Clinical outcomes in chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC) patients treated with abiraterone acetate stratified by prognosis

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Background

Patients with mCRPC can have very disparate outcomes. A prognostic index was developed from the COU-AA-301 trial in post-chemotherapy mCRPC pts treated with ABI (J Clin Oncol 31, 2013 (suppl; abstr 5013)). The model included 6 risk-factors (RF) associated with poor outcome: ECOG performance status (PS) ≥ 2, presence of liver metastases, time from start of LHRH agonists/antagonists to start of ABI ≤ 36 months, albumin ≤40 g/L, alkaline phosphatase (ALP) ≥ upper limit of normal (ULN) and lactate dehydrogenase (LDH) ≥ ULN. The aim of this study was to evaluate this model in an unselected, sequentially treated, population-based cohort of chemotherapy-naïve mCRPC patients treated with ABI.

Methods

246 mCRPC patients at 6 cancer centres
- Chemotherapy naïve
- Treated with abiraterone July 2009-February 2015

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197 mCRPC patients with complete risk factor information classified into prognostic groups:
- Good: 0-1 risk factors
- Intermediate: 2-3 risk factors
- Poor: 4-6 risk factors

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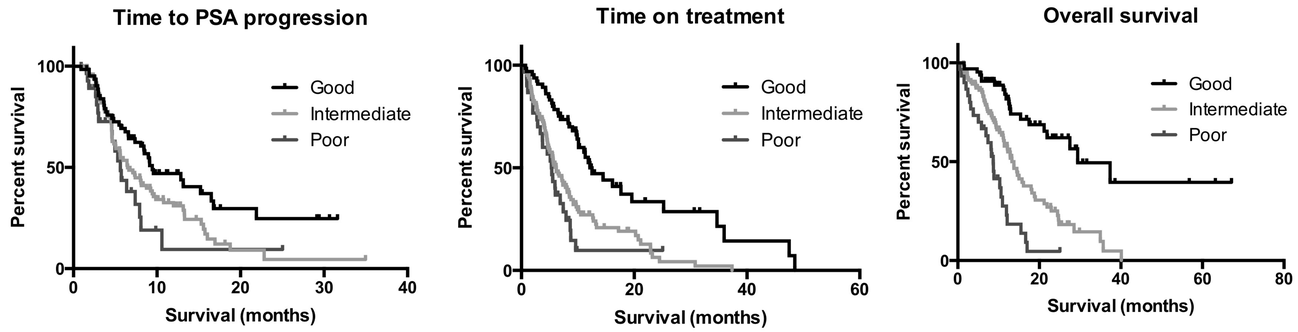
Outcomes assessed by prognostic group:
- PSA response (Decline ≥50%)
- Time to PSA progression (PCWG2 criteria)
- Overall survival

Univariate and multivariate analysis to examining association between baseline factors and survival outcomes

Baseline characteristics at initiation of abiraterone acetate (*n* = 197)

Characteristic	
Median Age, Years (IQR)	80 (71-84)
Gleason Score, n (%)	
6-7	57 (27)
8-10	109 (55)
Unknown	31 (16)
Disease sites, n (%)	
Bone	149 (76)
Lymph node	58 (29)
Liver	5 (3)
Median time since commencing ADT, months (IQR)	47 (22-93)
ECOG PS, n (%)	
0-1	122 (62)
≥ 2	75 (38)
Bone pain, n (%)	
Yes	65 (33)
No	129 (67)
Disease progression, n (%)	
PSA	175 (89)
Clinical	105 (53)
Radiographic	99 (50)
Laboratory	
Median LDH, U/L (IQR)	234 (176-355)
Elevated ≥ ULN, n (%)	59 (30)
Median ALP, U/L (IQR)	113 (80-221)
Elevated ≥ ULN, n (%)	69 (35)
Median Albumin, g/L (IQR)	38 (35-41)
Low < LLN, n (%)	130 (66)
Median Hemoglobin, g/L (IQR)	123 (111-132)
Low (< 100), n (%)	23 (12)
Prognostic Risk Group, n (%)	
Good: 0-1 risk factors	65 (31)
Intermediate: 2-3 risk factors	102 (52)
Poor: 4-6 risk factors	30 (17)

Clinical outcomes in chemotherapy-naïve mCRPC patients treated with abiraterone acetate stratified by six factor prognostic index model group: good (0-1 risk factors), intermediate (2-3 risk factors) and poor (4-6 risk factors).



Parameter	Good prognosis (0-1 RF) (n = 65)	Intermediate prognosis (2-3 RF) (n = 102)	Poor prognosis (4-6 RF) (n = 30)	*P*
PSA decline				
Decline ≥ 90%, n (%)	12 (18)	9 (8)	1 (3)	0.05
Decline ≥ 50%, n (%)	37 (57)	37 (36)	12 (40)	0.03
Decline ≥ 30%, n (%)	42 (65)	47 (46)	16 (53)	0.07
Median time on treatment, months (95% CI)	12.2 (8.7-15.6)	6.0 (4.4-7.5)	5.3 (4.0-6.6)	<0.001
Median time to PSA progression, months (95% CI)	9.4 (5.0-13.8)	6.5 (4.8-8.2)	5.6 (4.5-6.7)	0.01
Median overall survival, months (95% CI)	29.4 (17.8-41.0)	13.8 (11.5-16.0) HR 2.68 (1.60-4.47, P<0.001)	8.7 (7.8-9.6) HR 6.53 (3.56-11.95, p<0.001)	

On multivariate analysis, ECOG PS (HR 2.5, p<0.001), visceral metastases (HR 2.2, p=0.03) and ALP (HR 2.2, p=0.001) were confirmed as independent risk factors for decreased overall survival

Conclusions

- **The present analysis confirms that the prognostic index derived from the COU-301 study also prognostically discriminates chemotherapy-naïve patients receiving abiraterone acetate**
- **Patients with intermediate and poor prognosis also had a lower PSA response rate and shorter time to progression**
- **Identifying patients at risk of poor outcomes is important for informing clinical practice and clinical trial designs**