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## DISCLOSURE

The authors have declared no conflicts of interest.

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## Risk and severity of SARS-CoV-2 infection in breast cancer patients undergoing a structured infection screening program at the University and Hospital Trust of Verona

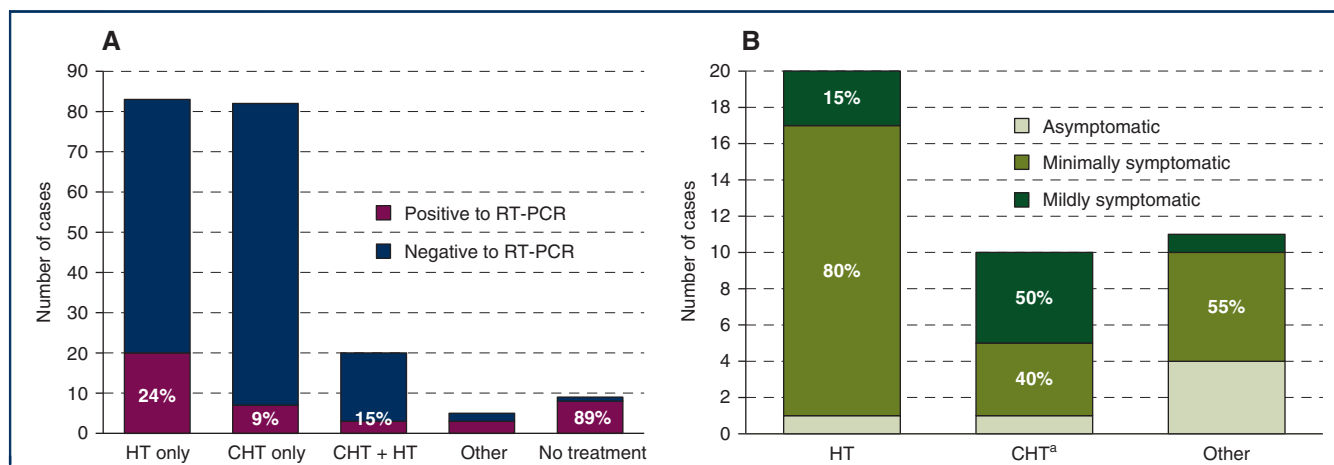


Cancer patients/survivors are at high risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and two- to threefold more likely to develop severe complications and death,<sup>1</sup> with female sex being relatively

protected.<sup>2</sup> Little evidence is currently available about specific associations between coronavirus disease-19 (COVID-19) and breast cancer (BC).

As part of a cohort of 979 oncological patients tested for SARS-CoV-2 by RT-PCR according to the strategy implemented by the Veneto Oncology Network (ROV),<sup>3</sup> we gathered data on 199 BC patients tested between 1 April 2020 and 30 April 2021. Forty-one BC patients tested positive [20.6%; 95% confidence interval (CI) 15.2% to 26.9%]; at a significance level of 0.05, BC patients were more likely to be infected with SARS-CoV-2 than patients with other cancer types (100/780, 12.8%, 95% CI 10.6% to 15.4%) (Fisher's exact test:  $P = 0.007$ ). Clinical characteristics, in particular menopausal status, did not significantly differ between infected and uninfected BC patients (Supplementary Table S1, available at <https://doi.org/10.1016/j.annonc.2022.02.227>). Anticancer treatment distribution at the time of testing significantly differed between the two groups (Figure 1A). The risk of infection was the lowest among BC patients undergoing chemotherapy (CHT), either alone (9%) or combined with hormonal treatment (HT) (15%), intermediate among those receiving HT only (24%), while nearly all patients not receiving active treatment (8/9) tested positive ( $P < 0.001$ ). None of the BC patients with SARS-CoV-2 infection developed severe COVID-19, six patients required hospitalization (two of which belonged to the CHT group) and none died of disease; patients undergoing CHT were more likely to develop symptomatic disease ( $P = 0.025$ ) (Figure 1B).

Epidemiological data gathered in the Veneto region between February and April 2020<sup>4</sup> suggested that BC patients might have a higher risk of hospitalization for COVID-19 and that anti-estrogenic treatment might reduce its prevalence in this patient population. However, in the first wave of the pandemic, SARS-CoV-2 testing was almost exclusively driven by symptoms, potentially missing asymptomatic cases. In our study, screening was targeted at asymptomatic subjects: under these conditions, HT did not appear to influence the risk and severity of SARS-CoV-2 infection within the BC population. However, the prevalence of infection among BC patients undergoing HT is still higher than that of the general population; this leaves open the possibility that menopausal status and HT might influence susceptibility to SARS-CoV-2 infection, even though the mechanistic explanation for such association remains elusive.<sup>5</sup> BC patients undergoing CHT were less likely to be infected, but when they did, they developed a more severe form of COVID-19, while patients not undergoing active treatment were at higher risk of infection. Consistently, recent epidemiological data showed that the risk of SARS-CoV-2 infection is higher in patients diagnosed with and treated for cancer >12 months before SARS-CoV-2 testing (prevalent-inactive cases), while the risk of death is higher for patients newly diagnosed or undergoing active treatment (incident or prevalent-active cases).<sup>6</sup> These results may be related to the stricter compliance of BC patients undergoing CHT with social distancing requirements, as well as to the more frequent SARS-CoV-2 screening in patients at high risk of myelosuppression.<sup>3</sup>



**Figure 1. SARS-CoV-2 infection characteristics in BC patients, according to the type of treatment ongoing at the time of testing.**

(A) Rates of SARS-CoV-2 positivity according to treatment. 'Other' includes five patients undergoing anti-HER2 monoclonal antibodies maintenance; 'No treatment' includes nine patients who had completed active anticancer therapy within the previous 6 months, only one of whom had been treated with CHT up to 4 months before testing. (B) Distribution of disease severity according to treatment. 'Other' includes three patients undergoing anti-HER2 monoclonal antibody maintenance and eight patients who had completed active anticancer therapy within the previous 6 months, only one of whom had completed chemotherapy 4 months before testing positive. Minimally symptomatic: fever, headache or mild respiratory symptoms (cough or sore throat), no hypoxemia and normal chest X-ray, excellent prognosis (phenotype 1 according to Rello et al.<sup>7</sup>); Mildly symptomatic: mild hypoxemia, small chest-X ray opacities, requiring close respiratory monitoring (respiratory rate and SpO<sub>2</sub>), 15% may progress to more severe disease (phenotype 2 according to Rello et al.<sup>7</sup>).

BC, breast cancer; CHT, chemotherapy; HER2, human epidermal growth factor receptor 2; HT, hormonal treatment; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. <sup>a</sup>Including patients undergoing CHT in association with luteinizing hormone-releasing hormone agonists.

Since such evidence might be useful to improve on current surveillance and management strategies, taking into account the circulation and clinical expressivity of different SARS-CoV-2 variants and the impact of the vaccination campaign, we plan to confirm our findings in a larger contemporary cohort from ROV and validate them using epidemiological data.

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