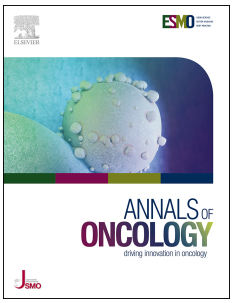

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Androgen deprivation and SARS-CoV-2 in men with prostate cancer

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Letter to the Editor

We read with great interest the very recent article by Montopoli *et al.*, which reports men with prostate cancer tested for SARS-CoV-2 in Veneto, Italy, by April 1, 2020 (1). The authors suggest that androgen deprivation therapy (ADT) could partially protect from SARS-CoV-2 infection (1). The biological premise for this observation is the androgen receptor-mediated regulation of TMPRSS2 (2), a type II transmembrane serine protease that is important for SARS-CoV-2 entry to host cells (3). Indeed, androgens regulate *TMPRSS2* expression also in a lung carcinoma cell line (4).

Encouraged by the findings of Montopoli *et al.*, we examined the health care records of patients with prostate cancer (ICD-10 code C61) in the Hospital District of Helsinki and Uusimaa (HUS), Finland, using automated text mining with manual verification and structured diagnostic codes. Altogether, 352 such men were tested for SARS-CoV-2 between March 7 and May 14, 2020. A patient was classified to be on ADT if he had a history of orchiectomy, or a valid prescription for a GnRH analogue, GnRH antagonist, and/or antiandrogens (flutamide, bicalutamide, enzalutamide) or the CYP17 inhibitor abiraterone before his SARS-CoV-2 test (n=134) (38%, 95% CI: 33%-43%). The mean age of these 134 men was 78.4 yrs ± 8.1 SD (range 58–96 yrs). The frequency of being on ADT was in agreement with that observed in a survey of a large cohort of UK men with prostate cancer (5). Conversely, a patient was classified not to be on ADT if no records of the above conditions were found or ADT had been ceased before a SARS-CoV-2 test (n=218; mean age 76.5 yrs ± 9.4 SD, range 51–96 yrs). The presence of SARS-CoV-2 RNA in nasopharyngeal swab samples was analyzed by reverse transcriptase polymerase chain reaction (RT-PCR) (details available upon request). This study was based on register data, provided by the registry holder, Helsinki University Hospital, and therefore no ethical permission was required according to the Finnish Medical Research Act.

Of the 352 prostate cancer patients, 17 (4.8%, 95% CI: 2.6%–7.0%) tested positive for SARS-CoV-2, and 6 (35%, 95% CI: 13%–58%) of them were on ADT. However, the frequency of being positive for SARS-CoV-2 was not associated with ADT (6/134 on ADT *vs.* 11/218 not on ADT; odds ratio (OR) 0.88; 95%CI 0.32 to 2.44, P=0.81). ADT was not associated with the severity of the disease, as assessed by occurrence of death or the need of intensive care (1/6 in ADT-positive group *vs.* 3/11 in the ADT-negative group; OR 0.53; 95%CI 0.04 to 6.66, P=0.63). There were no

differences in possible confounding comorbidities on COVID-19 severity between patients with and without ADT (6) (Table 1).

While we can only speculate on the difference between our results and those of Montopoli *et al.*, methodological differences stand out. Montopoli *et al.* collected data on 68 hospitals in Veneto region, and identified 118 SARS-CoV-2 positive patients with prostate cancer of whom 4 were on ADT and 114 were not (1). Thereafter, they compared the ratios of SARS-CoV-2 positive patients with and without ADT *per* all Venetian prostate cancer patients on (4/5273) or off ADT (114/37161) (OR 4.05; 95%CI, 1.55-10.59) (1). However, it can be estimated that the six provinces and the Venice metropolitan city had differences in the COVID-19 infection rates on April 1, 2020 (i.e. at the time of Venetian data acquisition), the greatest difference being over 4-fold (1, 7, 8). Thus, these apparent provincial differences in the infection rate represents a potential confounding factor. Accordingly, in our study we further restricted the analysis on the risk of SARS-CoV-2 infection in men with or without ADT only to the 163 patients living in Helsinki. Again, there was no significant relationship between ADT and the probability of being SARS-CoV-2 positive (*data not shown*).

In conclusion, our results do not support a role for ADT in the prevention of SARS-CoV-2 infection in men with prostate cancer via ADT-mediated decrease in the expression of *TMPRSS2*. These results do not encourage compassionate use of drugs that suppress pituitary gonadotropin secretion or inhibit androgen synthesis or androgen receptor in an attempt to decrease SARS-CoV-2 infection risk or to alleviate the course of COVID-19.

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Disclosure

The authors have declared no conflicts of interest.

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Table 1. The presence of potential confounding factors on COVID-19 severity in SARS-CoV-2 tested patients with prostate cancer classified on the basis of being on androgen deprivation therapy (ADT). The distributions of diagnoses from 2015 to two weeks before the SARS-CoV-2 test are shown. Smoking status was extracted by using automated text mining and manual verification. The data denote the number of patients with each condition.

	No ADT (n=218)	On ADT (n=134)	P-value[§]
Age >65 years	191	125	0.10
Hypertension[#]	47	30	0.89
Coronary artery disease[¤]	30	21	0.64
COPD[¥]	12	8	1.0
Diabetes[£]	17	16	0.26
Cardiac arrhythmia[Ω]	41	30	0.42
Current smoker	17	18	0.10

[§]Fisher exact test
[#]ICD-10 codes I10 and I15
[¤]ICD-10 codes I20, I21, I24 and I25
[¥]ICD-10 code J44
[£]ICD-10 code E11
[Ω]ICD-10 codes I48 and I49