Janavicius, R; Lazaro, C; Blanco, I; Feliubadalo, L; Brunet, J; Gayther, SA; Pharoah, PP; Odunsi, KO; Karlan, BY; Walsh, CS; Olah, E; Teo, SH; Ganz, PA; Beattie, MS; van Rensburg, EJ; Dorfling, CM; Diez, O; Kwong, A; Schmutzler, RK; Wappenschmidt, B; Engel, C; Meindl, A; Ditsch, N; Arnold, N; Heidemann, S; Niederacher, D; Preister-Adams, S; Gadzicki, D; Varon-Mateeva, R; Deissler, H; Gehrig, A; Sutter, C; Kast, K; Fiebig, B; Heinritz, W; Caldes, T; de la Hoya, M; Muranen, TA; Nevanlinna, H; Tischkowitz, MD; Spurdle, AB; Neuhausen, SL; Ding, YC; Lindor, NM; Fredericksen, Z; Pankratz, VS; Peterlongo, P; Manoukian, S; Peissel, B; Zaffaroni, D; Barile, M; Bernard, L; Viel, A; Giannini, G; Varesco, L; Radice, P; Greene, MH; Mai, PL; Easton, DF; Chenevix-Trench, G; kConFab investigators; Offit, K; Simard, J; Consortium of Investigators of Modifiers of BRCA1/2

Titel des Beitrags:
Common variants at the 19p13.1 and ZNF365 loci are associated with ER subtypes of breast cancer and ovarian cancer risk in BRCA1 and BRCA2 mutation carriers.

Abstract:
Genome-wide association studies (GWAS) identified variants at 19p13.1 and ZNF365 (10q21.2) as risk factors for breast cancer among BRCA1 and BRCA2 mutation carriers, respectively. We explored associations with ovarian cancer and with breast cancer by tumor histopathology for these variants in mutation carriers from the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA). Genotyping data for 12,599 BRCA1 and 7,132 BRCA2 mutation carriers from 40 studies were combined. We confirmed associations between rs8170 at 19p13.1 and breast cancer risk for BRCA1 mutation carriers [HR, 1.17; 95% confidence interval (CI), 1.07-1.27; P = 7.42 × 10(-4)] and between rs16917302 at ZNF365 (HR, 0.84; 95% CI, 0.73-0.97; P = 0.017) but not rs311499 at 20q13.3 (HR, 1.11; 95% CI, 0.94-1.31; P = 0.22) and breast cancer risk for BRCA2 mutation carriers. Analyses based on tumor histopathology showed that 19p13 variants were predominantly associated with estrogen receptor (ER)-negative breast cancer for both BRCA1 and BRCA2 mutation carriers, whereas rs16917302 at ZNF365 was mainly associated with ER-positive breast cancer for both BRCA1 and BRCA2 mutation carriers. We also found for the first time that rs67397200 at 19p13.1 was associated with an increased risk of ovarian cancer for both BRCA1 (HR, 1.16; 95% CI, 1.05-1.29; P = 3.8 × 10(-4)) and BRCA2 mutation carriers (HR, 1.30; 95% CI, 1.10-1.52; P = 1.8 × 10(-3)) and that rs19p13.1 and ZNF365 are susceptibility loci for ovarian cancer and ER subtypes of breast cancer among BRCA1 and BRCA2 mutation carriers. These findings can lead to an improved understanding of tumor development and may prove useful for breast and ovarian cancer risk prediction for BRCA1 and BRCA2 mutation carriers.