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BRCA1/BRCA2 GERMLINE MUTATIONS AND CHEMOTHERAPY RELATED HEMATOLOGIC TOXICITY IN BREAST CANCER PATIENTS

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Introduction: BRCA1 and BRCA2 genes are central to DNA repair. Germline mutations are found in 5% of breast cancers. As adjuvant breast cancer chemotherapy includes DNA-damaging agents, we hypothesize that mutation carriers may exhibit increased chemotherapy-related hematologic toxicity.
Méthode: We included female early breast cancer patients screened for BRCA1/BRCA2 germline mutations between 2001-2016 at the HUG and treated with (neo)adjuvant chemotherapy. Primary endpoint was febrile neutropenia after the first chemotherapy. Secondary endpoints were the incidence of severe neutropenia, hospitalizations, G-CSF use, chemotherapy dose-reductions and long term toxicity. We analyzed the correlation between mutation location in BRCA1/BRCA2 genes and neutropenia. A second cohort from Centre Leon Bérard was included for long-term toxicity.
Résultats: 249 patients were assessed for acute hematologic toxicity, including 28 BRCA1 and 26 BRCA2 carriers. Febrile neutropenia had an incidence of 16% (p=0.013), 8.7% (p=0.174) and 2.7% among BRCA1, BRCA2 and non-carriers, respectively. Severe neutropenia was found in 50% of BRCA1 (p=0.001), 18.2% of BRCA2 (p=0.772) and 16.9% of non-carriers. Among BRCA1 carriers, there was a trend toward increased hospitalizations (p=0.053) and dose reductions (p=0.068). 82.6% (p=0.005) of BRCA1 carriers required G-CSF support, 65.2% of BRCA2 (p=0.213) and 46.2% of non-carriers. BRCA1 carriers exhibited increased grade 3-4 neutropenia, except those with mutations in the RING domain (16.6%, p=1). Long-term toxicity among 934 patients (202 BRCA1, 95 BRCA2, 637 non-carriers) was equivalent.