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Prevalence of BRCA1 mutations among 403 women with triple-negative breast cancer: implications for genetic screening selection criteria: a Hellenic Cooperative Oncology Group Study.

Fostira F, Tsitlaidou M, Papadimitriou C, Pertesi M, Timotheadou E, Stavropoulou AV, Glentis S, Bournakis E, Bobos M, Pectasides D, Papakostas P, Pentheroudakis G, Gogas H, Skarlos P, Samantas E, Bafaloukos D, Kosmidis PA, Koutras A, Yannoukakos D, Konstantopoulou I, Fountzilas G.

Source

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Abstract

In spite the close association of the triple-negative breast cancer immunophenotype with hereditary breast cancers and the BRCA1 pathway, there is a lack of population studies that determine the frequency of BRCA1 mutations among triple-negative breast cancer patients. To address this, we have screened a large sample of 403 women diagnosed with triple-negative invasive breast cancer, independently of their age or family history, for germline BRCA1 mutations. Median age at diagnosis was 50 years (range 20-83). The overall prevalence of triple-negative cases among the initial patient group with invasive breast cancer was 8%. BRCA1 was screened by direct DNA sequencing in all patients, including all exons where a mutation was previously found in the Greek population (exons 5, 11, 12, 16, 20, 21, 22, 23, 24-77% of the BRCA1 coding region), including diagnostic PCRs to detect the three Greek founder large genomic rearrangements. Sixty-five deleterious BRCA1 mutations were identified among the 403 triple-negative breast cancer patients (16%). Median age of onset for mutation carriers was 39 years. Among a total of 106 women with early-onset triple-negative breast cancer (<40 years), 38 (36%) had a BRCA1 mutation, while 27% of women with triple-negative breast cancer diagnosed before 50 years (56/208) had a BRCA1 mutation. A mutation was found in 48% (50/105) of the triple-negative breast cancer patients with family history of breast or ovarian cancer. It is noteworthy, however, that of the 65 carriers, 15 (23%) had no reported family history of related cancers. All but one of the carriers had grade III tumors (98%). These results indicate that women with early-onset triple-negative breast cancer, and ideally all triple-negative breast cancer patients, are candidates for BRCA1 genetic testing even in the absence of a family history of breast or ovarian cancer.