

Key considerations when prescribing midostaurin with a strong CYP3A4 inhibitor

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Welcome to Managing AML. I am Dr. Alexander Perl, and today I will be discussing the practical considerations to be aware of when prescribing midostaurin with a strong CYP3A4 inhibitor. CYP3A4 is a hepatic microsome in the P450 class of enzymes that is responsible for metabolism of a number of medications, including midostaurin. We know that when a strong inhibitor of CYP3A4 is given, the midostaurin levels will be increased and many of the drugs that we use to treat patients with AML can have effects on CYP3A4 or are metabolized by CYP3A4. In particular, a couple of the standard medications that are given as supportive care, such as azole antifungal agents voriconazole or posaconazole, are strongly inhibiting CYP3A4. If these are given at the same time as midostaurin, the midostaurin levels could be higher. This in and of itself is not a contraindication to giving midostaurin, but you have to be aware that you could see more side effects from the midostaurin if the drug levels are higher.

What are these side effects that you might see? Well, if we look at the effects of midostaurin as a single agent, we often did see nausea, anorexia, vomiting, or diarrhea. Certainly when we look at studies of midostaurin added to chemotherapy, the vast majority of patients did not receive midostaurin with posaconazole or voriconazole, so we do not have a lot of data in terms of a direct increase in side effect profile, but that is what we would certainly expect. While again there is not a contraindication, you do need to monitor closely for side effects of midostaurin, and primarily it will be GI irritative symptoms that we might see. Again, one advantage of midostaurin in this context is it is typically only given for two weeks, and so even if the patient has side effects, they can be managed and usually this does not affect the ability to give the midostaurin at all, and usually you can kind of ride the patient through with supportive care (antiemetics, fluids, antidiarrheals), and those agents will allow you to continue to give the patient optimal therapy. Thank you for listening.