AURKA F31I polymorphism and breast cancer risk in BRCA1 and BRCA2 mutation carriers: a consortium of investigators of modifiers of BRCA1/2

Abstract:
The AURKA oncogene is associated with abnormal chromosome segregation and aneuploidy and predisposition to cancer. Amplification of AURKA has been detected at higher frequency in tumors from BRCA1 and BRCA2 mutation carriers than in sporadic breast tumors, suggesting that overexpression of AURKA and inactivation of BRCA1 and BRCA2 cooperate during tumor development and progression. The F31I polymorphism in AURKA has
been associated with breast cancer risk in the homozygous state in prior studies. We evaluated whether the AURKA F31I polymorphism modifies breast cancer risk in BRCA1 and BRCA2 mutation carriers from the Consortium of Investigators of Modifiers of BRCA1/2. Consortium of Investigators of Modifiers of BRCA1/2 was established to provide sufficient statistical power through increased numbers of mutation carriers to identify polymorphisms that act as modifiers of cancer risk and can refine breast cancer risk estimates in BRCA1 and BRCA2 mutation carriers. A total of 4,935 BRCA1 and 2,241 BRCA2 mutation carriers and 11 individuals carrying both BRCA1 and BRCA2 mutations was genotyped for F31I. Overall, homozygosity for the 31I allele was not significantly associated with breast cancer risk in BRCA1 and BRCA2 carriers combined (hazard ratio (HR), 0.91; 95% confidence interval (95% CI), 0.77-1.06). Similarly, no significant association was seen in BRCA1 (HR, 0.90; 95% CI, 0.75-1.08) or BRCA2 carriers (HR, 0.93; 95% CI, 0.67-1.29) or when assessing the modifying effects of either bilateral prophylactic oophorectomy or menopausal status of BRCA1 and BRCA2 carriers. In summary, the F31I polymorphism in AURKA is not associated with a modified risk of breast cancer in BRCA1 and BRCA2 carriers.