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Treatment of Patient With Low Risk of Gastrointestinal Absorption Impairment for Established VTE With Cancer

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

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Dr. Connors:
Hello, I'm Jean Connors, a Hematologist at Brigham and Women's Hospital and Dana Farber Cancer Institute in Boston. I'm the Medical Director of our Hemostatic Antithrombotic Stewardship Program, and Medical Director of Anticoagulation Management Services both at Brigham and Women's Hospital, and for our cancer patients at Dana Farber Cancer Institute.

The topic of this presentation today is Treatment of the Patient with Low Risk of Gastrointestinal Absorption Impairment for Established VTE in Patients with Cancer. In other words, no GI tract problems that would affect DOAC absorption.

And so, I'm going to start with a case. This is a case of a 57-year-old man with newly diagnosed localized pancreatic cancer, who's had two cycles of neoadjuvant FOLFOX chemotherapy. He presents with a 2-day history of worsening dyspnea on exertion with pleuritic chest pain and left lower extremity swelling. He is diagnosed with a right lower lobar segmental PE without right heart strain on imaging and a left lower extremity DVT when he is seen in the emergency department. The emergency department calls you and asks what anticoagulant to give.

Factors that contribute to deciding on which anticoagulant to use includes the type of cancer and the presence of intraluminal disease, anticancer treatments, decreased absorption possibilities through the GI tract, drug-drug interactions, or all of the above.

So we know that patients who have GI tract malignancies have an increased risk of bleeding with direct oral anticoagulants, specifically edoxaban and rivaroxaban. And then the data shown here in the graphs on the right-hand side, when we look at

Hokusai VTE cancer, in which edoxaban was compared to dalteparin, and we break out those that had major bleeding into those that had non-GI tract cancers and those with GI tract cancers, we can see that if you had lung cancer, breast cancer, or other cancers, there was no difference in the major bleeding rate between dalteparin and edoxaban. However, if patients in Hokusai VTE cancer were on edoxaban and had a GI tract malignancy, their rate of major bleeding, as represented by this blue line, was significantly higher. And so, this is a concern in some patients for risk of bleeding, never mind absorption.

Select-D also had an issue with that, in that halfway through the trial in which rivaroxaban was compared to dalteparin, the Data Safety Monitoring Board suggested not enrolling upper GI tract malignancies. I highlight this even though this case is about absorption issues, because we need to take into account the type of tumor. And it's thought that primarily upper GI tract tumors but also lower GI tract tumors with an intact luminal primary cancer and unresected colon cancer, unresected stomach cancer, unresected esophageal tumor, these tumors are high - have a higher likelihood of bleeding.

But we also know that there are potential DOAC oncology drug interactions, as seen in this table. And what we need to pay attention to when we're going to use a direct oral anticoagulant to treat a cancer-associated VTE in patients is whether or not the patient is taking other drugs that induce CYP3A4 or P-glycoprotein, which would lead to lower plasma concentrations of the DOAC, and therefore, less efficacy, or inhibitors of CYP3A4 and P-glycoprotein, which would then increase the DOAC plasma concentration, and therefore, put the patient at risk for bleeding. And there are lots of lists. And at the bottom of this, different agents depending on whether they induce or inhibit, and you can find from the publications at the bottom, more detailed lists about these drug-drug interactions.

But GI tract pathology of any time it can actually affect DOAC absorption, and therefore plasma concentration. And if you have a lower plasma concentration of DOAC because it's not absorbed, you will likely have decreased efficacy. I myself

have actually seen this in patients who have nausea and vomiting. I had a woman on rivaroxaban following ALL treatment, who got influenza and had 3 days of nausea and vomiting, and just could not keep the pills down. And she had a new pulmonary embolus simply in the setting of nausea and vomiting and not being able to keep the oral medication down.

Similarly, for those that have lots of large bowel movements, or profuse watery diarrhea, particularly if it's originating in the small intestine, or even the lower intestine, patients may have problems with absorbing the DOAC as well. And so we've heard nausea, vomiting, and diarrhea. I sometimes switch patients, or rather often switch patients, from DOAC to a low-molecular-weight heparin, so we can be sure that they're going to absorb the drug.

Patients who have resected sections of the stomach, the small intestine, and even the bowel will also have concerns for decreased absorption of DOACs. The drugs need to be absorbed many of them are absorbed in the small intestine, but then P-gp often dumps them back into the gut and they get reabsorbed in this circular mechanism of maintaining drug concentration. And so just like gastric bypass, somebody who's had their stomach resected for gastric cancer, there may be concerns with dumping syndrome and others about ability to absorb the drug. There is currently an ongoing discussion about the use of DOACs inpatients post gastric bypass and whether or not they can use a DOAC. There's still uncertainty about absorption in the immediate postoperative state.

Inflammatory bowel diseases, whether or not the patient has malignancy is also a concern for absorption as well as bleeding. We do have data for patients who require G-tubes or J-tubes that you can crush apixaban or rivaroxaban, and administer it through the J-tube and demonstrate good plasma levels. Usually, the G-tube or the J-tube are used in patients who might have head and neck cancer undergoing concurrent chemoradiation, but they have an intact bowel. And I think that that's important to note, because if they do not have an intact bowel, if they've had lots of resections, there may be concern for ability to absorb the DOAC.

So in this case, the answer to the question: factors that contribute to deciding on which anticoagulant to use include: type of cancer and intraluminal disease status, anticancer treatments, potential for decreased absorption, drug-drug interactions, the answer is all of the above.

Now, this patient has pancreatic cancer, and so he does not have an intraluminal primary disease and has not had any GI tract resection to impair absorption. We know that because we're giving him neoadjuvant chemotherapy before resecting localized pancreatic cancer. FOLFOX chemotherapy does not affect DOAC metabolism. And so, while nausea and vomiting, diarrhea can occur with FOLFOX, current antiemetic drugs usually give excellent control of these side effects. So there's no reason not to treat this patient with a DOAC at this point in time on his cancer journey with new diagnosis of PE and DVT but no obstacles to GI tract absorption or increased risk of GI tract bleeding.

I want to thank you for your attention, and hope that you will watch the rest of the videos in this series. Thank you.

Announcer:
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