In the third study, coBRIM, also presented at ESMO and published in NEJM, 495 previously untreated patients were randomly assigned to receive vemurafenib either with the MEK inhibitor cobimetinib (GDC-0973; Roche) or with placebo. Combination therapy resulted in improved PFS compared with the control group (9.9 months vs. 6.2 months) and a higher 9-month OS rate (81.1% vs. 72.5%; N Engl J Med 2014 September 29 [Epub ahead of print]).

Earlier this year, the FDA granted accelerated approval of GSK's dabrafenib–trametinib combination for melanoma patients with the *BRAF* V600 mutation, based on results from phase II studies. COMBI-v and COMBI-d validate that approval, says Ribas, and, along with coBRIM, pave the way for developing other BRAF–MEK combinations.

"BRAF–MEK inhibition is a very elegant combination that slows tumor activity while decreasing the main side effect of the single agent," says Ribas. "With these new data, there is no reason to consider starting a patient with *BRAF* mutation–positive melanoma on single-agent therapy." ■

PROMPT to Detail Breast Cancer Risk

When women undergo genetic testing to see if they have an increased risk for breast cancer, many learn that they have changes in genes other than *BRCA1* and *BRCA2*.

Although mutations in *p53*, *PALB2*, *RAD51C*, *CDH1*, and other genes have been associated with an increased risk of breast cancer, doctors don't know much about them—they don't know to what degree the mutations heighten risk, how those mutations might interact with others, or at what age the risk starts to climb.

Four major cancer institutions—Dana-Farber Cancer Institute (Boston, MA), Mayo Clinic (Rochester, MN), Memorial Sloan Kettering Cancer Center (MSKCC; New York, NY), and Penn Medicine (Philadelphia, PA)—are now teaming up to address these types of questions. By combining their expertise and partnering with commercial laboratories—Ambry Genetics, Gene Dx, Myriad Genetics, Pathway Genomics, and Quest Diagnostics have all agreed to participate—they hope to enroll enough patients in an online registry to better understand the effects of these genetic mutations. Although they are starting with breast cancer, the registry, called Prospective Registry Of Multi-Plex Testing, or PROMPT, will also gather information on other cancer-associated genes.

"We have had 20 years to get really great evidence for what to recommend for individuals with *BRCA1* and *BRCA2* mutations, and we want to quickly obtain such evidence for these other high, moderate, and unknown penetrant genes," says PROMPT co-founder Susan Domchek, MD, director of the Basser Research Center for BRCA in the University of Pennsylvania's Abramson Cancer Center in Philadelphia.

When doctors order multigene panel tests, several of the labs that conduct those tests will send information about the registry to patients and providers and invite them to participate, says Domchek. If patients choose to join, they can contribute their gene test results and family history to the registry. Over time, they will be informed of any relevant findings the consortium might make.

Findings will be made publicly available, and participants may volunteer for other studies as well. "We want to build a resource that many different investigators will use to try to [answer] questions as quickly as possible," says Mark Robson, MD, PROMPT co-founder and clinic director of the Clinical Genetics Service at MSKCC.

Each of these gene mutations is likely to be uncommon, which is why the group needs to enroll a large number of patients. However, that can take a long time. In a recent paper, for instance, researchers reported that it took them several years to enroll the 150 families needed to analyze, with sufficient statistical power, links between *PALB2* and breast cancer (N Engl J Med 2014; 371:497–506).

"To try to get the answers in a meaningful timeframe, we have to throw a much, much wider net and make [studies] available to a much, much broader group of people," Robson says. ■

For more news on cancer research, visit *Cancer Discovery* online at http://CDnews.aacrjournals.org.

NOTED

- Concluding that "the transaction is no longer in the best interests of stockholders at the agreed upon valuation," **AbbVie's Board of Directors has withdrawn its support for a proposed merger with the biopharmaceutical company Shire.** The decision was spurred by a U.S. Treasury notice regarding the tax implications of such a transaction. AbbVie will pay Shire a "break fee" of $1.635 billion.
- **The NCI launched the Exceptional Responders Initiative,** a study that will investigate the molecular factors associated with dramatic responses to cancer treatment relative to responses in other patients receiving the same therapy. Researchers plan to examine tissue and clinical data and conduct gene sequencing in as many as 300 cases.
- **The Indiana University Melvin and Bren Simon Cancer Center in Indianapolis has once again been recognized as an NCI-designated cancer center.** The designation will bring $7.8 million in federal grant money to the institution over the next 5 years, an increase of 20% from its previous award in 2008.
- **To help speed the development and approval of drugs for certain breast cancers, the FDA released a guidance document for industry** called "Pathological Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval," which defines pathological complete response, discusses endpoints for neoadjuvant trials, and identifies suitable patient populations. However, the agency acknowledges that "important regulatory questions remain."
- **New Canadian guidelines recommend against using the prostate-specific antigen test to screen for prostate cancer** based on evidence showing an increased risk of harm, such as false-positive results and unnecessary treatment, and little evidence of reduced mortality. The guidelines, published in the *Canadian Medical Association Journal*, are consistent with the recommendations of the U.S. Preventive Services Task Force and Cancer Council Australia; the UK does not have an organized screening program (CMAJ 2014;186:1225–34).