Cardiac biomarkers among men with metastatic castration-resistant prostate cancer during abiraterone acetate treatment – a prospective, single centre study.

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Background: Abiraterone acetate (ABI) thereapy is a valuable anti-cancer treatment option for men with metastatic castration resistant prostate cancer (mCRPC). The role of cardiac biomarkers (CB) on the course of ABI is not clear. We aimed to determine the correlation of CB and the lenght of ABI therapy (time to treatment failure – TTF).
Methods: This is a prospective, observational study. We enrolled 35 consecutive mCRPC Patients who were qualified to ABI therapy between 2018-2020. Troponin (T), NtproBNP, and age- adjusted d-dimer (DD) were evaluated before the initiation of ABI treatment. Survival curves and log-rank test were used to evaluate the impact of CB on time to treatment failure (TTF) of ABI therapy. The protocol of the study was approved by Bioethical Committees at the Centre of Postgraduate Medical Education in Poland (Resolution Number 83/PB/2016) and was in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Inclusion criteria: pathological diagnosis of prostate adenocarcinoma, a radiologic evidence of metastases, concurrent use of androgen deprivation therapy (surgical or pharmacological), with a serum testosterone level of 50 ng/dL or less (≤1.7 nmol/L), Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1, no significant hepatic dysfunction (only Child-Pugh class A was eligible), no unstable or uncontrolled cardiac disorders during inclusion, no history of prior abiraterone acetate, enzalutamide or ketoconazole therapy.
Patients' characteristics (table 1) were registered before the initiation of ABI treatment.

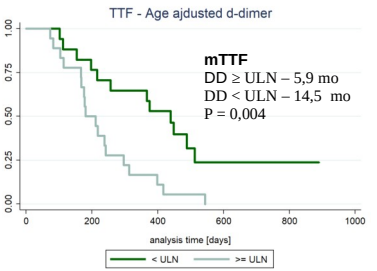
The primary endpoint of our analysis was the time to treatment failure (TTF), described as the time period between the initiation of ABI to the moment of its termination (defined as the cancer disease progression, unaccepted toxicity, hypersensitivity to the drug or the patient's death).
Disease progression was defined as the occurrence of at least 2 of the following 3 types of progression in total:
1) clinical, defined as pain progression (inclusion of a new opioid for more than 2 weeks), or the occurrence of skeletal related events, or deterioration of the patient's performance status to at least Grade 2 (according to the ECOG classification),
2) biochemical, defined as prostate specific antigen (PSA) progression (three consecutive increases in PSA, measured at least in weekly intervals, with proven increases of at least 50% from ABI baseline),
3) radiological, defined as the appearance of at least two new metastatic lesions, confirmed by scintigraphy.
Progression was also diagnosed if criteria of Response Evaluation Criteria In Solid Tumors ver. 1.1 were met (regardless of other types of progression mentioned above).

Table 1. Patient's characteristics.

Characteristic	Study population (n = 35)
Age - Median – yr (IQR)	70 (66-76)
Gleason score – No. (%)	
≤7	8 (24%)
8-10	24 (69%)
missing data	3 (9%)
Location of metastases – No. (%)	
Bone only	18 (51%)
Visceral	17 (49%)
PSA [ng/ml] - Median (IQR)	21,7 (7,45 – 106,5)
Cardiac comorbidity – No. (%)	
Hypertension	24 (72%)
Heart failure	4 (11%)
Hyperlipidemia	6 (17%)
Coronary artery disease	3 (9%)
Any of above	29 (83%)
LVEF – No. (%)	
>= 50%	30 (86%)
Cardiac biomarkers	
D-dimer [ng/ml] – median (IQR)	0,78 (0,47 – 1,29)
troponin T [ng/ml] – median (IQR)	0,01 (0,008 – 0,015)
NT-proBNP [pg/ml] – median (IQR)	218 (116,9 – 460,3)
Cardiac treatment – No. (%)	
Angiotensin system inhibitor	19 (54%)
B-blocker	20 (60%)
Statin	6 (17%)
Acetylsalicylic acid	11 (31%)
TTF – months - Median (95%CI)	8 (5,9 – 12,4)
Continue ABI – No. (%)	5 (14%)

Table 2. Univariate analysis.

Factor	HR (95% CI)	p
≥70 years (yes vs no)	1,32 (0,64 – 2,74)	0,44
BMI ≥25	0,42 (0,16 – 1,15)	0,09
Age adjusted d-dimer ≥ULN	**2,98 (1,39 – 6,39)**	**0,005**
Troponin ≥ULN	**3,02 (1,33 – 6,84)**	**0,008**
NT-proBNP ≥ULN	1,57 (0,69 – 3,54)	0,28
Gleason score ≥8	1,37 (0,59 – 3,22)	0,467
Visceral metastases	1,57 (0,76 – 3,23)	0,219
PSA ≥ median	1,81 (0,85 – 3,89)	0,126



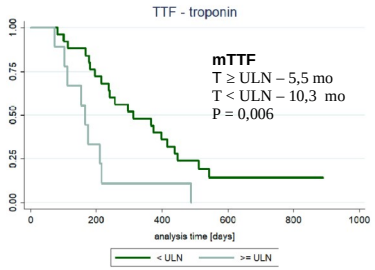


Table 3. Multivariate analysis.

Factor	HR (95% CI)	p
BMI ≥25	0,39 (0,14 – 1,12)	0,08
Age adjusted d-dimer ≥ULN	**2,78 (1,26 – 6,12)**	**0,011**
Troponin ≥ULN	**3,3 (1,39 – 7,78)**	**0,007**

TTF was significantly longer in patients with normal vs high DD (14,5 vs 5,9 months, p=0,004). Men with normal vs high T had statistically longer TTF (10,3 vs 5,5 months, p=0,006). Normal vs high concentration of NT-proBNP did not impact TTF (p=0,27). TTF among men who had normal DD and T, abnormal T or DD, or abnormal DD and T was 14,5 months, 7,8 months, 5,5 months, respectively. The difference was stastistically significant (p=0,0002).
In multivariate analysis age adjusted d-dimer ≥ ULN and troponin ≥ ULN were statistically significant factors for shorter TTF.
Conclusions: The study suggests that high levels of DD and T are correlated with shorter TTF of ABI in men with mCRPC. This correlation merits further study.