Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

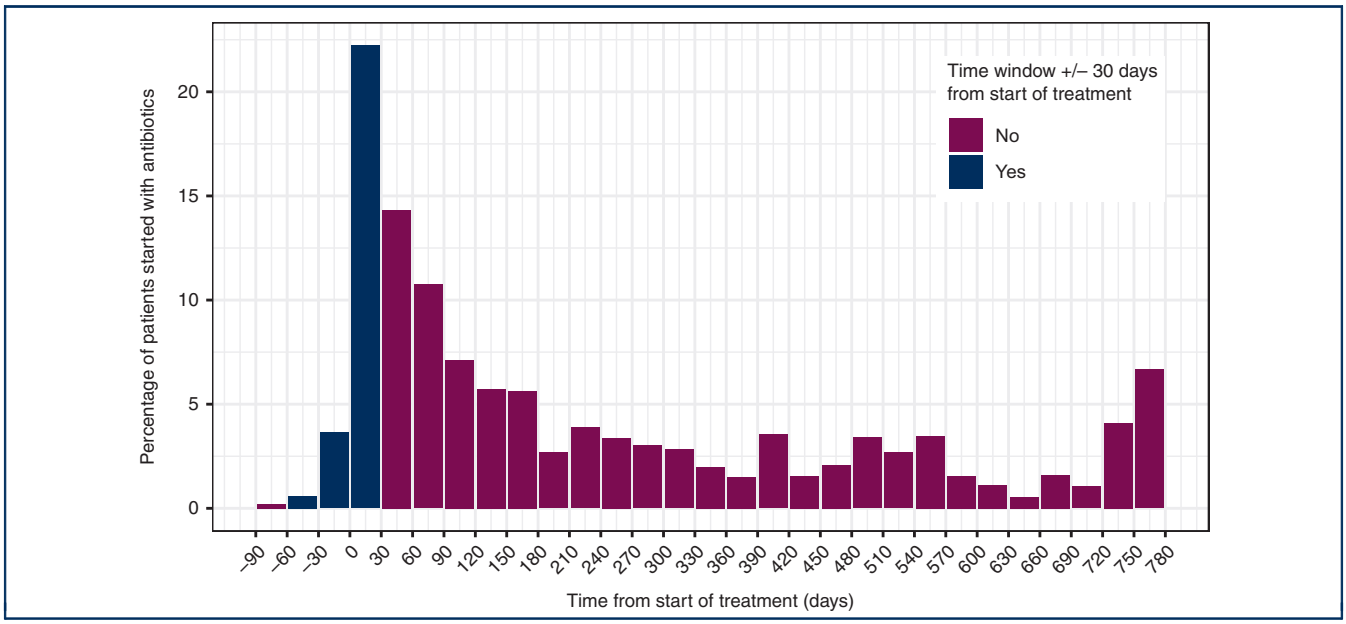

Figure 1. Percentage of patients (alive) who start antibiotics from 90 days before study treatment up to 780 days after start.
Bins are 30-day periods with the day marked on the *x*-axis included in the left bin.

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Available online 23 September 2020

https://doi.org/10.1016/j.annonc.2020.09.007

ACKNOWLEDGEMENTS

Data from the OAK (trial reference number: NCT02008227) and POPLAR trials (trial reference number: NCT01903993) were accessed according to Roche's policy and process for clinical study data sharing. Data analysis was supported by the foundation Personalized Healthcare Catalyst Alliance that aims to improve the personalized health care in The Netherlands.

FUNDING

This work was not supported by funding.

DISCLOSURE

The authors have declared no conflicts of interest.

REFERENCES

1. Chalabi M, Cardona A, Nagarkar DR, et al. Efficacy of chemotherapy and atezolizumab in patients with non-small-cell lung cancer receiving antibiotics and proton pump inhibitors: pooled post hoc analyses of the OAK and POPLAR trials. *Ann Oncol*. 2020;31(4):525—531.
2. Anderson JR, Cain KC, Gelber RD. Analysis of survival by tumor response. *J Clin Oncol*. 1983;1(11):710—719.
3. Hsu-Kim C, Hoag JB, Cheng G, Lund ME. The microbiology of post-obstructive pneumonia in lung cancer patients. *J Bronchology Interv Pulmonol*. 2013;20(3):266—270.

Androgen deprivation therapy in unlikely to be effective for treatment of COVID-19

Recent literature has reported that patients with prostate cancer treated with androgen deprivation therapy (ADT) have a lower incidence of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), an observation which has been widely reported by media outlets, together with speculation that ADT may be a potential treatment for coronavirus disease 2019 (COVID-19). The study by Montopoli et al.[1] was conducted at a population level in Italy, a region experiencing a high level of COVID-19 cases. They observed in a cohort of men with prostate cancer that those prescribed ADT were less likely to report COVID-19 (4/5273 cases versus 114/37 161, odds ratio 4.05, 95% confidence interval 1.55—10.59, $P = 0.00043$). Benefits were also observed for classification of mild and severe disease and were used as a basis of the conclusion that 'ADT, based on luteinizing hormone-releasing hormone (LHRH) agonist/antagonists or AR inhibitors, may be considered to reduce SARS-CoV-2 infections or complications in high-risk male populations.'

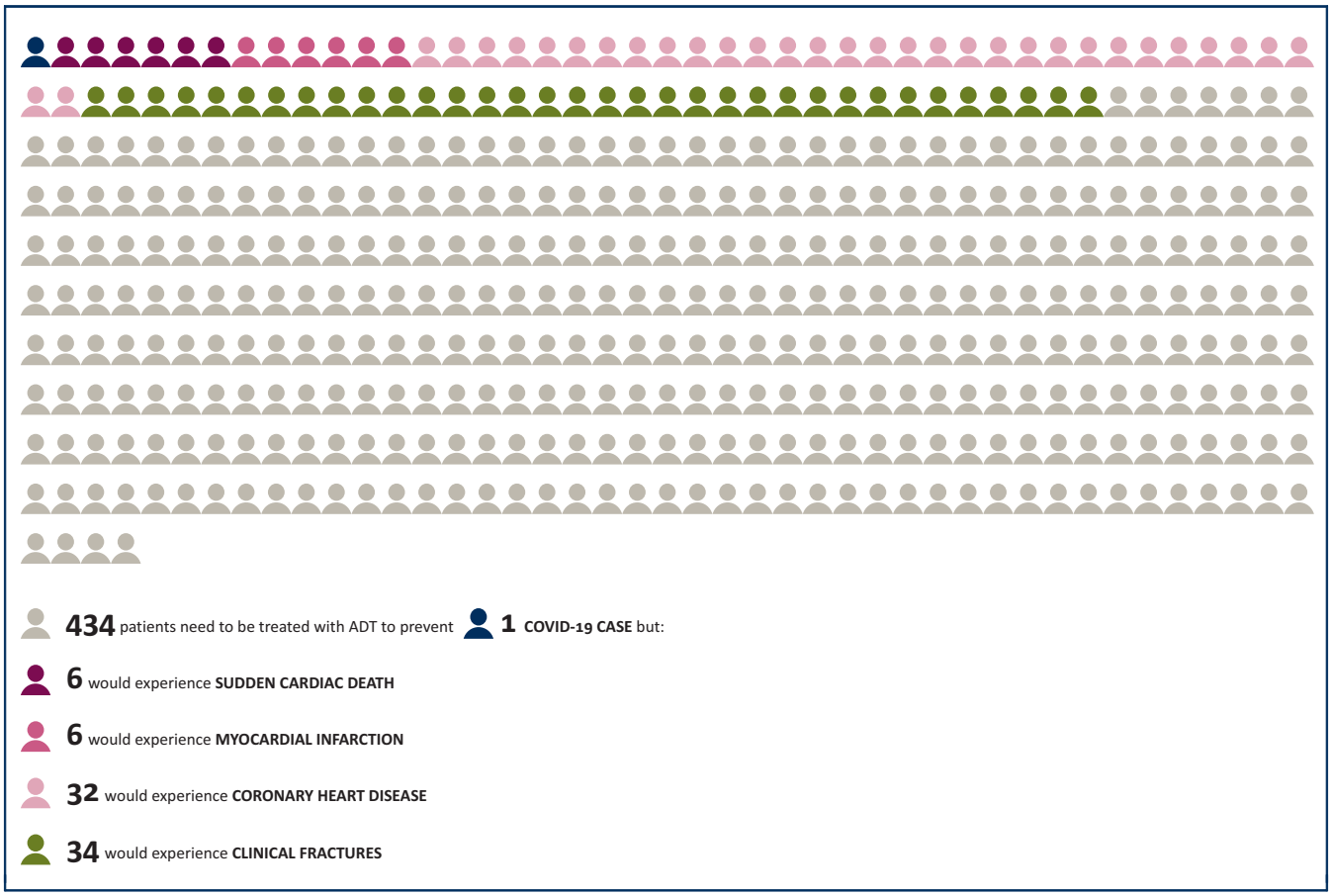

Figure 1. ADT treatment for COVID 19 in context.
ADT, androgen deprivation therapy; COVID-19, coronavirus disease 2019.

A useful metric to consider in this context is the number needed to treat, which is calculable from the data reported, but was not included by Montopoli et al.[1] We calculate that the number needed to treat with ADT for the prevention of one COVID-19 case is 434. Treatment of these cases is not without risk and this is shown in Figure 1 with data extracted from Bagrodia et al.[2] In addition, diabetes mellitus, decreased libido, hot flashes and erectile dysfunction would be expected in a high proportion of men. These adverse events are calculated per person-year, a time frame which may be relevant to prevention of COVID-19. Montopoli et al.[1] state that ADT could be administered transiently to minimise adverse events, though this hypothesis has not been tested in the data they present. Transient ADT treatment may be appropriate to reduce complications in those already infected with SARS-COV-2, although ADT adverse events are typically most common immediately after commencement.[3]

The mechanism of action which Montopoli et al.[1] describe may provide a novel target for COVID-19 treatments, but it seems unlikely that existing ADTs will provide a viable treatment option.

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Available online 30 September 2020

https://doi.org/10.1016/j.annonc.2020.09.014

FUNDING

None declared.

DISCLOSURE

The authors have declared no conflicts of interest.

REFERENCES

1. Montopoli M, Zumerle S, Vettor R, et al. Androgen-deprivation therapies for prostate cancer and risk of infection by SARS-CoV-2: a population-based study ($N = 4532$). *Ann Oncol*. 2020;31:1040-1045.
2. Bagrodia A, Diblasio CJ, Wake RW, Derweesh IH. Adverse effects of androgen deprivation therapy in prostate cancer: current management issues. *Indian J Urol*. 2009;25:169-176.
3. O'Farrell S, Garmo H, Holmberg L, Adolfsson J, Stattin P, Van Hemelrijck M. Risk and timing of cardiovascular disease after androgen-deprivation therapy in men with prostate cancer. *J Clin Oncol*. 2015;33:1243-1251.

Sequential treatment with NOTCH inhibitor crenigacestat followed by pazopanib in soft tissue sarcoma patients

Systemic treatment options are limited in patients with metastatic soft tissue sarcoma (STS). For instance, the objective response rate to pazopanib (a multikinase inhibitor approved in non-adipocytic STS) in this setting is 6%.[1]

After having received the investigational NOTCH inhibitor crenigacestat (LY3039478) in a phase I trial[2] (resulting in progressive disease after 1.8 months), a 53-year-old female patient with a heavily pretreated, advanced, radiation-induced breast angiosarcoma with lymph nodes metastases was treated with pazopanib 800 mg daily. After 2 days of treatment, we observed a complete clinical response that was confirmed 1 month later by an [^{18}F]2-fluoro-2-deoxy-D-glucose positron emission tomography. She underwent surgery 3 months later (showing a pathological complete response), and has remained free of disease after 62 months of follow-up.

Following this observation, an institutional decision was made to treat with pazopanib (400-800 mg daily, according to toxicity) all consecutive patients with metastatic STS who experienced progressive disease under crenigacestat.

Twelve patients [five males, median age: 55 years (range: 50-78)] were treated (including the first patient). The median number of previous treatment lines was two (range: one to five). Four patients had previously received pazopanib, with stable disease ($n = 2$) or progressive disease ($n = 2$) as best response. Patients' characteristics are shown in Table 1.

Table 1. Patients' characteristics before initiation of crenigacestat

Patient #	Primary tumor subtype and site	FNCLCC grade	Metastatic sites	Molecular characteristics	Previous systemic treatments	Best response to previous treatment by pazopanib
1	Angiosarcoma of the breast, in irradiated field	3	Skin, lymph nodes (locally advanced disease)	ND	FEC, docetaxel (for primary breast carcinoma); weekly paclitaxel, doxorubicin + ifosfamide	NA
2	Angiosarcoma of the heart	3	Bone, liver, pericardium	ND	Weekly paclitaxel	NA
3	Angiosarcoma of the breast, in irradiated field	3	Skin	*MYC* amplification	FEC, docetaxel (for primary breast carcinoma); doxorubicin + ifosfamide, weekly paclitaxel	NA
4	Angiosarcoma of the breast, in irradiated field	3	Skin, lymph nodes	ND	Weekly paclitaxel	NA
5	Dedifferentiated liposarcoma, retroperitoneal	ND	Peritoneum, skin	ND	Doxorubicin, trabectedin	NA
6	Leiomyosarcoma, retroperitoneal	2	Lungs, liver, pancreas, orbital cone	*TP53* mutation	Doxorubicin + dacarbazine, gemcitabine, trabectedin, ***pazopanib***	SD for 6 months
7	Leiomyosarcoma, retroperitoneal	3	Lungs, peritoneum	ND	Doxorubicin, gemcitabine, trabectedin, ***pazopanib***, oral cyclophosphamide	PD after 3 months
8	Leiomyosarcoma of the inferior vena cava	2	Lungs, liver, peritoneum	*RB* mutation (germinal)	Doxorubicin + Dacarbazine	NA
9	Leiomyosarcoma, retroperitoneal	3	Liver	*RB* mutation (germinal), *TP53* mutation	Doxorubicin + dacarbazine, gemcitabine	NA
10	Leiomyosarcoma, uterine	2	Lungs, liver, per itoneum, skin	ND	Gemcitabine, doxorubicin, trabectedin, dacabazine, ***pazopanib***	PD after 2 months
11	Pleiomorphic rhabdomyosarcoma of the thigh	3	Lungs, lymph nodes	*NOTCH2* translocation, *TSC1* loss, *RB* loss, *ATM* re-arrangement	Doxorubicin + ifosfamide, gemcitabine + dacarbazine	NA
12	Pleiomorphic rhabdomyosarcoma of the thigh	2	Lungs, lymph nodes	ND	Doxorubicin + ifosfamide + cisplatin, trabectedin, ***pazopanib***, pembrolizumab	SD for 12 months

FEC, 5-fluorouracil, epirubicin, and cyclophosphamide; NA, not applicable; ND, not determined; PD, progressive disease; SD, stable disease.