Clinical and cost impact of cabazitaxel versus a second androgen receptor-targeted agent (ARTA) for patients with metastatic castration-resistant prostate cancer (mCRPC) previously treated with docetaxel and the alternative ARTA (abiraterone or enzalutamide)

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BACKGROUND

- Docetaxel is the recommended first-line chemotherapy in patients with metastatic castration-resistant prostate cancer (mCRPC).[1] After receiving docetaxel, patients with low response to an androgen receptor-targeted agent (ARTA - arbiraterone or enzalutamide) may have a marginal response when switched to an alternative ARTA.[2, 3]
- In the CARD study, cabazitaxel demonstrated significant improvements in radiographic progression-free survival (rPFS), PFS, and overall survival (OS) compared with a second ARTA in patients with mCRPC who previously received docetaxel and an alternative ARTA.[4]
- Despite the encouraging clinical outcomes from the CARD trial, an optimal cost-effective third line (3L) treatment is currently unclear. Healthcare decision-makers face a significant challenge to optimize the treatment landscape in terms of cost and effectiveness in these patients.

OBJECTIVE

- Based on the results of the CARD study, we developed an economic model to quantify the clinical outcomes (rPFS, PFS, OS, hospitalization days, and intensive care unit [ICU] days) and determine potential healthcare resource utilization (HCRU) impact and associated costs that can be avoided in a hypothetical cohort of patients with mCRPC receiving cabazitaxel as a 3L treatment compared to a same-size cohort receiving a second ARTA from a US payer perspective.

METHODS

- **Table 1** presents an overview of this cost-consequence model, whereas a detailed summary of clinical inputs is provided in **Table 2**.

Table 1: Cost-consequence model overview

Parameters	Model Settings/Inputs
Model	Cost-consequence
Patient demographics	A cohort of patients (n=100) representative of the CARD study (mCRPC on 3L treatment post-docetaxel and ARTA)
Timepoints of assessment	• Reference case: 18 months • Scenario analyses: 6, 12, and 24 months
Clinical inputs - efficacy and safety	• Proportion of patients with rPFS, PFS, and OS • Incidence of symptomatic skeletal events (pathological fracture, radiation to bone, spinal cord compression, surgery to bone) • Incidence of Grade 3/4 adverse events • Proportion of patients with symptomatic skeletal events or Grade 3/4 adverse events to be hospitalized or placed in an ICU • Hospitalization days for symptomatic skeletal events, adverse events, and end-of-life care
Economic inputs - costs	• Cost for management of symptomatic skeletal events • Cost of adverse events • Cost of end-of-life care
Perspective	US payer perspective
Currency	2020 USD (translated in Euro (€) to suit local readers, 1 US dollar equals 0.85 Euro as per exchange rate as of 21st Jul 2021)
Inflation	Wherever the costs were only available from previous years, the costs were inflated using the health component of the Consumer Price Index.[5]

ARTA, androgen receptor-targeted agent; mCRPC, metastatic castration-resistant prostate cancer; OS, overall survival; PFS, progression-free survival; rPFS, radiographic progression-free survival; US, United States; USD, United States dollars; 3L, third line

Table 2: Cost-consequence model: Clinical inputs

Parameters	Data Source/Reference
Proportion of patients achieving rPFS, PFS, and OS at 6, 12, 18, and 24 months	CARD trial[4]
Distribution of type of SSE	CARD trial[6]
Incidences of SSEs	CARD trial[4]
Total number of SSEs	Overall monthly rate of SSEs based on the CARD trial[4] x Total months of OS based on the CARD trial[4]
Incidences of treatment-related Grade 3/4 AEs reported in ≥3% of patients	CARD trial[4]
Total number of AEs	Incidences of events in the CARD trial[4] x Hypothetical cohort size
Proportion of patients with SSEs or Grade 3/4 AEs to be hospitalized or placed in an ICU	Clinician input
Number of days in the hospital or ICU for SSEs or Grade 3/4 AEs	Clinician input
Number of hospitalization days for end-of-life care	Wilson et al. (2014)[7]

AEs, adverse events; ICU, intensive care unit; OS, overall survival; PFS, progression-free survival; rPFS, radiographic progression-free survival; SSE, symptomatic skeletal event

- The published costs for management of SSEs and Grade 3/4 AEs are provided in **Table 3.**

Table 3: Published US costs for management of SSEs and Grade 3/4 AEs

Event	Cost[a]
Symptomatic skeletal events*	
Radiation to bone[8]	$6,460 (€5,491)
Pathological fracture[8]	$31,387 (€26,679)
Spinal cord compression[8]	$46,382 (€39,425)
Grade 3/4 adverse events	
Asthenia or fatigue[9]	$27 (€23)
Diarrhea[10,b]	$8,268 (€7,028)
Infection[10,b]	$9,689 (€8,236)
Musculoskeletal pain or discomfort[9]	$19 (€16)
Peripheral neuropathy[11,c]	$748 (€636)
Renal disorder[10,b]	$11,713 (€9,956)
Cardiac disorder[10,b]	$13,126 (€11,157)
Febrile neutropenia[10,b]	$18,739 (€15,928)
Anemia[9]	$5,063 (€4,304)
Leukopenia[12]	$191 (€162)
Neutropenia[12]	$191 (€162)
Thrombocytopenia[9]	$1,266 (€1,076)
Hyponatremia[11,12,d,e,f]	$1,354 (€1,151)

*The cost for bone surgery was not included as the incidence was 0% for both arms in the CARD trial.[6]
[a]Reported costs were inflated to 2020 USD using the health component of the Consumer Price Index.[5]
[b]Costs reported by Bui et al. (2016)[10] assumed hospitalization (aligned with clinician input).
[c]Cost based on CPT 99214 (outpatient visit, $110.43 (€94))[13] and Red Book[14] cost for pregabalin ($11.19 (€10))
Pregabalin dosage: 300 mg/day for 3 days + 600 mg/day for 27 days.
[d]Assumed 92.5% outpatient management and 7.5% hospitalization with 3 days of LOS (based on clinician input).
[e]Cost of inpatient management: Bilir et al. (2016)[11], [f]Cost of outpatient management: Roy et al. (2015)[12].
AEs, adverse events; CPT, Current Procedural Terminology; LOS, length of stay; SSEs, symptomatic skeletal events; US, United States

- **Table 4** presents the cost per hospitalization day for Grade 3/4 AEs, SSEs, and end-of-life care. Based on clinician input, it was assumed that 10% of total deaths would happen following hospitalization. The cost of end-of-life care for patients who died during hospitalization was estimated to be $130,660 (€111,061).[7] This is the average cost of the last hospitalization for severe side effects for an average stay of 22 days.

Table 4: US Cost per hospitalization day for Grade 3/4 AEs, SSEs, and end-of-life care

Event	Cost per hospitalization day
Diarrhea[a]	$4,134 (€3,514)
Infection[a]	$2,422 (€2,059)
Renal disorder[a]	$2,928 (€2,489)
Cardiac disorder[a]	$3,282 (€2,790)
Febrile neutropenia[a]	$4,685 (€3,982)
Anemia[11,b]	$6,111 (€5,194)
Thrombocytopenia[11,b]	$5,099 (€4,334)
Hyponatremia[11,b]	$5,232 (€4,447)
Pathological fracture[a]	$6,277 (€5,335)
Spinal cord compression[a]	$9,276 (€7,885)
End-of-life[7]	$5,939 (€5,048)

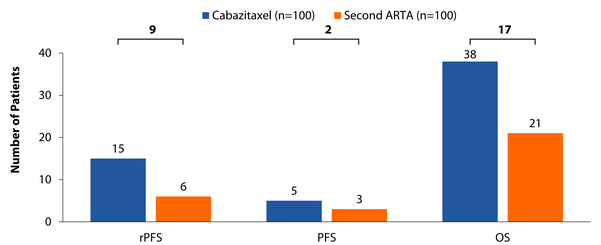
Note: ICU costs were assumed to be part of the hospitalization costs. [a]To obtain the respective costs, hospitalization costs per event were divided by the length of stay or expected days of hospitalization (based on clinician input). [b]Cost per day was obtained from Bilir et al. (2016)[11], which provided data on both mean inpatient cost and mean length of stay.
AEs, adverse events; SSEs, symptomatic skeletal events; US, United States

RESULTS

Reference Case Analysis at 18 months

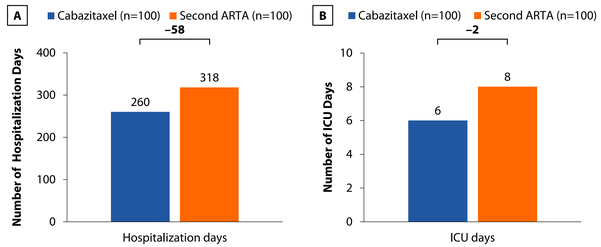
- The number of patients achieving rPFS, PFS, and OS at 18 months is presented in **Figure 1**, whereas hospitalization and ICU days are provided in **Figure 2**.
- The use of cabazitaxel as a 3L treatment was estimated to be associated with a 21% reduction in both SSE management and end-of-life care costs, and a 10% increase in AE costs compared to a second ARTA (**Figure 3**).
- Compared to a second ARTA, cabazitaxel as a 3L treatment was estimated to be associated with a 17% reduction in hospitalization and overall HCRU costs (**Figure 4**).

Figure 1: Number of patients in rPFS, PFS, and OS at 18 months



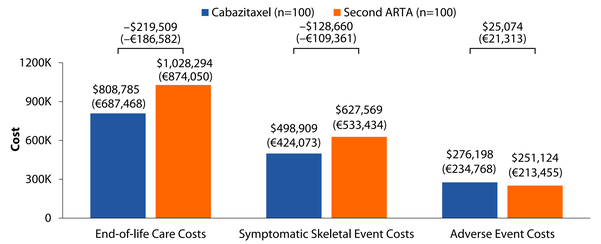
ARTA, androgen receptor-targeted agent; OS, overall survival; PFS, progression-free survival; rPFS, radiographic PFS

Figure 2: Hospitalization days (A) and ICU days (B) at 18 months



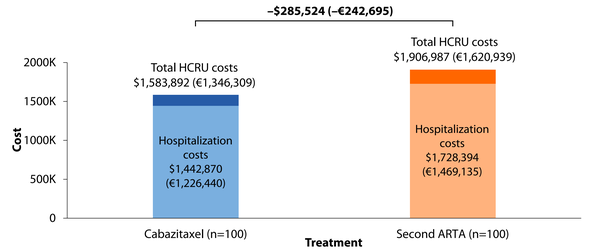
ARTA, androgen receptor-targeted agent; ICU, intensive care unit

Figure 3: Healthcare resource utilization costs at 18 months



ARTA, androgen receptor-targeted agent

Figure 4: Hospitalization and overall HCRU costs at 18 months



ARTA, androgen receptor-targeted agent; HCRU, healthcare resource utilization

Scenario Analyses at 6, 12, and 24 months

- Scenario analyses for clinical and cost results at 6, 12, and 24 months were consistent with the reference case results (**Table 5** and **Table 6**).

Table 5: Number of patients in rPFS, PFS, and OS at 6, 12, and 24 months

	6 months			12 months			24 months		
Outcome	Cabazitaxel	Second ARTA	Difference	Cabazitaxel	Second ARTA	Difference	Cabazitaxel	Second ARTA	Difference
rPFS (number of patients)	58	36	22	27	9	18	6	4	2
PFS (number of patients)[a]	36	16	21	10	3	7	0	0	0
OS (number of patients)	86	81	5	56	45	12	25	9	16
Hospitalization days	112	138	−26	206	250	−44	297	351	−54
ICU days	5	7	−2	6	8	−2	7	8	−1

Note: Values correspond to a cohort of 100 patients for each treatment. [a]No results available for 24 months as the number at risk for PFS was 0 for both arms in the CARD trial.
ARTA, androgen receptor-targeted agent; ICU, intensive care unit; OS, overall survival; PFS, progression-free survival; rPFS, radiographic progression-free survival

Table 6: Healthcare resource utilization costs at 6, 12, and 24 months

	6 months			12 months			24 months		
Outcome	Cabazitaxel	Second ARTA	Difference	Cabazitaxel	Second ARTA	Difference	Cabazitaxel	Second ARTA	Difference
SSEs	$219,191 (€186,312)	$309,285 (€262,892)	−$90,094 (−€76,580)	$394,870 (€335,640)	$519,906 (€441,920)	−$125,036 (−€106,281)	$566,887 (€481,854)	$674,083 (€572,971)	−$107,196 (−€91,117)
AEs	$226,750 (€192,738)	$202,843 (€172,417)	$23,907 (€20,321)	$267,456 (€227,338)	$234,821 (€199,598)	$32,635 (€27,740)	$277,018 (€235,465)	$256,140 (€217,719)	$20,878 (€17,746)
End-of-life care	$181,617 (€154,374)	$248,254 (€211,016)	−$66,637 (−€56,641)	$569,678 (€484,226)	$722,550 (€614,168)	−$152,872 (−€129,941)	$982,563 (€835,179)	$1,189,006 (€1,010,655)	−$206,443 (−€175,477)
Total	$627,559 (€533,425)	$760,382 (€646,325)	−$132,823 (−€112,900)	$1,232,003 (€1,047,203)	$1,477,277 (€1,255,685)	−$245,274 (−€208,483)	$1,826,468 (€1,552,498)	$2,119,229 (€1,801,345)	−$292,761 (−€248,847)

Note: Values correspond to a cohort of 100 patients for each treatment. AE, adverse event; ARTA, androgen receptor-targeted agent; SSE, symptomatic skeletal event

CONCLUSION

Compared to a second ARTA, the use of cabazitaxel as a 3L treatment after docetaxel and ARTA in patients with mCRPC is estimated to result in clinical benefits (longer rPFS, PFS, and OS) and lower healthcare resource utilization (fewer hospitalization and ICU days).

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Disclosures/Conflicts of Interest

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