In the third study, coBRIM, also presented at ESMO and published in NEJM, 493 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, and other providers—those with a mutation or at high-risk, moderate, and unknown penetrance, 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 own data and family history to the registry. Over time, they will be informed of any relevant findings the registry 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.