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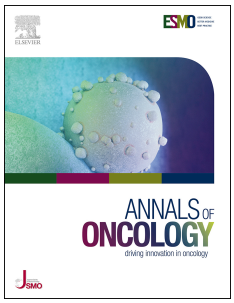

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Letter to the Editor

Androgen deprivation therapy and SARS-CoV-2 in men with prostate cancer: findings from the University of California Health System registry

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Conflicts of interest:

Rahul Aggarwal discloses the following potential conflicts of interest: Honoraria: Clovis Oncology. Consulting or Advisory Role: AstraZeneca, Dendreon, Advanced Accelerator Applications, Clovis Oncology, Axiom Biotechnologies. Research funding (for institution): Zenith Epigenetics, Novartis, Xynomic Pharma, Cancer Targeted Technology, Janssen, Merck, Abbvie, Amgen, AstraZeneca, Bioexcel Therapeutics

Atul Butte is a co-founder and consultant to Personalis and NuMedii; consultant to Samsung, Mango Tree Corporation, and in the recent past, 10x Genomics, Helix, Pathway Genomics, and Verinata (Illumina); has served on paid advisory panels or boards for Geisinger Health, Regenstrief Institute, Gerson Lehman Group, AlphaSights, Covance, Novartis, Genentech, Merck, and Roche; is a shareholder in Personalis and NuMedii; is a minor shareholder in Apple, Facebook, Alphabet (Google), Microsoft, Amazon, Snap, Snowflake, 10x Genomics, Illumina, Nuna Health, Assay Depot (Scientist.com), Vet24seven, Regeneron, Sanofi, Royalty Pharma, Pfizer, BioNTech, AstraZeneca, Moderna, Biogen, Twist Bioscience, Pacific Biosciences, Editas Medicine, Invitae, and Sutro, and several other non-health related companies and mutual funds; and has received honoraria and travel reimbursement for invited talks from Johnson and Johnson, Roche, Genentech, Pfizer, Merck, Lilly, Takeda, Varian, Mars, Siemens, Optum, Abbott, Celgene, AstraZeneca, AbbVie, Westat, several investment and venture capital firms, and many academic institutions, medical or disease specific foundations and associations, and health systems. Atul Butte receives royalty payments through Stanford University, for several patents and other disclosures licensed to NuMedii and Personalis. Atul Butte's research has been funded by NIH, Northrup Grumman (as the prime on an NIH contract), Genentech, Johnson and Johnson, FDA, Robert Wood Johnson Foundation, Leon Lowenstein Foundation, Intervalien Foundation, Priscilla Chan and Mark Zuckerberg, the Barbara and Gerson Bakar

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We read with great interest two studies on the association of androgen deprivation therapy (ADT), a widespread therapy for advanced prostate cancer, and COVID-19 published in the *Annals*.[1,2] SARS-CoV-2 entry into host cells is facilitated by the transmembrane protease TMPRSS2, whose expression can be modulated by the androgen receptor.[3] Pre-clinical data suggests that ADT may protect from SARS-CoV-2 infection and decrease COVID-19 severity.[3] A registry study reported by Montopoli et al.[1] demonstrated that ADT was associated with decreased COVID-19 incidence in Venetian men with prostate cancer. However, this relationship was not observed by Koskinen et al.[2] in a study of Finnish men. This relationship has not been examined in a diverse population.

We sought to determine the association between ADT and COVID-19 incidence in men with prostate cancer in the University of California Health System (UCHS) in California, USA. The UC Health COVID Research Data Set, which includes electronic health data of all patients who underwent testing for SARS-CoV-2 at 5 UCHS academic medical centers and 12 affiliated hospitals across California, was used for men tested between February 1, 2020 and December 20, 2020.[4] Association of SARS-CoV-2 positivity and ADT (GnRH agonist/antagonist) within 6 months of COVID-19 testing was determined using the Chi-squared test. Multivariable logistic regression to predict SARS-CoV-2 infection based on ADT, race/ethnicity, birth year, and co-morbidities was performed. This study was approved by the University of California, San Francisco Institutional Review Board.

Overall, 5,211 men with prostate cancer who underwent SARS-CoV-2 testing were identified, of whom 97 (1.9%) tested positive. Of these men, 3,812 (73%) were White; 369 (7%) Black or African-American; 350 (7%) Asian, American Indian/Alaska Native, or Native Hawaiian/Pacific-Islander; 238 (5%) Other/Multiple race; and 442 (8%) Unknown race. There were 385 (7%) Hispanic/Latinx men.

Of 799 men who received ADT, 18 (2.3%) tested positive. Of 4,412 men who did not receive ADT, 79 (1.8%) tested positive (OR 1.30, 95%CI 0.78-2.19, *P*=0.31). No statistically significant association between ADT and SARS-CoV-2 infection was found within race/ethnicity subgroups. Multivariable logistic regression revealed that ADT was not independently associated with SARS-CoV-2 infection (Table 1). By contrast, known risk factors (diabetes, Black race, Other/Multiple race, and Hispanic/Latinx ethnicity) were associated with infection.

Among 97 COVID-positive men with prostate cancer, 1/19 men (5.3%) who received ADT died, versus 7/78 men who did not (9.0%) (OR 0.56, 95%CI 0.07-4.88, *P*=0.60).

Our results do not suggest a benefit of ADT for SARS-CoV-2 infection or mortality, though deaths were few. Differences between our study and those in Italy and Finland are exclusion of oral anti-androgen therapies and COVID-19 community prevalence. Other factors such as socioeconomic determinants, stage, chemotherapy use, and ADT duration are unreported potential confounders. ADT duration may be important, as Patel et al.[5] recently reported that longer ADT duration was associated with decreased mortality.

In conclusion, no association between ADT and SARS-CoV-2 infection was identified in this large, diverse population of men with prostate cancer. Racial/ethnic disparities in SARS-CoV-2 infection rates described in the USA are also observed in men with prostate cancer.

Table 1. Multivariable logistic regression of SARS-CoV-2 infection in men with prostate cancer

Characteristic	*N*	Odds Ratio	95% CI	*P*-value
ADT				
Received	799	1.18	(0.70,1.99)	0.541
Birth year				
≤1955	3,999	0.91	(0.57,1.45)	0.680
Race				
White	3,812		Reference	
Black or African-American	369	1.96	(1.04,3.68)	0.037
Asian, Native Hawaiian/ Pacific Islander, or American Indian/Alaska Native	35	0.34	(0.08,1.41)	0.136
Other or Multiple	238	2.16	(1.03,4.50)	0.041
Unknown	442	1.59	(0.83,3.05)	0.165
Ethnicity				
Hispanic/Latinx	385	1.94	(1.04,3.63)	0.038
Co-morbidities				
Diabetes mellitus	763	1.86	(1.13,3.06)	0.015
Chronic kidney disease	658	1.08	(0.61,1.92)	0.800
Chronic obstructive pulmonary disease	321	1.60	(0.82,3.15)	0.171
Coronary artery disease	243	1.36	(0.62,3.02)	0.444
Congestive heart failure	334	0.99	(0.46,2.10)	0.974
Obesity	340	1.22	(0.62,2.44)	0.569

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