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CONFERENCE 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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