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Authors Reply: How to manage febrile neutropenia during the COVID pandemic? In response to, “A Practical Approach to the Management of Cancer Patients During the Novel Coronavirus Disease 2019 (COVID-19) Pandemic”

We agree with Boutayeb et al. that COVID-19 must be considered in patients presenting with febrile neutropenia; they may be a particularly high-risk population given their underlying immunocompromise and frequent interaction with the healthcare system. Viral respiratory infections, including COVID-19, should routinely be considered in differential diagnosis for febrile neutropenia as they are commonly identified even outside of the present pandemic.¹

The best evidence for sequential diagnostic algorithms for COVID-19 continues to evolve as emerging data is published. We believe that in patients who are admitted with febrile neutropenia, PCR-based diagnostic for COVID-19 should routinely be performed; in many of our centres as the turnaround time for such testing improves, we frequently obtain same-day results. Such patients would then be placed under appropriate precautions for a patient under investigation for COVID-19 to prevent nosocomial spread. Further, given the known limitations of the sensitivity for polymerase-chain-reaction (PCR) test to exclude the diagnosis of COVID-19, we would not necessarily withdraw precautions based on a single-negative assay and would consider repeat testing, particularly in the setting of ongoing fever or respiratory symptoms.²

There is not universal agreement on the use of routine chest radiography in patients with febrile neutropenia in the absence of respiratory symptoms;^{3,4} however, the European Society for Medical Oncology (ESMO) guidelines recommend chest-radiography. The Fleischner Society guidelines on the use of chest-imaging during the COVID-19 pandemic suggest that chest imaging should be used routinely at presentation in all patients with moderate-severe features of COVID-19 to establish a radiographic baseline, stratify risk of progression, and to supplement to diagnosis in patients with a negative PCR assay.⁵ For patients with febrile neutropenia, particularly in the setting of a negative PCR with ongoing clinical suspicion for COVID-19, a CT chest may further supplement the diagnosis given its

reported increased sensitivity.² Additionally, low-dose CT chest may be employed in resource constrained settings where radiologic assessment is more readily available than PCR testing and CT results may be quickly obtained. However, in the setting of PCR-confirmed COVID-19, a CT chest may not routinely be required and should be considered as clinically required on a case-by-case basis.

Additional considerations for the management of febrile neutropenia during the COVID-19 pandemic include primary prophylaxis with myeloid growth factors and outpatient management. We have not specifically recommended increased use of primary or secondary prophylaxis of myeloid growth factor, given anticipated resource constraints and lack of existing evidence related to COVID-19. However, we recognize that the American Society of Clinical Oncology (ASCO) guidelines support consideration of expanded use of myeloid growth factors for patients with a lower expected risk of febrile neutropenia.⁶ Further, in keeping with current ASCO recommendations, in low-risk clinically stable outpatients it may be preferable to maintain home isolation, outpatient investigation via tele-medicine consultation, and prescribe empiric antibiotic therapy to minimize additional exposures.⁶ Prospective investigation of these and other approaches to guide the evidence-based management of patients with cancer during the COVID-19 pandemic are highly anticipated.

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