Novel gene variants identified in male breast cancer

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Male breast cancer (MBC) is a very rare tumor type, occurring in just 1% of all breast cancer cases, and the underlying genetic causes and treatment of MBC is not well understood. In a paper published in the March issue of *Cold Spring Harbor Molecular Case Studies*, researchers from Italy and the U.S. describe novel genetic variants found in a hormone receptor positive (HR+) MBC patient, that are distinct from previously identified genetic variants found in ten MBC cases.

The authors present the treatment history of a HR+ male breast cancer patient. His disease stabilized from targeting of the PI3K/mTOR pathway using the PI3K/mTOR inhibitor BEZ235 in combination with everolimus as 3rd line treatment for his metastatic ductal carcinoma and experienced a prolonged stable disease. After 18 months he subsequently became resistant to the treatment and his disease progressed. The authors then investigated why the patient benefited and subsequently developed resistance to this combination treatment using genomic and immunohistochemical analysis.

Whole-exome sequencing was performed on pre-treatment and post-progression samples of the MBC patient, as compared to a whole blood normal control. The researchers found that a region of Chromosome 12p was deleted in the resistant tumor and that HR protein expression was increased in the resistant tumor. This research provides new insights into both male breast cancer and response to BEZ235/everolimus combination treatment. This study adds to our understanding of MBC development and resistance, and the authors commented that ""Breast cancer in men is a very rare disease, representing less than 1% of all breast cancer cases. So, very few and small studies have been conducted in this disease. Our analyses contributed to delineate the genomic landscape of male breast cancer and suggested a potential particular benefit in this disease by the combined treatment with Afinitor plus BEZ235 in order to achieve a complete blockade of the PI3K/Akt/mTOR pathway. "

More information: A. Rose Brannon et al. Biomarker analysis of a male breast cancer patient with prolonged stable disease under mTOR/PI3K inhibitors BEZ235/everolimus, *Molecular Case Studies* (2015). DOI: 10.1101/mcs.a000620

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