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Treatment implications of genetic heterogeneity detected by FISH testing of invasive ductal breast cancer

Standard screening of breast tumors involves morphologic, immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) analyses to assess pathogenicity and to identify possible treatment strategies. Among breast cancer types, invasive ductal carcinoma (IDC), in particular, exhibits amplification of the HER2 gene that can be detected by FISH as defined by the current American Society of Clinical Oncology/ College of American Pathologists (ASCO/CAP, 2013) scoring guidelines. One criterion for amplification of the HER2 gene; based on the ratio of HER2 gene signals to centromere 17 signals is measured from 20 cells by FISH. A second criterion is based on having an average of more than 6 copies of HER2 signals per cell out of 20 cells screened by FISH. If either of these criteria meets, then individualized therapy with adjuvant chemotherapy and the HER2-targeted drug Trastuzumab (Herceptin®) is indicated, which remarkably improves prognosis by decreasing local recurrence and metastasis. If HER2 is not amplified in the IDC of breast, then further testing is performed and alternative treatments are considered, which may have less favourable prognoses. Our research details cases of genetic heterogeneity (GH), which is when IDC of breast contains between 5%-50% of cells that are positive for HER2 amplification by FISH, yet fall short in meeting the amplified status criteria currently mandated by ASCO/CAP, resulting in the tumor being designated as non-amplified for the HER2 gene. Of the 998 specimens tested by FISH for HER2 amplification, 594 (60%) were non-amplified, 284 (28%) were amplified; 120 of the 998 (12%) had GH, of which 77 of 120 (64%) were non-amplified and 43 of 120 (36%) met the criteria for amplification. Based on these data, an update to the ASCO/CAP guideline criteria for positive amplification to include HER2 GH+ would extend to an additional 8% (77/998) of patients is the beneficial HER2-targeted therapy that is regulated by ASCO and FDA.

Speaker Biography

K H Ramesh is an alumnus of Bangalore University & Kidwai Memorial Institute of Oncology; obtained his Doctoral Degree in Human Cancer Cytogenetics under the guidance of Professors M Krishna Bhargava (MD) and B N Chowdaiah (PhD). He moved to the US in 1986 and completed his Clinical Cytogenetics training under the guidance of world renowned Geneticist Avery Sandberg, MD at Roswell Park Cancer Institute, Buffalo, NY. At present, he is the Director of Cancer CytoGenomics and Associate Professor of Pathology at Montefiore Medical Center & Albert Einstein College of Medicine, Bronx, NY. He is also Adjunct Associate Professor at The University of Texas MD Anderson Cancer Center. He is a Board Certified Clinical Cytogeneticist and a Diplomate of the American Board of Medical Genetics & Genomics, and Fellow of the American College of Medical Genetics & Genomics. His expertise is in genetic testing of leukemia, lymphoma, myeloma and soft and solid tumors. His interests include global education, football and music.

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