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

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Introduction and objectives

The treatment with AA or ENZ is one of the approved approaches in men with mCRPC in the post-docetaxel setting (1,2). However, a significant fraction of patients will not respond to treatment. We aimed at finding which characteristics could predict resistance to AA or ENZ.

Table

	sensitivity (%) 95% CI	specificity (%) 95% CI	AUC 95% CI	p-value
Diagnosis and castration treatment				
progresssion-free time <11 months	**82 (60-95)**	**33 (18-45)**	**0.53 (0.4-0.6)**	**0.69**
Chemotherapy after castration-resistance				
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 after progressing at 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**

TABLE. Univariate predictors of resistance

References

1. de Bono JS, Logothetis CJ, Molina A et al. Abiraterone and increased survival in metastatic prostate cancer. N Engl J Med 2011 May 26;364(21):1995-2005.
2. Loriot Y, Fizazi K, de Bono JS et al. Effect of enzalutamide on time to first skeletal-related event, pain, and quality of life in men with castration-resistant prostate cancer: results from the randomised, phase 3 AFFIRM trial. Lancet Oncol.2014 Sep;15(10):1147-56.

Methods and materials

From April 2015 to May 2019, 71 patient with mCRPC was
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, 22 patients (31%) resisted to therapy. 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 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, the resistance score conferred both high sensitivity [82 (57-96%; 95% CI)] and specificity [88 (74-96%)].

Conclusion

The suggested resistance score integrates the diagnostic performances of multiple predictors and may serve to decide which patient with mCRPC should be offered a treatment other than hormonal.