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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Primary Thromboprophylaxis of Patient at High-Risk of VTE Who Is Receiving Systemic Anticancer Therapy

Announcer:
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Dr. Ay:
Hello, I'm Cihan Ay. I am Professor of Hematology at the Medical University of Vienna. And welcome to the session on Primary Thromboprophylaxis of Patient with Cancer at High Risk of Venous Thromboembolism Who is Receiving Systemic Anticancer Therapy.

Let's start off with the case. A 66-year-old man with body mass index of 32 with metastatic pancreatic cancer. He has liver metastasis, is initiating ambulatory chemotherapy. The prechemotherapy blood counts are as follows: hemoglobin of 10.8, white blood cells of 12.9, platelets 412, D-dimer was also measured as 2.6 microgram per ml, and the Karnofsky Performance Status is 70%, corresponding to a ECOG performance status of 1.

The question here is: Does this patient have an indication for primary thromboprophylaxis?

In clinical practice, we have various settings where primary thromboprophylaxis is recommended and routinely administered like after major cancer surgery. Here even prolonged primary thromboprophylaxis with low-molecular-weight heparin after hospital discharge is recommended, also in hospitalized cancer patients with acute medical illnesses.

However, there is still a lot of discussion about primary thromboprophylaxis in the outpatient setting. And this is a very important topic because today the majority of patients with cancer are receiving the systemic cancer therapies in the ambulatory setting, and also the majority of thrombotic events are occurring outside of the hospital and are diagnosed in the ambulatory setting.

What are our options to identify patients at risk of venous thromboembolism? More than one decade ago, Dr. Khorana and colleagues have developed and validated a risk prediction model, the so-called Khorana Score, which consists of five readily available variables, including the type of cancer and blood count parameters and the body mass index. And based on the Khorana Score, our patient has 4 points. And this patient falls into the high-risk category of venous thromboembolism. And this Khorana Score was later refined and expanded by adding biomarkers, information on chemotherapy, and also the performance status.

There are also other project where a simplified risk prediction models for an individual VTE risk assessment have been developed. And one of them is developed by the - my group here in Vienna. And this risk assessment model just contains two variables, the type of cancer and D-dimer levels. And if we apply this risk assessment here to this patient, based on this nomogram here, so we have a patient with pancreatic cancer, we're getting 100 points, D-dimer was measured as around 2.6, getting 40 points, adds up to 140 points, which is corresponding to a 6-month cumulative incidence of 15%.

With regard to evidence for primary thromboprophylaxis, we have data with low-molecular-weight heparins in ambulatory cancer patients compared to no thromboprophylaxis. And in a systematic review and metaanalysis, it has been demonstrated that primary

thromboprophylaxis with low-molecular-weight heparin is significantly decreasing the VTE risk. However, the baseline risk of venous thromboembolism in the non-thromboprophylactic group was rather low, and lower than expected. And the reason for this was that in these studies, no risk assessment was applied; and therefore, novel trials for primary thromboprophylaxis with DOAC have based their decision on risk assessment.

And in two randomized controlled trials, the AVERT and the CASSINI study, the Khorana Score was used to identify patients at high risk of thrombosis. Patients with a score of 2 or higher were randomized to a DOAC or placebo. And in both of these studies, it has - it could be shown that in their own treatment group, the risk

of venous thromboembolism could be significantly reduced with apixaban or rivaroxaban for primary thromboprophylaxis in patients with cancer receiving ambulatory chemotherapy. And the bleeding risk overall was very low with DOAC in AVERT and the CASSINI study.

What are the updates of the latest guidelines on primary thromboprophylaxis in the ambulatory setting? Primary thromboprophylaxis is uniform formula in the guidelines recommended with low-molecular-weight heparins or with direct oral anticoagulants. In this case, with rivaroxaban or apixaban based on the evidence that I have presented, if there is a low risk of bleeding.

However, for certain cancer types, there are specific studies. So even there are guideline recommendation for ambulatory pancreatic cancer patients which recommend low-molecular-weight heparins at higher dose for a maximum duration of 3 months. Overall, the duration of primary thromboprophylaxis in ambulatory cancer patients starting systemic anticancer therapy is at least of 6 months with low-molecular-weight heparins and prophylactic dose or apixaban and rivaroxaban in this prophylactic dose.

The question now is: How should we select in clinical practice such patients? And here the guidelines clearly say patients receiving systemic anticancer therapy who are at intermediate to high risk of venous thromboembolism could be identified by validated risk assessment models. For instance, the Khorana Score of 2 or higher or with other validated risk assessment models, like the COMPASS-CAT or the Vienna-CAT nomograms score.

So we have evidence from randomized controlled trials and recommendation suggestions of various international guidelines of different organizations that recommend primary thromboprophylaxis in high - intermediate to high-risk patients who are not at high risk of bleeding.

Are we already implementing this new evidence in clinical practice? And according to my observation, we are quite slow in implementing this new evidence in everyday clinical practice; and therefore, the next step would be to develop implementation strategies. And also own local protocols are needed to implement the latest evidence on primary thromboprophylaxis in cancer patients receiving systemic anticancer therapy in the ambulatory setting.

Thank you so much for listening.

Announcer:
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