Testing the accuracy of FDA-approved and lab-developed cancer genetics tests

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Cancer molecular testing can drive clinical decision making and help a clinician determine if a patient is a good candidate for a targeted therapeutic drug. Clinical tests for common cancer causing-mutations in the genes BRAF, EGFR and KRAS abound, and include U.S. Food and Drug Administration (FDA)-approved companion diagnostics (FDA-CDs) as well as laboratory-developed tests (LDTs). LDTs are tests that have been designed and implemented in a single laboratory - some are completely homegrown while others are commercial kits, including "off label" uses of FDA-CDs (also known as in vitro diagnostics). Amid the debate about how much these tests should be regulated by the FDA, one question has gone unanswered: how well do LDTs and FDA-CDs perform? A new study published this week in *JAMA Oncology*, which analyzed data from almost 7,000 tests, finds that the answer is: very well and very comparably.

"We find that both laboratory-developed tests and FDA-approved companion diagnostics demonstrate excellent performance on proficiency testing," said corresponding author Annette Kim, MD, PhD, of BWH's Department of Pathology. "And, importantly, more than 60 percent of the laboratories in our study that were using an FDA-CD kit report using it with modifications - rendering those assays LDTs. These modifications appear to be driven by the exigencies of real day-to-day clinical practice that requires altering the assays to meet the needs of a variety of clinical situations that may not be accommodated by the FDA-approved protocol."

These modifications include, for example, the testing of other tumor types that may carry targetable variants, different types of input specimen preparations available in pathology such as cytology smears or other fresh specimens rather than paraffin blocks and availability of different methods of DNA quantification than those mandated by FDA approval based upon pre-existing technologies in the laboratories.

"In the clinical lab, we are always acutely aware that there is a patient awaiting this result and we validate our assays to ensure that we can provide reliable and accurate results from our laboratory under as many varied clinical situations as possible," said Kim.

The research team used data from proficiency tests provided by the College of American Pathologists Molecular Oncology Committee which provides external proficiency testing for labs to determine the accuracy of testing. Combing through data from 6,897 proficiency testing responses, the team found that both LDTs and FDA-CDs exceeded 97 percent accuracy combined across the three cancer genes.

The team's results also indicate that the majority of laboratories purchasing in vitro diagnostics for FDA-CDs are in fact modifying their use - making them into laboratory-developed tests.

"These data question the distinction between FDA-CDs and LDTs from a regulatory standpoint and note the greater clinically relevant applications of LDTs," the authors write.

More information: Kim, AS et al. "Comparison of Laboratory-Developed Tests and FDA-Approved Assays for BRAF, EGFR, and KRAS Testing" *JAMA Oncology*, DOI: 10.1001/jamaoncol.2017.4021

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