Real-world evidence in patient-reported outcomes (PROs) of metastatic castrate-resistant prostate cancer (mCRPC) patients treated with abiraterone acetate + prednisone (AA+P) across Canada: Final results of COSMiC

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Abstract

Introduction: Abiraterone acetate plus prednisone (AA+P) has shown to significantly improve survival. COSMiC, a Canadian Observational Study in Metastatic Cancer of the Prostate, set out to prospectively amass real-world data on metastatic castration-resistant prostate cancer (mCRPC) patients managed with AA+P in Canada. Herein, we report their patient-reported outcomes (PROs).
Methods: After a median followup of 67.1 weeks, 254 patients were enrolled across 39 sites. Functional Assessment of Cancer Therapy-Prostate (FACT-P), Montreal Cognitive Assessment (MoCA), Brief Pain Inventory-Short Form (BPI-SF), Brief Fatigue Inventory (BFI), and Current Health Satisfaction in Prostate Cancer (CHS-PCa) were evaluated at baseline, as well as at weeks 12, 24, 48, and 72 after AA+P initiation. Descriptive analysis was used with continuous variables. Changes from baseline were summarized using mean (standard deviation [SD]).
Results: At a median age of 76.6 (8.94), baseline FACT-P total score was 111.3 (19.56) with no significant change in their functional status observed from baseline over time. The median baseline MoCA score was 25.2 (4.52), yet subsequent assessments showed an absence of cognitive decline while under treatment. Similarly, no meaningful changes were detected in BPI, BFI, and CHS-PCa during the 72-week study period, thus suggesting that patients' PROs were well-maintained throughout AA+P treatment. Prostate-specific antigen (PSA) response with >50% decline was 66.4%. Safety profile was consistent with the known side effect of AA+P.
Conclusions: COSMiC represents the largest Canadian mCRPC cohort treated with AA+P with real-world, prospective evaluation of PROs. This data demonstrated the maintenance in quality of life and cognitive status over the course of the study and underscores the importance of PRO use in this complex patient population.

Introduction

In the past decade, major advances have taken place in the treatment of advanced prostate cancer. With a deeper understanding of the androgen receptor's central role in the pathogenesis of advanced disease, novel androgen receptor axis-targeted therapies (ARATs) are now first options in guidelines worldwide for the treatment of metastatic castration-resistant prostate cancer (mCRPC). Abiraterone acetate (AA), an oral prodrug of abiraterone, which is an androgen biosynthesis inhibitor of the CYP17 enzyme, plus prednisone (P) was the first ARAT to show significant delay in disease progression and improvement in survival in metastatic disease.[1,2] While level 1 evidence for the efficacy of AA+P is abundant, patient-reported outcomes (PROs) in the real-world setting remain sparse in this population and are highly critical to complement the existing efficacy and safety information. The objective of this study was to quantify the impact of AA+P treatment on patients' experience during routine clinical management of mCRPC. Herein, we describe the results of a Canadian prospective, multi-institutional, non-interventional study (ClinicalTrials.gov NCT02364531 for a Canadian Observational Study in Metastatic Cancer of the Prostate, or "COSMiC") that was specifically designed to examine PROs in asymptomatic or mildly symptomatic (chemotherapy-naive) mCRPC patients managed with AA+P.

Methods

From October 2014 to May 2017, 254 chemotherapy-naive patients with mCRPC who were to receive AA+P as part of their optimal clinical care were enrolled across 39 Canadian sites (29 sites in the community and 10 sites at academic centers). Their mCRPC therapies were initiated and man-

aged primarily by urology (31/39 sites) than radiation oncology (4/39 sites) and medical oncology (4/39 sites). Patients receiving AA+P treatment were asked to complete a series of self-reported questionnaires and scales pertaining to health-related quality of life (QoL) and cognition at baseline visit and subsequent followup visits at weeks 12, 24, 48, and week 72 (end of study). Safety, including any adverse events (AEs), whether they were serious or not, related or not related to AA+P, were prospectively collected as part of the clinical outcome. For those who discontinued AA+P prior to disease progression, patients were encouraged to continue with their PROs self-evaluation until week 72. The following validated measures were recorded:

- The Functional Assessment of Cancer Therapy-Prostate (FACT-P) consists of the FACT-General (Version 4) and a prostate cancer subscale. The FACT-G contains a 27-item questionnaire and is composed of four subscales of health-related QoL: physical well-being, social/family well-being, emotional well-being, and functional well-being. The prostate cancer subscale asks prostate-specific questions, which include sexuality, bowel/bladder function, and pain. Degradation of 10 points from baseline in total score and three points from baseline in prostate-cancer specific subscale were predefined as minimum clinically meaningful differences (MCMD).[3]
- Montreal Cognitive Assessment (MoCA) is a rapid screening instrument for mild cognitive impairment. It was only conducted at academic sites since the assistance of another individual is required to administer the test. The total possible score is 30 points, with a score of ≥26 being considered normal. Though the specific range to grade severity remains to be established, the following have generally been used: 18–25 as mild, 10–17 as moderate, and <10 as severe cognitive impairment.[4]
- Brief Pain Inventory-Short Form (BPI-SF) assesses the severity of pain with four items and the impact of pain on daily functions with seven items using a 11-point numerical rating scales. Scores for both pain intensity and pain interference ranges from 0–10, where higher scores indicate higher severity of pain.[5]
- Brief Fatigue Inventory (BFI) assesses the severity of fatigue and the impact of fatigue on daily functioning.[6]
- Current Health Satisfaction in Prostate Cancer (CHS-PCa) is an exploratory tool to assess patient satisfaction with their current status adopted from its original questionnaire in diabetic patients.[7]

Data were analyzed and reported using descriptive statistics (number of observations; mean, standard deviation [SD]; and minimum/maximum) of scores at baseline and at followup assessments for continuous variables, and number of observations and percentages for categorical variables; 95% confidence interval (CI) for the mean were also calculated for change scores of QoL from baseline. This analysis includes all functional data while under treatment of the 254 patients at baseline visit, 227 patients at week 12, 205 patients at week 24, 161 patients at week 48, and 125 at week 72. Of the 133 patients who had withdrawn from the study, death was the most common cause (n=34), followed by discontinuation of AA+P (n=27), unequivocal disease progression (n=25), withdrawal of consent (n=15), loss to followup (n=13) and adverse events (n=2).

Results

Two hundred fifty-four patients with mCRPC patients were recruited across Canada during the study period. Table 1 lists their baseline demographics. The mean age at study entry was 76.6 (SD 8.94) years old, with an average prostate cancer diagnosis of 6.5 years preceding mCRPC treatment. Metastases to bones were the most common (84%).

At a median followup of 67.1 weeks, the mean time on treatment was 452.6 days (SD 12.76). The prostate-specific antigen (PSA) values had been measured in 223 patients throughout their AA+P treatment; the median baseline PSA was 21.2 ng/mL (1.0–2603.0). The proportion of patients achieving a PSA decline of at least 90% was 30.0% (n=87), achieving a decline of at least 50% was 66.4% (n=148), and achieving a decline of at least 30% was 71.7% (n=160) of patients. The median overall survival (OS) was not reached since only 36 events had occurred at time of data cutoff; however, the mean estimate of OS was 17.2 months.

The change in patients' functional status over time was assessed by comparing their FACT-P scores at different followup visits to their respective baseline assessment. Table 2

Table 1. Patients' baseline characteristics

Time since diagnosis in mean years (SD)	6.5 years (5.63)
Gleason score ≥8	115 (47%)
Prior treatment	
ADT	218 (89.0%)
Radiation	89 (36.3%)
Radical prostatectomy	67 (27.3%)
TURP	32 (13.1%)
Brachytherapy	3 (1.2%)
Cryotherapy	9 (3.7%)
Time since metastasis in mean months (SD)	16.6 months (25.82)
Age in mean years (SD)	76.6 (8.94)
Location of metastases at study enrollment*	
Bone	205 (84.0%)
Lymph nodes	50 (20.5%)
Lung	14 (5.7%)
Other visceral sites	11 (4.5%)

*Patients may report more than one location of metastasis. ADT: androgen deprivation therapy; SD: standard deviation; TURP: transurethral resection of the prostate.

Table 2. FACT-P scores over 72-week study period

	Baseline mean (SD) n=252	Week 12 n=210	Week 24 n=186	Week 48 n=150	Week 72 n=118
		Mean change from baseline (SD)			
Physical well-being	22.8 (4.78)	0.6 (3.72)	-0.4 (3.99)	-0.7 (4.31)	-0.4 (4.55)
Social/family well-being	21.4 (4.70)	-0.5 (4.53)	-0.4 (4.62)	-0.3 (4.77)	-0.0 (5.03)
Emotional well-being	17.9 (4.57)	0.9 (4.12)	0.8 (4.35)	0.7 (4.00)	0.8 (3.72)
Functional well-being	18.5 (5.78)	0.1 (4.38)	-0.7 (5.61)	-1.0 (5.03)	-1.3 (5.03)
FACT-G total score	80.6 (14.94)	1.2 (11.45)	-0.6 (12.65)	-1.3 (12.34)	-0.9 (12.03)
FACT-P total score	111.3 (19.56)	2.6 (13.77)	0.0 (15.72)	-1.1 (15.54)	-1.4 (14.76)

FACT-G: Functional Assessment of Cancer Therapy-General; FACT-P: Functional Assessment of Cancer Therapy-Prostate; SD: standard deviation.

depicts changes in every FACT-P general function; its subscales were all below the clinical threshold of MCMD, therefore, no significant difference was detected in their functional status over time.

In terms of cognitive function (Table 3), their baseline MoCA score of 25.2 fell slightly below the diagnostic threshold of normal (i.e., ≥26). The changes over time at each followup visits were also less than an absolute value of one, suggesting that the grading of their cognitive function did not change from baseline.

The impact of pain was determined using BPI, with increases ≥30% from baseline as significant change threshold.[8,9] Table 4 shows neither the change from baseline in pain intensity nor interference met the predefined threshold, therefore, pain was not worsened over the course of the study. Other PROs examined, including fatigue and patients' health satisfaction, were evaluated using BFI and CHS-PCa, respectively. Both also demonstrated minimal change from its baseline value (Table 4).

AEs or reactions were reported in 69.7% patients (n=177). AEs that were determined to be treatment-related occurred in 31.9% of patients (n=81), with 16.1% (n=41) leading to study discontinuation. No new safety signals were identified. AEs reported by >5% of patients include peripheral edema (8.3%), fatigue (5.9%), and back pain (5.1%). AEs of special interests were selected from the safety profile of prior studies with AA+P[1,2] and are listed in Table 5. Most AEs were reported as mild-to-moderate in nature. Grade 3+ AEs consisted of ALT elevation in 0.4%, hypertension in 0.4%, and cardiac disorder in 5.9%.

Discussion

To date, COSMiC generated the largest real-world evidence in the PROs of mCRPC patients treated with AA+P in Canada. This study has shown that the functional status, cognitive abilities, pain level, and fatigue level, as well as patients' health satisfaction are consistently maintained throughout AA+P treatment.

In COU-AA-302, a phase 3, randomized, double-blinded, placebo-controlled trial of AA+P in patients with asymptomatic or mildly symptomatic mCRPC, AA+P delayed the deterioration of health-related QoL in patients when compared to those treated with prednisone alone.[10] They observed a median time to health-related QoL deterioration of 55.2 weeks using the same FACT-P assessment tool as COSMiC, which complements this finding in the real-world setting, where the FACT-P scores did not achieve MCMD from baseline throughout the 72-week treatment with AA+P. Another phase 2 trial with a shorter study timeframe of 24 weeks also observed a high proportion of patients in AA+P group (n=101) with "clinically significant improvement or no change" in FACT-P domains than those who exhibited "clinically worsening" in their randomized study of mCRPC patients treated with AA+P vs. enzalutamide.[11] Hence, the available literature is in keeping with the observation in COSMiC, where the functional status in patients treated AA+P was well-preserved over time.

In addition to FACT-P, Khalaf et al also evaluated the cognitive function of AA+P patients using MoCA. Among the 92 patients treated with AA+P and who completed their MoCA, their baseline score was 25 at a median age of 72.9 years old, with minimal change in MoCA scores over the 24-week study period.[11] Their finding is consistent to our observation in COSMiC, where patients with a baseline MoCA score of 25.2 at a median age of 77 did not show significant clinical change in cognition over the 72 weeks.

Another important factor that can negatively affect QoL is pain. Indeed, COU-AA-302 administered BPI to system-

Table 3. MoCA scores over 72-week study period

	Baseline mean (SD) n=69	Week 12 n=46	Week 24 n=38	Week 48 n=25	Week 72 n=16
		Mean change from baseline (SD)			
MoCA	25.2 (4.52)	0.7 (2.71)	-0.0 (3.50)	0.2 (5.26)	-0.9 (6.19)

MoCA: Montreal Cognitive Assessment; SD: standard deviation.

Table 4. Other PROs measures over 72-week study period

		Baseline mean (SD)	Week 12	Week 24	Week 48	Week 72
			Mean change from baseline (SD)			
BPI	N-value	248	209	180	143	115
	Intensity	3.1 (2.42)	-0.6 (1.97)	-0.5 (2.13)	-0.2 (1.92)	-0.1 (1.91)
	Interference	2.9 (2.58)	-0.7 (2.20)	-0.2 (2.31)	0.0 (2.15)	0.1 (2.19)
BFI	N-value	250	209	187	147	116
	Fatigue level	2.8 (2.47)	-0.2 (1.96)	-0.1 (2.12)	0.4 (2.15)	0.1 (2.08)
CHS-PCa	N-value	251	209	189	148	118
	Physical	4.7 (1.35)	0.3 (1.14)	0.1 (1.31)	0.0 (1.34)	0.1 (1.44)
	Emotional	5.4 (1.46)	0.3 (1.26)	0.3 (1.49)	-0.0 (1.48)	0.0 (1.57)

BPI: Brief Pain Inventory; BFI: Brief Fatigue Inventory; CHS-PCa: Current Health Satisfaction in Prostate Cancer; SD: standard deviation.

atically assess the impact of AA+P treatment on pain. They reported a significant delay in the progression of patient-reported pain in the AA+P group as compared with the prednisone alone group. The AA+P group had a median time to progression of pain intensity of 116.1 weeks and a median time to progression of pain interference of 44.8 weeks.[10] This is in line with the absence of meaningful change in pain scores over the 72 weeks seen in COSMiC, further supporting the control on pain progression in mCRPC patients treated with AA+P.

To expand the breadth of PROs measures in this real-world mCRPC cohort, we also deployed BFI and CHS-PCa to evaluate patients' fatigue level and overall health satisfaction living with prostate cancer. The lack of meaningful change from baseline detected in both questionnaires is consistent with the other results measured here (i.e., FACT-P, MoCA, and BPI).

From an efficacy and safety perspective, it was reassuring to find comparable clinical outcomes in the trial setting of COU-AA-302 vs. the real-world cohort in COSMiC; 62% of the patients in the COU-AA-302 trial achieved a ≥50% PSA decline with AA+P and had a median treatment duration of 60 weeks,[2,12] while COSMiC demonstrates a ≥50% PSA response in 66.4% of patients with an equivalent of 64.7 weeks of treatment. The two studies nearly mirror one another in numerical values in those efficacy endpoints. The safety of AA+P observed in COSMiC was also similar to that reported in COU-AA-302. AEs such as peripheral edema, fatigue, and back pain were the most common in both studies. In terms of serious AEs, a slightly lower incidence of grade 3+ alanine transferase elevation (0.4%) and hypertension (0.4%) were observed in COSMIC than that seen in COU-AA-302 (6% and 4%, respectively); this is likely attributed to proper patient selection, greater awareness, and experience in the management of AA+P-related side-effects among treaters. However, the incidence of serious cardiac disorders is comparable in COSMiC (5.9%) and COU-AA-302 (7%) and is perhaps owing to how common such comorbid conditions are among the elderly or those with an underlying predisposition. In fact, 43.0% (n=107) of COSMiC patients reported having a medical history of cardiovascular disease and hence confirm the need for patients with complex comorbid conditions to be comanaged with other specialists.

Study limitations

A major limitation of COSMiC is that we may have inadvertently selected for motivated or well patients to participate in and remain on study. Although, as part of the study design, any asymptomatic or mildly symptomatic mCRPC patients identified as candidates for AA+P treatment were enrolled on study and were requested to complete their PROs until the end of study, it is understandable too that those with declining health may have preferred to opt out of additional paperwork that would not alter their medical care. Second,

Table 5. Adverse events of special interest

	All reports		Mild/moderate		Severe or life-threatening	
	n	%	n	%	n	%
ALT increased	3	1.2%	2	0.8%	1	0.4%
AST increased	1	0.4%	1	0.4%		
Cardiac disorders*	21	8.3%	6	5.3%	15	5.9%
Edema/fluid retention	26	10.2%	26	9.1%		
Hypertension	8	3.1%	7	2.3%	1	0.4%
Hypokalemia	3	1.2%	3	1.1%		

*Cardiac disorders included acute coronary syndrome (n=1), angina pectoris (n=1), atrial fibrillation (n=6), atrioventricular block complete (n=2), bradycardia (n=2), cardiac arrest (n=1), congestive heart failure (n=3), myocardial infarction (n=3), and palpitation (n=2). ALT: alanine aminotransferase; AST: aspartate aminotransferase.

missing data resulting in smaller cohorts at longer followup is always suboptimal but an inevitable part of any clinical study, especially in the septuagenarian (or older) population studied here. Third, another consideration is the PRO measures used. While all questionnaires and scales used in COSMiC have been validated and are frequently used in clinical trials, MoCA was not developed to assess cognition in prostate cancer patients, thus its sensitivity may be put into question. In the rapidly changing landscape of advanced prostate cancer, ARATs are being used prior to disease becoming metastatic and its implication on the efficacy and PROs of AA+P or any other mCRPC agents remain to be determined.

Conclusions

COSMiC represents the first and largest pan-Canadian mCRPC cohort treated with AA+P with real-world prospective with an extensive evaluation of PROs. The data consistently demonstrated the maintenance in the overall quality of life and cognitive status over time among mCRPC patients treated by various medical specialties across the country. Equally important was the absence of unexpected AEs observed in the real-world setting while achieving similar efficacy outcomes as those seen in landmark trials. COSMiC further confirms the safety and clinical benefit in the maintenance of QoL as measured by PROs, as well as disease control of AA+P in a Canadian patient population.

Competing interests: Dr. Gotto has been an advisory board member for and received honoraria from Amgen, Astellas, Bayer, Janssen, Merck, Roche, and Sanofi; and has participated in clinical trials supported by Amgen, Astellas, AstraZeneca, Bayer, Janssen, Myovant, and Pfizer. Dr Chin has been an advisory board member for AbbVie, Astellas, Janssen, Profound Medical Inc., Sanofi-Aventis, and TerSera; has received payment from AbbVie, Astellas, Profound Medical Inc., Sanofi-Aventis, and TerSera. Dr. Fradet has had meeting-related travel expenses covered by Ferring; and has received research grants from Astellas and Sanofi. Dr Shayegan has been an advisory board member for AbbVie, Astellas, AstraZeneca, Bayer, Ferring, Janssen, Merck, and Sanofi; has recede honoraria from Janssen; and has participated in clinical trials supported by Astellas, Janssen, and Merck. Dr. Rendon has been an advisory board and speakers' bureau member for, and has received honoraria from AbbVie, Amgen, Astellas, AstraZeneca, Bayer, Ferring, Jansen, and Sanofi. Dr. Danielson has received speakers' fees and advisory board honoraria from Amgen, Astellas, Bayer, and Janssen. Mr. Camacho, Ms. Zardan, Mr. Plante, Ms. Hew, and Ms. Chan are employees of Janssen, Inc. Dr. Feifer has attended advisory board meetings for and received unrestricted educational grants from Astellas, Bayer, and Janssen. The remaining authors report no competing personal or financial interests related to this work.

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References

1. de Bono JS, Logothetis CJ, Molina A, et al. Abiraterone and increased survival in metastatic prostate cancer. *N Engl J Med* 2011;364:1995-2005. https://doi.org/10.1056/NEJMoa1014618
2. Ryan CJ, Smith MR, Fizazi K, et al. Abiraterone acetate plus prednisone vs. placebo plus prednisone in chemotherapy-naive men with metastatic castration-resistant prostate cancer (COU-AA-302): Final overall survival analysis of a randomized, double-blind, placebo-controlled phase 3 study. *Lancet Oncol* 2015;16:152-60. https://doi.org/10.1016/S1470-2045(14)71205-7
3. Cella D, Nichol MB, Eton D et al. Estimating clinically meaningful changes for the Functional Assessment of Cancer Therapy-Prostate: Results from a clinical trial of patients with metastatic hormone-refractory prostate cancer. *Value Health* 2009;12:124-9. https://doi.org/10.1111/j.1524-4733.2008.00409.x
4. Ziad Nasreddine. Quebec: MoCA Test Inc.; [updated 2019]. Available at: https://www.mocatest.org/faq/. Accessed Dec. 10, 2019.
5. Cleeland CS, Ryan KM. Pain assessment: Global use of Brief Pain Inventory. *Ann Acad Med* 1994;23:129-38.
6. Mendoza TR, Wang XS, Cleeland CS, et al. The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. *Cancer* 1999;85:1186-96. https://doi.org/10.1002/(SICI)1097-0142(19990301)85:5<1186::AID-CNCR24>3.0.CO;2-N
7. Traina SB, Colwell HH, Crosby RD, et al. Pragmatic measurement of health satisfaction in people with type 2 diabetes mellitus using the Current Health Satisfaction Questionnaire. *Patient Relat Outcome Meas* 2015;6:103-15. https://doi.org/10.2147/PROM.S79368
8. Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain* 2008;9:105-21. https://doi.org/10.1016/j.jpain.2007.09.005
9. Farrar JT, Young JP, LaMoreaux L, et al. Clinical importance of changes in chronic pain intensity measured on a 11-point numerical pain rating scale. *Pain* 2001;94:149-58. https://doi.org/10.1016/S0304-3959(01)00349-9
10. Basch E, Autio K, Ryan CJ, et al. Abiraterone acetate plus prednisone versus prednisone alone in chemotherapy-naive men with metastatic castration-resistant prostate cancer: Patient-reported outcome results of a randomized phase 3 trial. *Lancet Oncol* 2013;14:1193-9. https://doi.org/10.1016/S1470-2045(13)70424-8
11. Khalaf DJ, Sunderland K, Eigl BJ, et al. Health-related quality of life for abiraterone plus prednisone vs. enzalutamide in patients with metastatic castration-resistant prostate cancer: Results from a phase 2 randomized trial. *Eur Urol* 2019;75:940-7. https://doi.org/10.1016/j.eururo.2018.12.015
12. Ryan CJ, Smith MR, de Bono JS, et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. *N Engl J Med* 2013;368:138-48. https://doi.org/10.1056/NEJMoa1209096

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