Body composition and the efficacy of pre-operative hormone therapy (HT) for men with localized and/or locally advanced prostate cancer

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Background: In localized prostate cancer, adiposity increases the risk for recurrence and lethal disease, yet in metastatic castration-resistant prostate cancer (mCRPC), recent studies suggest that increasing adiposity may be associated with improved response to AR signaling inhibitors (ARSI). Given these paradoxical findings, it is critical to determine whether the influence of adiposity on prostate cancer is driven by stage or by exposure to treatment with ARSI. Herein, we test the hypothesis that adiposity and/or muscle are associated with resistance to HT in men treated with pre-operative HT.

Methods: Men with localized high-risk or locally advanced prostate cancer (HRPCa) who received 3-6 months of pre-operative ADT +/- ARSI on 3 clinical trials were eligible if they had CT imaging of L3 prior to HT. Body composition was measured using an AI segmentation tool prior to HT, after HT and at time of RP, and % change was calculated. Pathologic response was defined a T2N0 disease, and differences in proportions was tested with chi-square tests. PSA progression-free survival was defined as time from radical prostatectomy (RP) to date of PSA ≥ 0.2 ng/mL or date adjuvant/salvage XRT if PSA < 0.2 and calculated by Kaplan-Meier methods.

Results: In 104 men treated with pre-operative HT, median age was 63 years and pre-treatment median PSA was 12.7 (IQR 7.7, 25.7). 76.9% of men had Gleason grade group 4 or 5 disease, 45% had clinical T3-4 disease, and 12.5% had N1 disease. After pre-operative HT, men had a median loss of skeletal muscle mass (SMMi) of 8.6% (IQR -12.9%, -6.1), gain in subcutaneous adiposity (SATi) of 13.2% (IQR -4.7%, 23.9%), and loss of visceral adiposity (VATi) of 2.2% (IQR -18.3%, 11.0%). Pathologic response was significantly associated with lower levels of visceral (p=0.002), subcutaneous (p=0.004), and total adiposity (TATi, p=0.001) after exposure to HT (**Table**). Similar trends were observed with pre-treatment adiposity measures, but they were not statistically significant (**Table**). Increasing visceral, subcutaneous, and total adiposity after exposure to HT was associated with a significant increase in the hazard for PSA progression (VATi HR 1.09 for 10 unit increase, p=0.04; SATi HR 1.14 for 10 unit increase, p=0.03; TATi HR 1.08, p=0.01).

Conclusions: In men with localized high-risk or locally advanced prostate cancer, elevated adiposity levels after treatment with pre-operative HT were associated with inferior clinical outcomes. These findings suggest that the influence of adiposity on prostate cancer is dictated by stage rather than exposure to HT. Future analyses will evaluate how baseline disease characteristics differ by adiposity groupings.

Funding Acknowledgements: This work is supported by the Rob Heyvaert and Paul Heynen Prostate Cancer Foundation Young Investigator Award (21YOUN33). AWH is also supported by an Early Investigator Research Award by the Department of Defense (W81XWH2210117), an ASCO Conquer Cancer Foundation Career Development Award, and philanthropic donations from the Hiley Family and Michael and Patricia Berns.

Conflict of Interest Statement: AWH reports advisory board consulting for Johnson & Johnson Innovative Medicine, Intellisphere, Exelixis, Eisai, and Pfizer; honoraria from Medscape, Projects in Knowledge, and Binaytara Foundation; travel support from DAVA Oncology, and institutional research funding from Bayer and Eisai. PGP has received honoraria for service on scientific advisory board for Janssen and AstraZeneca. JRG is a consultant and advisory board member for Bayer. BAS reports advisory board consulting to Merck, travel support from Merck, and institutional research funding from Regeneron. JLM reports honoraria from Merck, Bristol-Myers Squibb, and Novartis. CJL reports honoraria from Bayer, Amgen, Novartis, Boehringer Ingelheim, Merck Sharp & Dohme, and Exelixis; and institutional research funding from Janssen, ORIC Pharmaceuticals, Novartis, and Aragon Pharmaceuticals. DEF has received research funding from GTx, Inc, and has a familial relationship with Biocity Biopharmaceuticals, Hummingbird Bioscience, Bellicum Pharmaceuticals, Maia Biotechnology, Alms Therapeutics, Hinova Pharmaceuticals, and Barricade Therapeutics.

Body composition metric	**No pathologic response** (n=65)	**Pathologic response** (n=39)	**Full cohort** (n=104)	**P value**
Pre-treatment body composition				
Subcutaneous adipose tissue index (IQR)	63.0 (50.9, 72.5)	55.5 (38.8, 71.6)	59.1 (46.7, 72.4)	0.12
Visceral adipose tissue index (IQR)	70.9 (49.6, 96.2)	63.9 (39.0, 90.0)	66.5 (45.8, 92.0)	0.18
Total adipose tissue index (IQR)	137.0 (106.5, 178.5)	121.6 (86.1, 167.7)	133.0 (99.9, 170.7)	0.07
Skeletal muscle mass index (IQR)	55.3 (52.1, 60.8)	52.9 (48.6, 60.4)	55.0 (50.0, 60.8)	0.20
Skeletal muscle density (IQR)	44.0 (37.3, 49.1)	45.1 (40.7, 51.6)	44.3 (38.9, 49.3)	0.18
Intramusclar adipose index (IQR)	3.0 (1.9, 4.5)	2.6 (1.7, 4.8)	2.7 (1.8, 4.6)	0.47
Body composition after hormone therapy				
Subcutaneous adipose tissue index (IQR)	68.5 (58.1, 80.3)	52.6 (41.3, 59.8)	66.5 (52.0, 76.6)	**0.004**
Visceral adipose tissue index (IQR)	71.6 (46.8, 105.6)	39.4 (20.9, 58.5)	59.3 (39.4, 93.2)	**0.002**
Total adipose tissue index (IQR)	149.0 (105.7, 189.9)	96.2 (68.6, 112.6)	127.2 (96.4, 170.6)	**0.001**
Skeletal muscle mass index (IQR)	52.4 (48.2, 57.0)	49.9 (46.0, 54.4)	51.7 (48.0, 55.5)	0.19
Skeletal muscle density (IQR)	38.8 (30.9, 43.6)	43.1 (38.9, 46.5)	40.3 (33.3, 45.3)	0.13
Intramusclar adipose index (IQR)	3.1 (2.1, 5.6)	2.5 (1.9, 3.6)	2.7 (2.0, 4.5)	0.29