CONFERENCES ABSTRACT

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Contribution of germline TP53 variants and assessment of HER-2 status among young breast cancer patients in Malaysia

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Abstract: Background: Li-Fraumeni Syndrome (LFS) is caused by a mutation in the TP53 tumour suppressor gene. This rare hereditary condition predisposes individuals to an increased risk of cancers including breast cancer in women at a relatively young age, which accounts for nearly 25%–30% of all LFS-associated cancers. Studies have shown that breast tumours in women with a germline TP53 deleterious variants are associated with a human epidermal growth factor receptor 2 (HER2)-positive phenotype. Taken together, this study aimed to investigate the contribution of germline TP53 variants and its association with tumour HER-2 status in a cohort of young women with breast cancer.

Methods: From 2002 to 2017, 4048 women with breast cancer treated at University Malaya Medical Centre or Sime Darby Medical Centre participated in the Malaysian Breast Cancer Genetics Study. Of which, 87 patients were diagnosed before 30 years of age. All patients were analysed for germline TP53 single nucleotide variants, small insertions or deletions by amplicon-based targeted sequencing and validated by Sanger sequencing. DNA from patients who tested negative for sequencing were subsequently evaluated for the presence of TP53 exon deletions or duplications by multiplex ligation-dependent probe amplification. HER-2 status of breast tumours was defined by immunohistochemistry, fluorescence in situ hybridisation and/or silver in situ hybridisation. Results: 5 distinct TP53 variants were detected in 5 individuals. 3 out of 5 TP53 variants were classified as frameshift mutations, one nonsense mutation and one in-frame duplication. Variants in other genes were detected in 17 individuals. No large genomic rearrangements were detected in the remaining 65 sequencing-negative patients. The assessment of HER-2 status will be presented. Conclusions: Our results suggest that alterations in TP53 gene were identified in approximately 5.7% (5/87) of this cohort of young women with breast cancer. Although early-onset breast cancer accounts for approximately 2.1% of all breast cancer cases in this cohort, identification of TP53 carriers is important as this group of patients should be closely monitored for other LFS-related cancers. Finally, the data from this study may be useful in the selection of BRCA1/2-negative patients for TP53 screening.

Keywords: TP53 variant; breast cancer; Li-Fraumeni Syndrome (LFS)


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