CORRESPONDENCE

Helicobacter pylori and gastric cancer risk in *BRCA 1/2* pathogenic germline variant carriers

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TO THE EDITOR:

In "Clinical risk management of breast, ovarian, pancreatic, and prostatic cancers for BRCA1/2 variant carriers", Ueki et al. nicely reviewed recommendations for measures to diagnosis earlier cancers associated with *BRCA1/2* pathogenic germline variants (PGVs). They noted that BRCA carriers "might" also be at risk for stomach cancer [1]. Although there is not substantial evidence suggesting that *BRCA1/2* PGV carriers should be routinely screened for stomach cancer, there is emerging evidence that those with *BRCA 1/2* PGVs who are infected and not treated for *H. pylori* are at a substantially increased risk for stomach cancer.

In a recent New England Journal of Medicine article, Usui et al. demonstrated that persons with an *H. pylori* infection and homologous-recombination pathogenic germline variants (PGVs)-including *BRCA* PGVs-have a cumulative lifetime risk of 45.5% for developing gastric cancer [2]. For those with *CDH1* PGVs, the lifetime gastric cancer risk is roughly 38%, and prophylactic gastrectomy or screening for gastric cancer is recommended [3, 4]. Therefore, it might seem reasonable to consider screening all *BRCA1/2* carriers for *H. pylori* and, if detected, it would seem worthwhile to also screen those patients for gastric cancer and aggressively treat *H. pylori* in those not found to have gastric cancer.

Based on a comprehensive review of *H. pylori* incidence and its relationship to the development of gastric cancer, the International Agency for Research on Cancer recommends "tailored" surveillance and eradication of *H. pylori* [2, 5]. A randomized, controlled trial showed that eradication of *H. pylori* reduced gastric cancer incidence [6]. Such an approach to screening, treatment and surveillance of *H. pylori* would be particularly reasonable for *BRCA 1/2* carriers. Usui et al. showed that both *BRCA1* and *BRCA 2* carriers had similar age of gastric cancer diagnosis (roughly age 64) and similar Odds Ratios for developing gastric cancer (4.81 and 5.08, respectively) [2]. Usui et al. also noted that the average age of gastric cancer diagnosis was "more than 10 years younger" among PGV carriers compared to non-PGV carriers [2].

Genes are typically classified as PGVs related to their penetrance for developing a particular cancer without respect to environmental influences. The thorough review of Ueki et al. illustrates why defining *BRCA1/2* penetrance for developing gastric cancer independent of environmental influences excludes patients from recommendations that might profoundly help them in part because Usui et al. demonstrated that *BRCA1/2* and other homologous-recombination PGVs in the context of *H. pylori* infection as are gastric cancer predisposing. If *BRCA1/2* PGVs are reclassified as gastric cancer predisposing in the setting of *H. pylori* infection, management recommendations-such as those described by Ueki et al.-will include more testing for, treatment of, and eradication of *H. pylori* in this group and their high risk for developing gastric cancer will hopefully be mitigated.

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COMPETING INTERESTS

Dr. Sorscher was formerly and briefly employed by Invitae, Corp.

ADDITIONAL INFORMATION

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