Dehydroepiandrosterone (DHEA) as a biomarker for subsequent therapy in metastatic castration-resistant prostate cancer (mCRPC): preliminary results from the SU2C-PCF West Coast Dream Team (WCDT).

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BACKGROUND
Low serum DHEA is associated with poor prognosis in patients with mCRPC, and may be predictive of treatment response and resistance. Here, we investigate the relationship between baseline serum DHEA and response to subsequent therapy following biopsy in the WCDT.

METHODS
Patients with progressive mCRPC enrolled to the WCDT were included in this preliminary analysis. A previously validated, high throughput, high pressure liquid chromatographic method with triple quadrupole mass spectral detection was used for the measurement of serum androgens, including DHEA. The limit of quantitation (LQ) of DHEA was 0.2ng/mL. PSA response was defined as PSA decline ≥50%.

RESULTS
Serum specimens from 59 men were included in this analysis. Seventeen men had treatment-naïve mCRPC, and 42 men had received prior abiraterone (20), enzalutamide (14), or both (8). Median DHEA for the entire cohort was 0.388ng/mL (<LQ to 4.07). Median DHEA levels were lower in patients with prior AR-targeted therapy compared to treatment-naïve patients (0.261 vs 0.706, p=0.0046), as expected; 18/28 patients with prior abiraterone exposure had DHEA <LQ, compared to 7/22 patients with prior enzalutamide. There was no difference in DHEA levels in PSA responders versus nonresponders overall. In patients with DHEA <LQ, 2/11 (18%) had PSA responses to AR-targeted therapy, while 6/8 (75%) had PSA responses to chemotherapy. In patients with DHEA ≥LQ, 9/18 (50%) had PSA responses to AR-targeted therapy, while 3/11 (27%) has PSA responses to chemotherapy. The relationship between DHEA levels (<LQ vs ≥LQ) and PSA response was significantly different between the treatment groups (AR-targeted vs chemotherapy (p=0.04). DHEA levels were significantly higher in men with PSA response to AR-targeted therapy compared to those without PSA response (0.840 vs 0.226, p=0.008). 10/23 (43%) patients with DHEA <LQ had inadequate (or indeterminate) tumor specimen for histology, while only 2/37 (5%) patients with DHEA ≥LQ had inadequate (or indeterminate) tumor specimen for histology.

CONCLUSIONS
In this exploratory analysis, there was a significant difference in the relationship between DHEA levels and PSA responses to AR-targeted therapy versus chemotherapy. Interestingly, there was a high rate of biopsy failure in patients with undetectable DHEA levels compared to those with detectable DHEA levels. Ongoing work include the following: serum analysis in >30 additional specimens, including mass array for full characterization of circulating steroid hormones; acquisition of sequencing data in specimens with paired biopsy specimens, for correlation of serum androgens with AR expression (including AR-v7), AR signature, and other exploratory analyses; analysis of sequential and paired (biopsy) specimens to explore changes in serum androgens over time with treatment and the impact on gene expression and outcomes; validation of a functional assay to provide “integrated” read-out of “pan-androgens” for potential clinical application.
CONFLICTS OF INTEREST
None

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