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Treatment of Patients With Established VTE With Cancer and COVID-19

Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.

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Dr. Khorana:

Hi, my name is Alok Khorana, and I'm a Medical Oncologist and Director of the GI Cancer Program at the Cleveland Clinic in Cleveland, Ohio. And today I will be discussing the Treatment of Patients with Established VTE with Cancer and COVID-19.

As background, people with cancer are at higher risk for COVID-19 and its complications, including thromboembolism, severe disease, and mortality. The inflammatory response to SARS-CoV-2 infection can cause an acute - both and acute phase response and endothelial cell dysfunction. And together, this contributes to COVID-19-associated coagulopathy on a background of a hypercoagulable state of cancer in the first place.

D-dimer and other inflammatory and hemostatic biomarkers have been associated with worse outcomes in the general population with COVID, and may be also associated with worse outcomes in the cancer population.

In terms of thrombosis, VTE rates vary substantially by report, depending on whether patients were in the earlier part of the pandemic, the later part of the pandemic, pre vaccine, post vaccine, ambulatory setting, or hospital setting.

The most recent U.S. data that represented by a group in ASH in December, we found about - in a national dataset, found a 3% thromboembolism rate that's both venous and arterial, in a population that was different types of tumors including solid tumors and hematologic malignancies, and a mix of inpatients and outpatients.

Why COVID-19 leads to venous thromboembolism is displayed in this graph of mechanisms here. As you can see, many different factors contribute to the prothrombotic state in this setting, including complement activation, organ injury that leads to a very proinflammatory state which in turn can lead to increased factor VIII and a von Willebrand factor, endothelial cell dysfunction, platelet activation. And all of these things can lead to both fibrin formation and elevation on D-dimer.

In cancer patients specifically, certain factors have been found to be associated with increased COVID severity, including, as displayed here in this large registry data from the COVID and Cancer Registry, the absolute lymphocyte count, absolute neutrophil count, platelet counts, creatinine, a D dimer, LDH, and C-reactive protein.

Once cancer patients with acute COVID-19 get a blood clot, the treatment is similar as it is for treatment of acute VTE in cancer. For many years, this treatment used to be 6 months of low-molecular-weight heparin monotherapy, but in recent multiple randomized trials, as shown here on the slide, recurrent VTE appears to be a little bit less with direct oral anticoagulants, although this is associated with a slightly increased risk of major bleeding, seen in some but not all clinical trials of DOACs. And this increased risk of major bleeding appears to be primarily in the GI cancer population, as shown on the graph on the left. In non-GI cancer patients, you don't really see an

increased association of major bleeding with the direct oral anticoagulants.

So the algorithm that's followed in my practice is if you have a patient with COVID and cancer-associated VTE, if they don't have major GI, hepatic, or renal dysfunction, if they don't have any drug-drug interactions with drugs that they're on, if they don't have a high risk of bleeding, such as an unresected esophageal cancer, which is about most patients, about 70% of patients, then we would start with a direct oral anticoagulant, apixaban, rivaroxaban, or edoxaban. If they have one of those issues, then we would prefer to do the low-molecular-weight heparin.

Generally speaking, the duration of treatment should be at least 6 months, although it should be reassessed for both risk of bleeding and risk of recurrent VTE at 3 months and 6 months. At 6 months, we generally stop if the cancer is in remission and there's no active cancer therapy, or we continue if there is active cancer. This recommendation is concordant with guidelines from ASCO and ITAC, as shown here.

So to summarize, cancer patients are at risk for COVID-related complications given their immunocompromised status, the hypercoagulable state of cancer is enhanced during an acute COVID-19 infection. In terms of treatment, standard treatment guidelines for cancer-associated VTE should be followed. Anticoagulant approaches include Warfarin, low-molecular-weight heparins, and direct oral agents, and treatment should be continued for at least 6 months.

Thank you so much for your attention.

Announcer:
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