Transcript Details

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DPYD Testing Before Fluoropyrimidine Therapy: Benefits, Risks, and Guidance

Announcer:
You're listening to *Project Oncology* on ReachMD. On this episode, we'll hear from Dr. Daniel Hertz, who's an Associate Professor of Clinical Pharmacy at the University of Michigan College of Pharmacy and the Medical Advisor to The Advocates for Universal DPD/DPYD Testing Organization. He'll be discussing the clinical benefits and risks of DPYD testing in patients receiving fluoropyrimidine-based therapy, which he spoke about at the 2026 American Society of Clinical Oncology Annual Meeting. Here's Dr. Hertz now.

Dr. Hertz:
Although previously it was thought that DPD deficiency was a rare occurrence, we now know that about one in 20 patients carry a DPYD variant leading to DPD deficiency, so this is not at all a rare occurrence. So there has been increasing attention and awareness of the importance of DPYD testing prior to fluoropyrimidine chemotherapy over the last few years. A lot of this is driven by recent scientific evidence and really passionate work by the advocates from the Universal DPD/DPYD Testing Organization.

So there has been an increase in testing over the last few years at some sites, and we've really seen rapid momentum towards increased testing since October of 2025 when the FDA added a statement to the drug labels stating that DPYD testing should be performed prior to fluoropyrimidine chemotherapy use. In response to that, ASCO and NCCN guidelines have also been updated to recommend pretreatment DPYD testing. This has now essentially become standard of care in the United States. There are some statements in the FDA drug label saying that if a patient needs to start treatment immediately, then starting without the DPYD testing results may be appropriate. But other than those very rare cases, all patients should receive DPYD testing prior to starting fluoropyrimidine chemotherapy.

I think that the evidence strongly supports that DPYD testing improves treatment safety, and that is across all patients who are receiving systemic fluoropyrimidine chemotherapy, either IV 5-FU or oral capecitabine. I think that all patients should be tested for DPYD prior to initiating treatment as there's no way to know which patients have DPD deficiency and are at high risk for severe toxicity if they aren't tested.

There are some key limitations that clinicians should keep in mind. The first is that if a patient is tested and isn't found to be DPD deficient, that doesn't mean that they won't have toxicity. There's still about a 25 to 30 percent risk of severe toxicity, so all patients should be monitored as any patient would be.

The other limitation is that the current testing does not include all known DPYD variants. There is a lot of ongoing research to find all those variants, especially variants that are carried by non-European patients. But not all those variants are included on all testing panels, which is part of the reason why patients who are tested and are not found to be carrying a variant may still have severe toxicity risk.

The other risk that we know of is that in patients who carry a DPYD variant who receive an empiric dose reduction as is recommended by CPIC guidelines, there is some risk of undertreatment in those patients. So all patients who start out with a dose reduction should be monitored for tolerability, and they should be dose escalated as allowable based on how they're tolerating their dosing.

From my presentation specifically, I want clinicians to understand that there is strong evidence of the clinical utility of DPYD testing and that it is recommended by the FDA and NCCN and ASCO guidelines. The other thing to understand is that with the recent addition to the FDA drug labels and the clinical practice guidelines, there's broad insurance reimbursement for DPYD testing, so there's no longer a concern that insurance won't cover the testing.

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From our educational session more broadly, I want clinicians to understand that testing is very feasible. It's been widely implemented across the United States in the VA, in major academic medical centers, and in lower-resource settings, including community oncology practices and cancer centers outside the U.S. which have less resources, but they have still found ways to implement DPYD testing in practice to ensure that all patients receive safe and effective chemotherapy treatment.

Announcer:
That was Dr. Daniel Hertz talking about the clinical benefits and risks of DPYD testing. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!

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