Caveat Emptor

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In 2003, ASCO published the seminal guideline for genetic risk assessment and genetic testing.¹ The guideline established that genetic testing should be employed only when a patient has a personal or family history suggesting an inherited cancer syndrome, the patient can participate in the informed consent process, the results of the test are reproducible, and the results lead to a change in management for the patient. The recently updated ASCO guideline for the use of genetic testing for genes of low to variable penetrance applies the same criteria to testing for genetic alterations that may increase the risk of cancer but, unlike genes more familiar to the oncology professional such as *BRCA*, do not directly cause a malignancy.² Companies market these tests directly to consumers, often through Internet portals. An array of genomic risk profiles and individual genetic tests are offered.³ These direct-to-consumer marketing practices are the basis of the updated guideline recently published in *Journal of Clinical Oncology*.²

Increasingly, genes of low penetrance are being identified through genome-wide association studies. These genes may be true mutations or single nucleotide polymorphisms that when combined with lifestyle and environment increase an individual's risk for malignancy. Unfortunately, many of these gene tests are not reproducible, nor can knowledge of the results change therapy or risk reduction.

The ultimate goal of any diagnostic test is to give meaningful results that will ultimately affect treatment or prevention. Many of the gene tests currently being offered directly to patients may result in information that is ambiguous or misleading. This may lead to unnecessary anxiety and testing or a false sense of security in an individual who requests such a test with an *a priori* perception of risk.

Direct-to-consumer genetic testing allows an individual to select a test without a clear understanding of the limitations of the test itself; the risk-benefit ratio of a positive, negative, or ambiguous result; or whether additional testing and/or management is necessary to manage that individual's risk of cancer. The goal of the health care provider in evaluating a patient for a genetic test is genetic risk assessment, of which the test itself is only a component. For example, a patient with Lynch Syndrome may meet Amsterdam criteria by family history, have a personal history of a Lynch-defining cancer, and have a negative comprehensive genetic test for a mutation in a mismatch repair gene. Such a patient would be assessed in the context of a genetic risk assessment visit, and an individual risk-reduction plan would be

provided to the patient. A direct-to-consumer test may have given such a patient a false sense of security and presented a missed opportunity for cancer prevention. Additionally, direct-to-consumer testing may not be subject to the stringent Health Insurance Portability and Accountability Act regulations governing provider-patient encounters, and as such, the protection of the consumer's genetic test results may not be what the individual presumes.

Oncology providers are increasingly asked to interpret tests that are patient self-directed for cancer risk determination. The knowledge gap for an oncologist may be such that interpretation is difficult, if not impossible. ASCO's updated guideline² calls for increased physician education regarding genomic testing as well as increased clinical trial testing to determine the true risk carried by these genes of low penetrance. The guideline also calls on the US Food and Drug Administration and Centers for Medicare & Medicaid Services to regulate these tests in the interest of consumer protection. Oncology providers must also play a role in educating not only our patients but also our colleagues as to the limitations and lack of reproducibility of such testing.

The era of patient-directed genetic testing is here, and the role of the oncology provider is often to sort out truth from perception once an individual is faced with an ambiguous result. Innovation will lead to more tests, and concerned patients will drive demand higher. Oncologists will need more education to counsel such patients who present with test results, and the primary care community will need our expertise to guide them as patients ask about testing. Until there is a clearer understanding of the role that these genes of low penetrance play in cancer risk, the best advice may be: Buyer beware.

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