxel	10 (1.6)	1 (2.0)
Docetaxel chemotherapy		
Initial dose		
75 mg/m^2	116 (19.0)	10 (20.4)
70 mg/m^2	223 (36.6)	11 (22.5)
60 mg/m^2	117 (19.2)	14 (28.6)
Other	124 (20.3)	13 (26.5)
Missing data[a]	30 (4.9)	1 (2.0)
Number of cycles[b]		
Mean ± SD	12.4 ± 11.2	14.6 ± 21.4
Median (range)	9.0 (1–83)	8.5 (1–143)

Values are expressed as number (%) of patients, unless specified otherwise.
SD, standard deviation; ECOG PS, Eastern Cooperative Oncology Group performance status; PSA, prostate-specific antigen; AR, androgen receptor.
[a] Missing data for prior treatment history, prior docetaxel treatment, or prior docetaxel dose.
[b] The number of cycles was available for 581 patients aged <80 years and 48 patients aged ≥80 years.

Table 2
Cabazitaxel exposure.

	<80 years old (n = 610)	≥80 years old (n = 49)
Initial cabazitaxel dose, mg/m^2	20.0 (10.0–26.3)	20.0 (10.0–25.0)
<15	14 (2.3)	3 (6.1)
≥15 to <20	105 (17.2)	12 (24.5)
≥20 to <25	299 (49.0)	27 (55.1)
≥25	192 (31.5)	7 (14.3)
Average cabazitaxel dose, mg/m^2/cycle	20.0 (10.0–25.5)	20.0 (11.9–25.0)
<15	11 (1.8)	4 (8.2)
≥15 to <20	137 (22.5)	14 (28.6)
≥20 to <25	348 (57.1)	27 (55.1)
≥25	114 (18.7)	4 (8.2)
Cumulative dose, mg/m^2	85.0 (10.0–445.0)	80.0 (18.0–350.0)
Actual dose intensity, mg/m^2/week	5.63 (1.48–8.41)	5.16 (2.51–8.33)
Relative dose intensity, %	67.5 (17.8–101.0)	61.9 (30.2–100.0)
Number of cycles	4 (1–18)	4 (1–15)
Prophylactic G-CSF at any time during the treatment period	496 (81.3)	40 (81.6)

Values are expressed as median (range) or number (%) of patients.
G-CSF, granulocyte colony-stimulating factor.

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Table 3
Summary of the most common adverse drug reactions.

	<80 years old (n = 610)		≥80 years old (n = 49)	
	All grades	Grade ≥3	All grades	Grade ≥3
Patients with any ADR	471 (77.2)	377 (61.8)	39 (79.6)	31 (63.3)
Number of ADRs	1050	602	62	41
Non-hematologic ADRs				
Diarrhea	64 (10.5)	20 (3.3)	2 (4.1)	1 (2.0)
Decreased appetite	48 (7.9)	11 (1.8)	1 (2.0)	0
Malaise	38 (6.2)	2 (0.3)	2 (4.1)	1 (2.0)
Pyrexia	21 (3.4)	3 (0.5)	1 (2.0)	1 (2.0)
Dysgeusia	14 (2.3)	0	1 (2.0)	0
Interstitial lung disease	8 (1.3)	6 (1.0)	1 (2.0)	1 (2.0)
Pneumonia	5 (0.8)	4 (0.7)	1 (2.0)	1 (2.0)
Rash	1 (0.2)	0	1 (2.0)	0
Urinary tract infection	0	0	1 (2.0)	1 (2.0)
Restlessness	0	0	1 (2.0)	1 (2.0)
Meningitis	0	0	1 (2.0)	0
Hematologic ADRs				
Neutropenia	295 (48.4)	241 (39.5)	28 (57.1)	21 (42.9)
Febrile neutropenia	112 (18.4)	107 (17.5)	7 (14.3)	6 (12.2)
Anemia	98 (16.1)	58 (9.5)	3 (6.1)	2 (4.1)
Thrombocytopenia	74 (12.1)	35 (5.7)	5 (10.2)	1 (2.0)
Leukopenia	70 (11.5)	45 (7.4)	4 (8.2)	3 (6.1)
Lymphocytopenia	2 (0.3)	1 (0.2)	1 (2.0)	0

Values are expressed as number (%) of patients.
ADR, adverse drug reaction.

Non-hematologic ADRs observed in two or more patients in the ≥80 year-old group were malaise and diarrhea (two patients each). In the <80 year-old group, notable ADRs were decreased appetite (48 [7.9%]), pyrexia (21 [3.4%]), interstitial lung disease (eight [1.3%]), and pneumonia (five [0.8%]).

In the ≤80 year-old group, neutropenia and febrile neutropenia occurred in 57.1% and 14.3% of patients, respectively. In the <80 year-old group, these ADRs occurred in 48.4% and 18.4% of patients, respectively. Anemia or leukopenia occurred in 6.1% and 8.2% of patients in the ≥80 year-old group (Table 3).

Grade four ADRs observed in the ≥80 year-old group were neutropenia in 14 patients, leukocytopenia in one patient, and thrombocytopenia in one patient.

3.4. Efficacy

Median OS was 319 days (95% CI 296.0–not reached) in the <80 year-old group and 292 days (95% CI 199.0–not reached) in the ≥80 year-old group, based on 308 (50.7%) and 26 (54.2%) patients with events (Fig. 2). The median TTF was about 116 days (95% CI 108.0–135.0) in the <80 year-old group and 125 days (95% CI 79.0–172.0) in the ≥80 year-old group (Fig. 3).

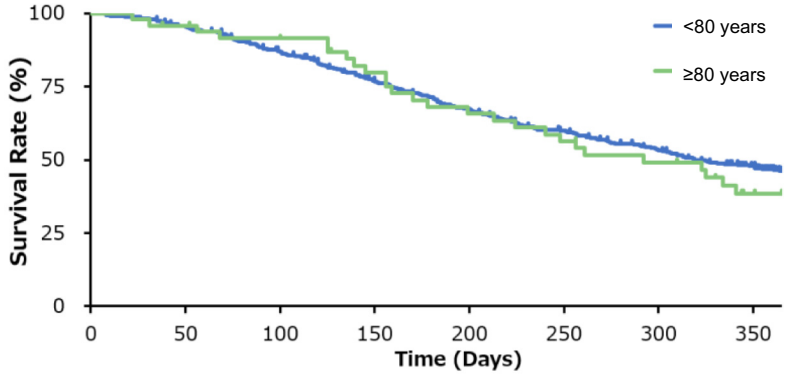
The PSA response was assessed in terms of the percentage of patients with a reduction in PSA levels of ≥50% or ≥30% from baseline levels exceeding ≥5 ng/mL. As shown in Fig. 4, the percentage of patients with a reduction in PSA of ≥30% or ≥50% was 28.3% and 23.9%, respectively, in the ≥80 year-old group. The corresponding values in the <80 year-old group were 29.7% and 17.7%.

4. Discussion

In this report, we describe the results of post-hoc subgroup analyses of patients aged <80 or ≥80 years old at the start of treatment with cabazitaxel registered in a large PMS. The aims of these subgroup analyses were to investigate the safety and efficacy of cabazitaxel for the treatment of CRPC in older patients in real-world settings.

The key finding of this subgroup analysis is that patients aged ≥80 years old with CRPC treated with cabazitaxel have previously received appropriate therapies, including prior docetaxel and anti-AR agents enzalutamide and abiraterone, as observed in younger patients. The initial dose of 25 mg cabazitaxel was selected in a small proportion of patients aged ≥80 years. This implies that the physicians carefully selected the cabazitaxel dose in the ≥80 year-old group in real-world settings, although the average dose per cycle was numerically similar between patients aged ≥80 years old and patients aged <80 years old included in this PMS.

It is interesting to see that the overall frequency of ADRs was comparable in both age-groups, with ADRs in 77.2% and 79.6% of patients aged <80 and ≥80 years old, respectively. Although no consistent trends were observed in individual event rates of non-hematologic and hematologic ADRs, there was no increase in febrile neutropenia in patients aged ≥80 years, possibly because physicians might have carefully selected the cabazitaxel dose and patients.



N at risk								
<80 years	607	578	517	446	386	337	294	247
≥80 years	48	45	41	34	28	24	20	12

Group	Events, n (%)	Censored/died, n (%)	Median OS (95% CI)
<80 years	308 (50.7)	299 (49.3)	319 (296, not reached)
≥80 years	26 (54.2)	22 (45.8)	292 (199, not reached)

Fig. 2. Overall survival. CI, confidence interval; OS, overall survival.

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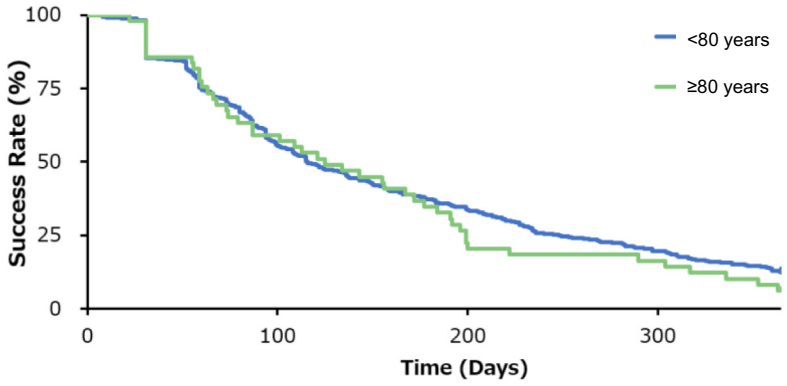

N at risk								
<80 years	610	515	341	261	207	150	120	89
≥80 years	49	42	29	22	11	9	8	5

Group	Events, n (%)	Censored/died, n (%)	Median TTF (95% CI)
<80 years	534 (87.5)	76 (12.5)	116 (108, 135)
≥80 years	46 (93.9)	3 (6.1)	125 (79, 172)

Fig. 3. Time to treatment failure. CI, confidence interval; TTF, time to treatment failure.

The Japanese Phase I study enrolled 44 patients aged 50–74 years with a similar median age of 67.0 years (vs 70.0 years in patients aged <80 years in this PMS) [16]. All 44 patients were started on cabazitaxel at 25 mg/m^2, and 28 (63.6%) discontinued treatment due to disease progression in 16 (36.4%) patients, AEs in nine (20.5%) patients, and consent withdrawal in three (6.8%) patients. The median number of cycles was 7.5 (range 1–29).

Although the rates of treatment-emergent adverse events (TEAEs) in the Phase I study and ADRs in the present PMS should not be directly compared as TEAEs are not necessarily related to the study drug, the frequent types of TEAEs and ADRs among patients aged <80 years in our PMS were similar to those in patients aged <75 years in the Phase I study. Similar types of ADRs were also observed among patients aged ≥80 years, and no ADRs that have not previously been reported with cabazitaxel in other studies [9,15,16] were observed in either age-group in this PMS.

Prophylactic G-CSF was used in over 80% of patients in both age-groups in any cycle. This is perhaps unsurprising because, in December 2014, about 6 months after the approval of cabazitaxel, the package insert was amended to include a recommendation for prophylactic G-CSF, especially in patients susceptible to febrile neutropenia.

These findings suggest that the tolerability of cabazitaxel in patients aged ≥80 years and <80 years in this real-world setting is consistent with the findings of prior international trials [9,16].

In the PROSELICA study, the PSA response rate defined as a decline of ≥50% was 29.5% and 42.9% at 20 mg/m^2 and 25 mg/m^2, respectively, with a baseline PSA ≥10 ng/mL [17]. In the present PMS, among 497 patients aged <80 years with baseline PSA ≥5 ng/mL, the reduction in PSA was ≥50% in 100 (17.7%) patients and ≥30% in 168 (29.7%) patients, with similar values in patients aged ≥80 years (11/46 [23.9%] and 13/46 [28.3%], respectively). The difference in the PSA response rate between PROSELICA and this PMS may be due to an evidence–practice gap.

Median OS in the Phase III TROPIC study was 15.1 months in the cabazitaxel group [9]. In the present PMS, the median OS was 319 days in patients aged <80 years and 292 days in patients aged ≥80 years. A longer follow-up period might be necessary to fully evaluate the longer-term outcomes of cabazitaxel in real-world settings. The present findings provide further support for the use of cabazitaxel in

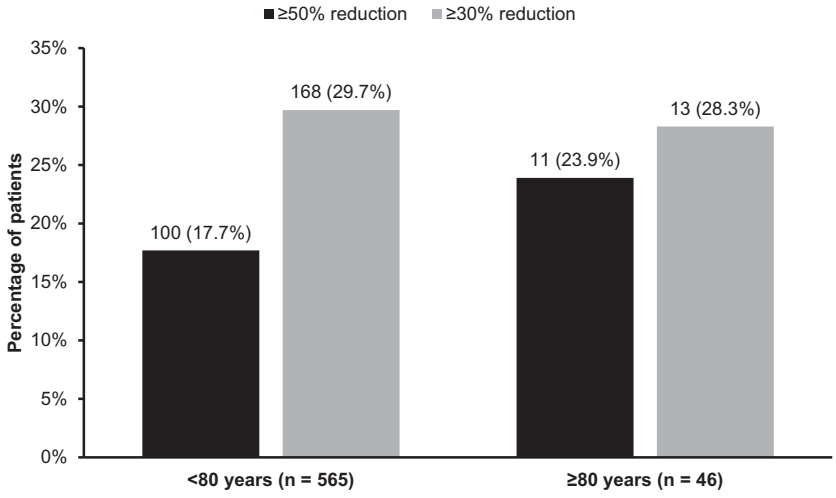

Fig. 4. Prostate-specific antigen (PSA) responder rates according to age-group and baseline PSA (≥5 ng/mL).

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fit or vulnerable older patients who had previously undergone androgen deprivation therapy followed by docetaxel and/or androgen signaling inhibitors, as proposed in recent treatment recommendations [18].

Further research might also be helpful to evaluate standard or adapted cabazitaxel dose and schedule in frail patients with CRPC. An international Phase III trial revealed that a reduced-dose regimen of cabazitaxel (20 mg/m^2) was noninferior to the standard-dose regimen (25 mg/m^2) in terms of median OS (13.4 vs 14.5 months, HR 1.024) although the PSA response rate was significantly lower (29.5% vs 42.9%, $p < .001$) [17]. Nevertheless, the reduced-dose regimen was associated with a lower rate of grade three/four TEAEs (39.7% vs 54.5%). It is possible that older patients with deteriorated performance status might benefit from a reduced-dose cabazitaxel regimen in order to reduce the risk of ADRs while maintaining favorable OS and PSA responses.

4.1. Limitations

Several limitations warrant mention. First, patients aged ≥80 years accounted for only 7.4% of the overall population, so this imbalance in patient numbers might introduce some bias. Second, as this was a PMS of patients treated in a real-world setting, it is possible that the data collection might be less extensive than in clinical trial settings. Accordingly, it is possible that some AEs/ADRs were omitted or misclassified by the attending clinician/investigator. Additionally, some safety and efficacy data assessed in clinical trials (e.g. PSA levels, RECIST criteria) might not be recorded as frequently in routine clinical practice. We must also acknowledge that the observation period of 1 year might be insufficient to fully evaluate the safety and efficacy of cabazitaxel; longer follow-up might be necessary to accumulate further data. In addition, our investigation cannot reveal which patients are fit or unfit for cabazitaxel treatment because data were not obtained to evaluate comorbidities, frailty, or vulnerability, which may be needed to identify such patients.

4.2. Conclusions

In conclusion, the results of this PMS performed in real-world settings in Japan indicate that cabazitaxel is tolerable in patients aged ≥80 years and in younger patients (<80 years old), with no newly described ADRs that had not occurred in prior clinical trials [9,16]. Despite a relatively short observation period of 1 year, the results of this PMS also suggest that cabazitaxel shows promising real-world efficacy in terms of OS, TTF, and PSA response in patients aged ≥80 years and in patients aged <80 years. Overall, the results of this PMS indicate that cabazitaxel is suitable for use in older patients (≥80 years old) whose general condition is good, and in younger patients (<80 years old) in real-world clinical practice.

Author Contributions

All authors have approved the final version of the manuscript before submission to the *Journal of Geriatric Oncology*.
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Data Sharing Statement

This post-marketing surveillance was conducted under the post-marketing regulation in Japan, and due to the characteristics of the surveillance in the regulation, the scope of permission for data sharing is limited to the content described in the paper.

Declaration of Competing Interest

Nobuaki Matsubara has received personal fees from Janssen, MSD, AstraZeneca, and Sanofi, and research grants from Janssen, MSD, Roche, Lilly, Taiho, BMS, and AstraZeneca.

Hideyasu Matsuyama has served on an advisory board for Sanofi.

Kazuhiro Suzuki has received personal fees from Sanofi, Takeda, Astellas, AstraZeneca, Janssen, Daiichi-Sankyo, Chugai, Kyowa-Kirin, and Bayer, and research grants from Takeda, Astellas, AstraZeneca, Daiichi-Sankyo, Chugai, Kyowa-Kirin, and Bayer.

Hirotaka Kazama, Shoko Tsukube, and Takeshi Seto are employees of Sanofi.

Acknowledgements

This PMS was supported by Sanofi. The authors thank Nicholas D. Smith (EMC K.K.) for medical writing support, which was funded by Sanofi. The authors also acknowledge the support of EPS Corporation (Tokyo, Japan) for conducting data analyses.

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