#EMUC19-0125

PROSTATE CANCER REGISTRY

Real-World Outcomes With Abiraterone Plus Prednisone or Prednisolone in Metastatic Castration-Resistant Prostate Cancer: The Prostate Cancer Registry

Anders Bjartell,[1] Nicolaas Lumen,[2] Pablo Maroto,[3] Thomas Paiss,[4] Francisco Gomez Veiga,[5] Alison Birtle,[6] Gero Kramer,[7] Ewa Kalinka,[8] Dominique Spaëth,[9] Susan Feyerabend,[10] Vsevolod Matveev,[11] Florence Lefresne,[12] Martin Lukac,[13] Robert Wapenaar,[14] Luis Costa,[15] Simon Chowdhury[16]

[1]Department of Urology, Skåne University Hospital Malmö, Lund University Sweden; [2]Department of Urology, Ghent University Hospital, Ghent, Belgium; [3]Department of Medical Oncology, Hospital de la Santa Creu i Sant Pau, Autonomous University of Barcelona, Barcelona, Spain; [4]Urologie team Ulm, Ulm, Germany; [5]Urology Department and Kidney Transplant Unit, Translational Research Group of Urology GITUR-IBSAL, Salamanca University Hospital, Salamanca, Spain; [6]Royal Preston Hospital, Preston, UK; [7]Department of Urology, Medical University of Vienna, Vienna, Austria; [8]Clinic of Oncology, Polish Mother's Memorial Hospital – Research Institute, Lodz, Poland; [9]Centre d'Oncologie de Gentilly, Nancy, France; [10]Studienpraxis Urologie, Nürtingen, Germany; [11]N.N. Blokhin National Cancer Research Center, Moscow, Russia; [12]EMEA Oncology, Janssen Pharmaceutica N.V., Beerse, Belgium; [13]Parexel International Czech Republic s.r.o, on behalf of Janssen Pharmaceutica N.V., Beerse, Belgium; [14]Janssen-Cilag B.V., Breda, The Netherlands; [15]Oncology Division, Hospital de Santa Maria, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal; [16]Guy's and St Thomas' NHS Foundation Trust and Sarah Cannon Research Institute, London, UK

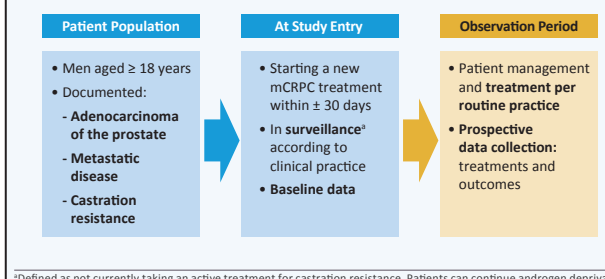
INTRODUCTION AND OBJECTIVE

- In randomised controlled trials, abiraterone acetate plus prednisone or prednisolone (AAP) prolonged overall survival in patients with chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC)[1] and those with mCRPC previously treated with docetaxel.[2]
- This analysis evaluated real-world characteristics, efficacy outcomes and safety of patients with mCRPC, and the subgroup with cardiovascular (CV) comorbidities, receiving AAP as first- or second-line (after docetaxel only) treatment, using final data from the international Prostate Cancer Registry (PCR) (NCT02236637).
  - CV comorbidities are defined as hypertension, angina pectoris, history of myocardial infarction, arrhythmia, thromboembolic disease, transient ischaemic attack, cerebrovascular accident and/or other CV event.

METHODS

- The included patient population and data collection are shown in Figure 1.

Figure 1. Study Design and Data Collection



[a]Defined as not currently taking an active treatment for castration resistance. Patients can continue androgen deprivation therapy and bone-targeted therapy.

Patients

- Patients from 16 countries in Europe, Russia and Turkey were enrolled between 2013 and 2016, consecutively, irrespective of their treatment, to avoid selection bias.
- Patients and disease characteristics were collected at baseline, and patients were followed for up to 3 years.

Outcomes Evaluated

- Treatment exposure, overall survival and full safety
  - Data are presented descriptively
- Time to progression was defined as (1) evidence of radiographic progression by investigator's assessment; (2) evidence of clinical progression by investigator's assessment; (3) first-line mCRPC treatment stopped due to progression; or (4) new mCRPC treatment started due to progression.
- Analysis groups:
  - All patients receiving first-line AAP
  - Patients with CV comorbidities receiving first-line AAP
  - All patients receiving second-line AAP (after docetaxel only)
  - Patients with CV comorbidities receiving second-line AAP (after docetaxel only)
    - Second-line AAP-treated patients had received first-line docetaxel prior to the study (n = 203) or during the study (n = 191).

RESULTS

- Patient demographics and disease characteristics at study entry are shown in Table 1.

Table 1. Demographics and Disease Characteristics at Study Entry

	First-line AAP		Second-line AAP	
	All patients (n = 754)	Patients with CV comorbidities (n = 504)	All patients (n = 394)	Patients with CV comorbidities (n = 234)
Age, years, median (range)	76.0 (43-98)	77.0 (50-94)	70.0 (46-89)	72.0 (48-89)
Time from initial prostate cancer diagnosis to study inclusion, years, median (range)	5.0 (0-29)	5.3 (0-29)	3.7 (0-20)	4.3 (0-180)
Disease location, n (%)	*(n = 612)*	*(n = 402)*	*(n = 345)*	*(n = 202)*
Node	249 (40.7)	167 (41.5)	155 (44.9)	96 (47.5)
Liver and lung	7 (1.1)	5 (1.2)	7 (2.0)	4 (2.0)
Liver only	13 (2.1)	7 (1.7)	25 (7.2)	17 (8.4)
Lung only	39 (6.4)	25 (6.2)	29 (8.4)	19 (9.4)
Local recurrence	85 (13.9)	54 (13.4)	70 (20.3)	42 (20.8)
Bone	463 (75.7)	296 (73.6)	261 (75.7)	155 (76.7)
Other	52 (8.5)	31 (7.7)	37 (10.7)	21 (10.4)
Biological parameters, median (range)				
Prostate-specific antigen, ng/mL	34.4 (0.0-10,710.0)	34.0 (0.1-10,710.0)	50.5 (0.0-2108.0)	52.4 (0.1-1445.0)
Lactic acid dehydrogenase, U/L	268.0 (3.0-3870.0)	255.0 (3.0-3870.0)	307.0 (40.0-3537.0)	291.0 (103.0-1553.0)
Alkaline phosphatase, U/L	111.0 (1.0-2890.0)	112.5 (1.0-2890.0)	103.2 (1.0-1850.0)	104.0 (1.0-1433.0)
Haemoglobin, g/dL	12.9 (7.0-17.0)	12.7 (7.0-16.0)	12.5 (7.0-17.0)	12.4 (7.0-16.0)
Gleason score at initial diagnosis, n (%)	*(n = 674)*	*(n = 448)*	*(n = 367)*	*(n = 220)*
2-6	100 (14.8)	71 (15.8)	44 (12.0)	31 (14.1)
7	230 (34.1)	154 (34.4)	106 (28.9)	63 (28.6)
8-10	344 (51.0)	223 (49.8)	217 (59.1)	126 (57.3)
M stage at initial diagnosis, n (%)	*(n = 732)*	*(n = 488)*	*(n = 388)*	*(n = 230)*
Mx	161 (22.0)	114 (23.4)	73 (18.8)	44 (19.1)
M0	315 (43.0)	217 (44.5)	138 (35.6)	89 (38.7)
M1, M1a, M1b, M1c	256 (35.0)	157 (32.2)	177 (45.6)	97 (42.2)
ECOG performance status, n (%)	*(n = 715)*	*(n = 477)*	*(n = 371)*	*(n = 221)*
0	340 (47.6)	218 (45.7)	133 (35.8)	72 (32.6)
1	318 (44.5)	214 (44.9)	208 (56.1)	127 (57.5)
2	48 (6.7)	36 (7.5)	26 (7.0)	19 (8.6)
3	9 (1.3)	9 (1.9)	4 (1.1)	3 (1.4)
4	0.0	0.0	0.0	0.0
FACT-P pain score, mean (SD)	11.1 (4.2)	11.1 (4.3)	10.0 (4.3)	9.8 (4.3)

ECOG, Eastern Cooperative Oncology Group; FACT-P, Functional Assessment of Cancer Therapy-Prostate.

- CV comorbidities at study entry are shown in Table 2.
  - 67% of first-line and 59% of second-line patients treated with AAP had CV comorbidities.
- 80% of patients were receiving concomitant therapies.

Table 2. Cardiovascular Comorbidities at Study Entry

CV comorbidity, n (%)	First-line AAP (n = 754)	Second-line AAP (n = 394)
Patients with CV comorbidities	504 (66.8)	234 (59.4)
Hypertension	411 (81.5)	187 (79.9)
Angina pectoris	34 (6.7)	19 (8.1)
Myocardial infarction	48 (9.5)	25 (10.7)
Arrhythmia	62 (12.3)	26 (11.1)
Thromboembolic disease	21 (4.2)	8 (3.4)
Transient ischaemic attack	14 (2.8)	8 (3.4)
Cerebrovascular accident	19 (3.8)	8 (3.4)
Other CV	139 (27.6)	61 (26.1)

- Dosing information is given in Table 3.
  - The recommended daily dose of abiraterone was 1000 mg.

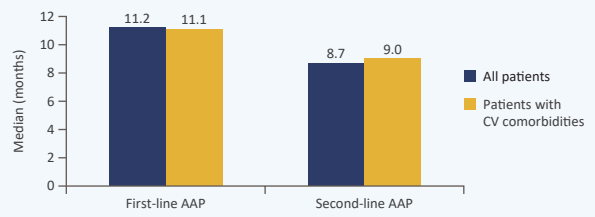
Table 3. Dosing Information

	First-line AAP		Second-line AAP	
	All patients (n = 754)	Patients with CV comorbidities (n = 504)	All patients (n = 394)	Patients with CV comorbidities (n = 234)
Abiraterone dose, n (%)				
250 mg	1 (0.1)	1 (0.2)	1 (0.3)	0 (0.0)
500 mg	8 (1.1)	7 (1.4)	0 (0.0)	0 (0.0)
750 mg	2 (0.3)	2 (0.4)	2 (0.5)	2 (0.9)
1000 mg	743 (98.5)	494 (98.0)	391 (99.2)	232 (99.2)
Corticosteroid given with abiraterone, n (%)[a]	746 (98.9)	499 (99.0)	387 (98.2)	228 (97.4)
Prednisone, n (%)	410 (54.4)	277 (55.0)	251 (63.7)	142 (60.7)
Prednisone dose, n (%)				
5 mg	23 (5.6)	13 (4.7)	6 (2.4)	4 (2.8)
10 mg	382 (93.6)	262 (94.6)	239 (95.2)	134 (94.4)
> 10 mg	3 (0.7)	2 (0.7)	6 (2.4)	4 (2.8)
Prednisolone, n (%)	299 (39.7)	195 (38.7)	119 (30.2)	71 (30.3)
Prednisolone dose, n (%)				
2 mg	1 (0.3)	1 (0.5)	1 (0.8)	1 (1.4)
5 mg	50 (16.7)	30 (15.4)	9 (7.6)	5 (7.0)
8 mg	4 (1.3)	3 (1.5)	0 (0.0)	0 (0.0)
10 mg	236 (78.9)	156 (80.0)	98 (82.4)	57 (80.3)
> 10 mg	8 (2.7)	5 (2.6)	6 (5.0)	4 (5.6)
Not reported	0 (0.0)	0 (0.0)	5 (4.2)	4 (5.6)

[a]Includes prednisone, prednisolone and other corticosteroids.

- Treatment duration was longer for patients receiving first- versus second-line AAP and similar between all patients and those with CV comorbidities (Figure 2).
- No new safety signals were observed with first- or second-line AAP in the overall patient population or in the subgroups of patients with CV comorbidities (Table 4).
- In the group that received first-line AAP, 7.1% of all patients discontinued because of toxicity compared with 8.9% patients with CV comorbidities; in the group that received second-line AAP, 7.5% and 9.6% of patients, respectively, discontinued.

Figure 2. Treatment Duration[a]



[a]Median duration of treatment by Kaplan-Meier estimates and censoring of patients with ongoing treatment at end of Registry.

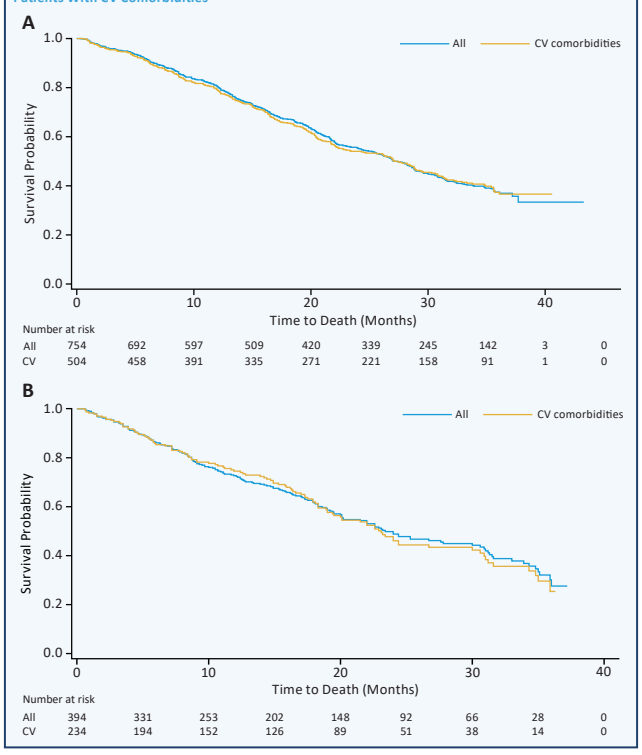
Table 4. Safety (Treatment-Emergent Adverse Events Reported in ≥ 10% of Patients)[a]

	First-line AAP		Second-line AAP	
	All patients (n = 754)	Patients with CV comorbidities (n = 504)	All patients (n = 394)	Patients with CV comorbidities (n = 234)
Patients with at least 1 treatment-emergent adverse event	487 (64.6)	338 (67.1)	222 (56.3)	132 (56.4)
General disorders and administration site conditions	219 (29.0)	156 (31.0)	101 (25.6)	65 (27.8)
Fatigue	56 (7.4)	37 (7.3)	22 (5.6)	17 (7.3)
Asthenia	54 (7.2)	39 (7.7)	22 (5.6)	14 (6.0)
Oedema peripheral	51 (6.8)	34 (6.7)	16 (4.1)	11 (4.7)
Musculoskeletal and connective tissue disorders	173 (22.9)	113 (22.4)	70 (17.8)	44 (18.8)
Back pain	57 (7.6)	41 (8.1)	12 (3.0)	8 (3.4)
Arthralgia	36 (4.8)	21 (4.2)	9 (2.3)	5 (2.1)
Bone pain	29 (3.8)	17 (3.4)	19 (4.8)	12 (5.1)
Gastrointestinal disorders	139 (18.4)	94 (18.7))	54 (13.7)	34 (14.5)
Diarrhoea	36 (4.8)	26 (5.2)	9 (2.3)	6 (2.6)
Constipation	28 (3.7)	19 (3.8)	8 (2.0)	6 (2.6)
Nausea	22 (2.9)	15 (3.0)	13 (3.3)	10 (4.3)
Infections and infestations	121 (16.0)	80 (15.9)	43 (10.9)	25 (10.7)
Urinary tract infection	29 (3.8)	21 (4.2)	11 (2.8)	7 (3.0)
Pneumonia	18 (2.4)	14 (2.8)	3 (0.8)	3 (1.3)
Sepsis	13 (1.7)	7 (1.4)	-	-
Renal and urinary disorders	84 (11.1)	60 (11.9)	31 (7.9)	20 (8.5)
Haematuria	36 (4.8)	27 (5.4)	11 (2.8)	8 (3.4)
Urinary retention	11 (1.5)	9 (1.8)	1 (0.3)	1 (0.4)
Dysuria	10 (1.3)	6 (1.2)	3 (0.8)	2 (0.9)
Nervous system disorders	76 (10.1)	48 (9.5)	22 (5.6)	17 (7.3)
Paraesthesia	15 (2.0)	6 (1.2)	-	-
Headache	11 (1.5)	7 (1.4)	5 (1.3)	3 (1.3)
Dizziness	7 (0.9)	4 (0.8)	2 (0.5)	2 (0.9)

[a]Adverse events occurring in ≥ 10% of patients by system organ class (SOC). The 3 most common preferred terms in each SOC for all patients are shown.

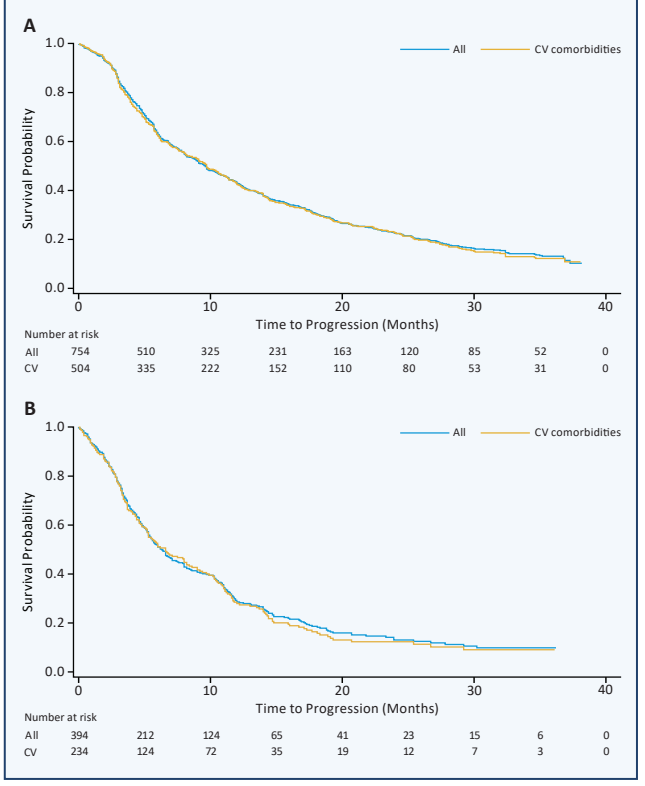
- Median (95% CI) overall survival is shown in Figure 3.
  - In patients receiving first-line AAP, median overall survival was:
    - 27.1 (25.3-28.9) months for all patients
    - 27.4 (23.0-30.3) months for patients with CV comorbidities
  - In patients receiving second-line AAP, median overall survival was:
    - 23.4 (20.1-30.6) months for all patients
    - 23.1 (19.4-30.0) months for patients with CV comorbidities

Figure 3. Overall Survival in First-Line (A) and Second-Line (B) AAP Treatment in All Patients and in Patients With CV Comorbidities



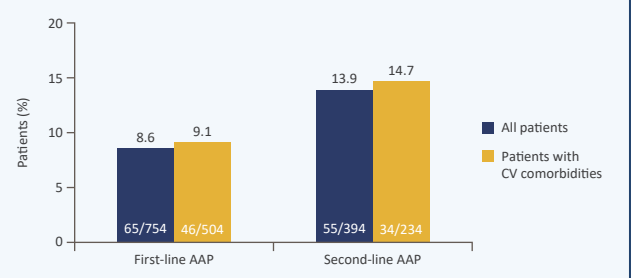
- Median (95% CI) time to progression is shown in Figure 4.
  - In patients receiving first-line AAP, median time to progression was:
    - 9.60 (8.40-10.80) months for all patients
    - 9.70 (8.20-11.20) months for patients with CV comorbidities
  - In patients receiving second-line AAP, median time to progression was:
    - 6.30 (5.40-7.50) months for all patients
    - 6.60 (5.30-8.40) months for patients with CV comorbidities

Figure 4. Time to Progression in First-Line (A) and Second-Line (B) AAP Treatment in All Patients and in Patients With CV Comorbidities



- The 6-month total mortality rates were similar between all patients and those with CV comorbidities among patients who were treated with AAP first (~9%) and second line (~14%) (Figure 5).

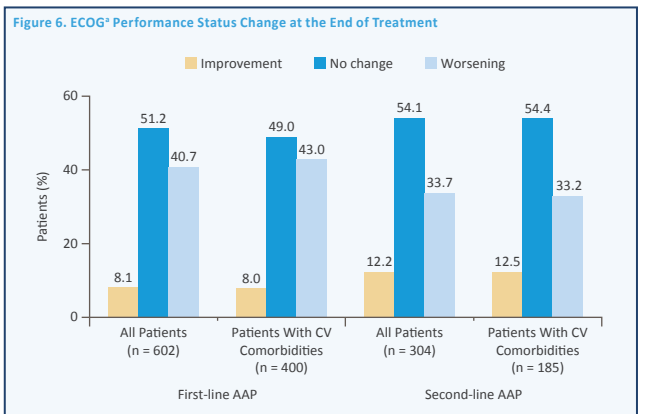
Figure 5. 6-Month Total Mortality Rate[a]



[a]By Kaplan-Meier estimates and censoring of patients alive at end of Registry.

- There was an improvement or no change in ECOG performance status in the majority of patients at the end of treatment with AAP first or second line, including in those patients with CV comorbidities, when compared with the start of treatment (Figure 6).

Figure 6. ECOG[a] Performance Status Change at the End of Treatment



[a]The ECOG scale ranges from 0 to 4, with 0 being fully functional and asymptomatic, and 4 being bedridden; improvement is reduction in score, worsening is increase in score.

CONCLUSIONS

- These real-world data confirm those from randomised trials and indicate that first- and second-line AAP is effective for treating mCRPC in a patient group in whom specific comorbidities were not excluded.
- In this real-world setting, AAP was well tolerated, including among patients who had CV comorbidities.
- Most patients were treated with AAP first line, including the substantial majority who had CV comorbidities.
- Efficacy outcomes were similar between the total patient group and the substantial subgroup of patients with baseline CV comorbidities, suggesting that AAP is effective in this latter group of patients.
- The PCR included a large number of patients from a variety of countries and had robust data collection (baseline characteristics, treatment initiation, closely monitored adverse events).
  - The results confirm real-world clinical outcomes in a broader population of patients than usually included in randomised clinical trials.

REFERENCES

1. Ryan CJ, et al. *Lancet Oncol.* 2015;16:152-160.
2. de Bono JS, et al. *N Engl J Med.* 2011;364:1995-2005.

DISCLOSURES

Anders Bjartell has received remuneration from Janssen, Astellas and Bayer for lectures and for participation in advisory boards.

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Author contact: anders.bjartell@med.lu.se

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