

Predictors of resistance to abiraterone acetate (AA) or enzalutamide (ENZ) in patients with metastatic castration-resistant prostate cancer (mCRPC) in the post-docetaxel setting

EUR Urol Suppl 2019;18(11):e3491

Omrčen T.¹, Eterovic D.², Vrdoljak E.¹

¹University Hospital of Split, Dept. of Oncology and Radiotherapy, Split, Croatia, ²University of Split, Dept. of Medical Physics, Split, Croatia

Introduction & Objectives: The treatment with AA or ENZ is one of the approved approaches in men with mCRPC in the post-docetaxel setting. However, a significant fraction of patients will not respond to treatment. We aimed at finding which characteristics could predict resistance to AA or ENZ.

Materials & Methods: From April 2015 to May 2019, 71 patients with mCRPC were treated with AA (N=34) or ENZ (N=37) at our institution. Resistance to treatment was defined as radiological progression within 3 months, documented at first visit.

Results: After a median follow up of 14.9 months, resistance was detected in 22 patients (31%). Many of the baseline characteristics differed between responders and non-responders, but on individual basis could not serve as predictors with clinically acceptable certainty (Table). In order to overcome this, a resistance score with a joint predictive power was obtained from the following clinical and laboratory predictors (lactate dehydrogenase sampled in only 35 patients and therefore omitted):

1. not only biochemical progression during or after docetaxel
2. ECOG performance status >1
3. duration of metastatic disease <41 months
4. serum PSA >52 ng/mL
5. serum alkaline phosphatase >119 g/L
6. serum hemoglobin concentration <126 g/L

Most patients with resistance and few responders had >3 positive predictors. Therefore, using the cut-off of 4 out of 6 predictive factors, the resistance score conferred both high sensitivity [82 (57-96%; 95% CI)] and specificity [88 (74-96%)].

TABLE. Univariate predictors of resistance

	sensitivity (%) 95% CI	specificity (%) 95% CI	AUC* 95% CI	p-value
Diagnosis and castration treatment				
Duration of response to castration <11 months	82 (60-95)	33 (18-45)	0.53 (0.4-0.6)	0.69

Type of progression during/after docetaxel				
not only biochemical progression	95 (72-100)	31 (18-45)	0.63 (0.5-0.7)	0.001
symptomatic progression	95 (77-100)	33 (20-48)	0.64 (0.5-0.8)	0.001
At study entry during/after progressing on docetaxel				
duration of metastatic disease <41 months	90.9 (71-99)	47 (32-66)	0.65 (0.5-0.8)	0.03
ECOG performance status >1	32 (14-55)	92 (80-98)	0.62 (0.5-0.7)	0.03
presence of visceral metastases	27 (11-50)	88 (93-100)	0.58 (0.5-0.7)	0.16
lactate dehydrogenase >252 (U/L)	100 (63-100)	93 (76-99)	0.95 (0.8-1)	<0.0001
PSA >52 ng/mL	76 (67-81)	68.4 (43-87)	0.77 (0.6-0.9)	<0.0001
hemoglobin <126 g/L	74 (49-91)	53 (39-69)	0.66 (0.5-0.8)	0.03
alkaline phosphatase >119 U/L	79 (63-90)	77 (50-93)	0.74 (0.6-0.9)	0.003

* Area under receiver-operating curve

Conclusions: The suggested resistance score integrates the diagnostic performances of multiple predictors and may serve in deciding which patient with mCRPC should be offered a treatment other than hormonal. However, our results should be evaluated in a larger prospective manner.