NCCN Guideline Expands Lynch Syndrome Screening

Updates to the newest version of the National Comprehensive Cancer Network's Guideline for Genetic/Familial High-Risk Assessment for Colorectal Cancers have widened the criteria for which screening for Lynch Syndrome can be considered.

The updated guideline separates testing criteria for Lynch syndrome into two sections: "Clinical Testing Criteria for Lynch Syndrome (based on personal and family history)" and "Routine Tumor Testing Criteria for Lynch Syndrome"—which was intended to make it easier for clinicians to navigate those recommendations considering the broadening differences in the testing strategies for the sections, Kory Jasperson, MS, CGC, Vice-Chair of the NCCN Guidelines Panel for Genetic/Familial High-Risk Assessment: Colorectal and Licensed Genetic Counselor at Huntsman Cancer Institute at the University of Utah, explained in an email.

"One of the take-home points is that the preferred method for routine tumor testing is IHC [immunohistochemistry] or MSI [microsatellite instability] alone, whereas the preferred method for personal and family history based testing is MSI and IHC together," Jasperson said. "And, for individuals who meet criteria for routine tumor testing, but tumor

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testing cannot be done because no tumor is available (or there is insufficient tumor), testing of all four MMR [mismatch repair] genes and EpCAM [epithelial cell adhesion molecule] should be considered, which can be done concurrently."

Key updates regarding Lynch syndrome screening in the guideline are:

- All patients who meet a five percent or greater risk threshold for Lynch syndrome (based on any prediction model) may be appropriate for testing;
- When tumor testing cannot be performed in a patient suspected to have Lynch syndrome, testing of all four MMR genes and EpCAM concurrently may be considered;
- Individuals with an EpCAM mutation should undergo the same surveillance as those with MLH1 and MSH2 mutations; and
- Surveillance recommendations for individuals with MSH6 and PMS2 mutations now include earlier and more frequent colonoscopies.

The updated guideline also notes that individuals with abnormal IHC testing results and no germline mutation detected in the corresponding genes may still have undetected Lynch syndrome or sporadic cancer due to somatic changes in the mismatch repair genes—and therefore the limitations and benefits of Lynch syndrome screening and risk-reducing options in these patients and their close relatives should be discussed.

Patients with Lynch syndrome have an 80 percent risk of developing colorectal cancer, as well as higher risks of stomach cancer, hepatobiliary tract cancer, urinary tract cancer, small bowel cancer, and brain cancer. For women with Lynch syndrome, the risk of endometrial and ovarian cancers also increases.