LOBULAR BREAST CANCER
NEW OPPORTUNITIES & PERSONALIZED TREATMENT

Lobular Breast Cancer

Invasive Breast Cancer refers to a type of cancer that has extended to the tissue surrounding a duct or lobule and may spread to other parts of the body. Infiltrating Ductal Cancer - IDC, which is the most common type of breast cancer, begins in the milk ducts, then breaks through, invading nearby tissue. Invasive Lobular Cancer - ILC is a type of breast cancer that begins in the milk-producing glands, lobules of the breast, which means the cancer cells have broken out of the lobule where they began and have the potential to spread to other areas of the body. Invasive lobular carcinoma typically doesn't form a lump, as most women expect with breast cancer. Instead, invasive lobular carcinoma more often causes a thickening of the tissue or fullness in one part of the breast.

ILC – Invasive lobular breast cancer makes up a small portion of all breast cancers. Since ILC make up only 5% to 10% of all BC cases, there hasn’t been much effort to treat them with a different strategy. But now, an increasing number of molecular and treatment-response studies are finding characteristics that set ILC apart from IDC…

Having an understanding on the basic biology of ILC - Invasive Lobular Cancer, I would like to share the outcomes of the sessions held at SABCS 2014 at the Henry B. Gonzalez Convention Center in San Antonio, TX where over 7500 physicians, researchers, patient advocates, including myself and healthcare professionals from over 90 countries attended and shared the latest research results on breast cancer…

Dr. Giovanni Ciriello, from MSKCC is a member of TCGA - The Cancer Genome Atlas BC Analysis Working Group - AWG, presented the research undertaken with 817 BC - Breast Cancer samples with complete genomic profiles to find out results of the following items:

• What are the genetic drivers of Lobular BC,
• What distinguishes ILC from IDC,
• And could this data be used to identify new therapeutic opportunities for patients with ILC?

The study as a phase of TCGA - The Cancer Genome Atlas BC Breast Cancer Project, aimed at exploring and explaining the diversity of a certain subset of breast tumors like luminal tumors. As we know Breast Cancer is a heterogeneous disease that could be thought as a collection of distinct diseases and these diseases are mostly characterized by the status of hormone receptors; ER - estrogen receptor, PR - progesterone receptor and growth factor receptor HER2. And the largest fractions of breast tumors are positive for the ER and PR but negative for HER2. This definition largely identifies what we call luminal breast cancer. Luminal tumors have been further stratified using mRNA signature into luminal A and luminal B, with luminal A being less aggressive, generally associated with a better prognosis, and overall, the most frequently occurring breast cancer subtype in the population. The great diversity
and abundance of genomic data resulted to more in-depth, specific analysis on the subtypes and identification of integrating multiple datasets. And from these datasets there were different data types. Almost all of them, had copy number alterations, somatic mutation and mRNA expression. ‘It was interesting that both luminal A’s and luminal B’s are associated with multiple and distinct copy number cluster suggesting an intrinsic heterogeneity in terms of copy number alteration, a similar picture emerged when looking at somatic mutation’ said Dr. Ciriello…

The results achieved showed that these subtypes have a greater heterogeneity at the molecular level. But this heterogeneity is not only molecular; indeed, luminal A is quite as heterogeneous also in clinics while it has the highest median overall survival, it also has the most variable one and it is actually greater in these subtypes than in the others in the long-term. So, given this overall preliminary observation, it was decided to focus specifically on this subtype of breast cancer, the luminal A breast cancer, as it looks like the most heterogeneous, both molecularly and clinically. And the TCGA BC Analysis Working Group wanted to address some fundamental question, like could they link the variability of certain clinical outcomes with the underlying molecular diversity, Dr. Ciriello discussed a number of specific molecular characterizations in ILC that his group identified, such as CDH1 loss of function mutations, FOXA1 mutations, lack of GATA3 mutations and PTEN loss of function mutations. Further, he showed that luminal type A Invasive Lobular Cancer shows increased RTK/AKT activation compared to luminal type A IDC, which opens the door to a therapeutic opportunity for AKT inhibitors in ILC.

Characterization and Clinical Relevance of the Genomic Alterations defining Lobular Breast Cancer that was presented by Christine Desmedt, PhD, Bio – Engineer and Translational Research Coordinator in Jules Bordet Institute referring to different histological subtypes of Invasive Lobular BC. The research aimed to enumerate the recurrent genomic alterations occurring in cancer related genes in a well characterized cohort of ILC - invasive lobular cancer patients and to correlate those with clinical and pathological features. Based on the results achieved the research team believes that there are some new therapeutic opportunities for lobular breast cancer patients.

Findings and Conclusions

Invasive Lobular Breast Cancers are molecularly distinct diseases.

There is a therapeutic opportunity for AKT inhibitors in ILC.

These findings deserve further attention to personalize the treatment of the ILC patients that needs to be validated.

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References:


24. Zhang J, CNTools: Convert segment data into a region by sample matrix to allow for other high level computational analyses. R package (Version 1.6.0.)


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