Li-fraumeni syndrome in females with early onset breast cancer in a mexican population.

Lenny Gallardo[1], Teresa Tusie-Luna[2], Isabel Tusie-Luna[2], José Díaz-Chávez[1], Enrique Macario Herrera Medina[2], Mariana Chavez-Mac Gregor[3], Enrique Bargallo Rocha[1], Luis Alonso Herrera Montalvo[1], David Franciso Cantu-de Leon[1]
Instituto Nacional de Cancerologia, Mexico City, Mexico; Unidad de Biología Molecular y Medicina Genómica. Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán"; Mexico, Mexico; The University of Texas MD Anderson Cancer Center, Houston, TX.

Background: Breast cancer in Mexican patients presents in average 10 year earlier compared to other populations. Among patients with *TP53* mutations, breast cancer is the most common malignancy. In this study we aim to determine the rate of *TP53* mutations among young Mexican breast cancer patients. **Methods:** Breast cancer patients younger that 45 were retrospectively identified, only patients without BRCA1/2 mutations were included. Clinical records and pedigrees were reviewed. Next generation sequencing test for *TP53* was performed from blood specimens. All pathogenic mutations were confirmed by Sanger sequencing and verified if were included in the IACR TP53 database. **Results:** Among the 78 patients younger than 45yo evaluated and tested with next generation sequencing, we identified 5 patients with a *TP53* mutation (6.4%). All were younger than 36 corresponding to a rate of 9.4% of mutations in this group of individuals (n = 53). Two, not previously described, frameshift mutations were found (c.291delC and c.273dupG) and three missense mutations (c.844C>T, c.517G>A, c.604C>T). A VUS c.672G>A that causes a silent mutation in a splicing-donor site was identified. All patients with a *TP53* mutation had locally advanced disease and tumors were high grade and Her2 positive. **Conclusions:** Among Mexican women younger than 45yo, the rate of *TP53* mutations was higher than in other populations where it's estimated to be 1%. Among patients younger than 36 the proportion was even higher. All patients had a family history suggestive of Li-Fraumeni syndrome. The VUS found in our series needs a deeper analysis (family segregation, structure and function of the resulting protein). Our results support the international recommendation of performing molecular testing for *TP53* in breast cancer patients younger than 35 years. Identification of patients with *TP53* mutation has important prognostic, therapeutic and quality of life implications for the proband in addition of the risk reduction strategies and intensive surveillance recommended in their families.