"An **international scientific symposium** for interaction and exchange among basic scientists and clinicians in breast cancer."

SAN ANTONIO BREAST CANCER SYMPOSIUM®

2016 DEC. 6-10

SAN ANTONIO BREAST CANCER SYMPOSIUM

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ISSUE 2

Plenary Lecture #2: Cell Free Plasma Tumor DNA in Breast Oncology

Thursday, December 8, 9:00 AM, Hall 3

Ben Ho Park, MD, PhD
The Sidney Kimmel Comprehensive Cancer Center
Johns Hopkins, Baltimore, MD

Crediting the success of his research to being at the right place at the right time and to the researchers and assistants in his lab, Dr. Ben H. Park, clinical oncologist and researcher at the Sidney Kimmel Comprehensive Cancer Center at John Hopkins, will speak this morning on the potential of using a blood-based marker to help guide decisions in breast cancer therapy. Circulating cell-free plasma tumor DNA could be a marker of whether micrometastatic disease is present, even to the point where it can become an everyday test.

By covering historic and recent studies on the clinical potential of measuring plasma tumor DNA (ptDNA) in breast cancer patients for early stage and metastatic disease, Dr. Park hopes to underscore that this is not as easy as some people may think. He responds with a quote by Dan Hayes, MD, the current ASCO president: "A bad test can be just as dangerous as a bad drug." Understanding the severity of this statement, Dr. Park is especially meticulous in how to develop these markers and how to validate them. In his talk, he will discuss the steps needed to translate liquid biopsies from research use to clinical practice, highlighting preanalytical and analytical validation. The crux of the research is to show that ptDNA could determine in early stage breast cancer who is cured and who is not. There is currently no way for doctors to provide individual-specific answers to their patients' questions regarding whether they are cured. Instead of providing general statistical data, having a blood test that could, at a microscopic level, reveal if a patient is cured would provide an immense peace of mind for them and their families. In addition, work in metastatic disease and drug resistance using ptDNA will be discussed. For example, ESR1 mutations in drug resistant metastatic disease have been detected in ptDNA, suggesting that they may be prognostic for worse outcomes. This provides opportunities for using ptDNA to serially monitor these patients and determine if new therapies can overcome breast cancer metastases that harbor these ESR1 mutations.

Another important problem Dr. Park hopes to tackle is overtreatment. In 5-10 years, doctors may be able to stop treating patients with a "one size fits all" model. By detecting microscopic disease in early stage

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SYMPOSIUM UPDATES

EXHIBITORS

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THURSDAY, DECEMBER 8TH

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*AT PRESS TIME

Plenary Lecture #2: *continued*

patients, this blood test will allow for truly personalized treatment. Thus, breast oncologists will no longer need to administer all forms of treatment including surgery, chemotherapy, radiation therapy, etc. to all patients. This is the current paradigm, with the logic that across a population of patients, more good than harm will be done. However, by measuring microscopic disease via a blood test, individualized or "precision medicine" could truly be carried out, sparing many women toxic therapies. For example, chemotherapy is not completely benign, yet most women who receive it do not need it for early stage disease. These blood tests could identify those patients who are cured with surgery only, thus sparing hundreds of thousands of women from chemotherapy, a concept that would be paradigm shifting.

The most exciting component of the talk covers the new prospective trial (TBCRC 040) that has, after 2.5 years, finally started. This neoadjuvant, multi-institutional (14 sites) study that opened this past summer at Hopkins aims to clinically validate the prior research. It is for higher risk individuals with the intent to analyze blood between modalities, particularly prior to chemotherapy and prior to surgery to determine if surgery for breast cancer can be avoided. 30% of patients or more who receive neoadjuvant therapy have a pathologic complete response. Dr. Park argues that if there is no tumor left in the breasts and the blood is found to be negative for disease, in the future, these women may not need surgery for their breast cancer treatment.

Incredibly excited and hopeful for the trial that has just begun, he says that this could "change the way we treat breast cancer."

AACR Distinguished Lectureship in Breast Cancer Research
funded by AFLAC

Targeting Breast Cancer Stem Cells: Challenges and Opportunities

Max S. Wicha, MD
University of Michigan Comprehensive Cancer Center, Ann Arbor, MI

Thursday, December 8, 11:30 am, Hall 3

The AACR Distinguished Lectureship in Breast Cancer Research has been established to recognize outstanding science that has inspired or has the potential to inspire new perspectives on the etiology, diagnosis, treatment, or prevention of breast cancer.

Dr. Max S. Wicha is recognized for his leadership in breast cancer research and as a pioneer in the field of cancer stem cells (CSCs). Dr. Wicha is among the most highly cited investigators in the field. His group was part of the team that first identified CSCs in human breast cancers, the first in any solid tumor. His laboratory has developed many of the techniques and assays used to study these cells and to elucidate the pathways which regulate their behavior. These pathways have provided targets for the development of drugs aimed at targeting CSCs. Dr. Wicha is cofounder of OncoMed Pharmaceuticals, a company focused on developing CSC therapeutics, which has produced five agents currently in clinical testing.

Dr. Max Wicha received his medical degree from Stanford University and trained in internal medicine at the University of Chicago. He then went on to the National Cancer Institute, where he trained in clinical oncology and cancer biology. Dr. Wicha joined the faculty of the University of Michigan in 1980 and served as chief in the Division of Hematology/Oncology in the Department of Internal Medicine, from 1984 to 1993. He was the director of the University of Michigan Comprehensive Cancer Center since its inception in 1986 until 2015, when he became director emeritus. Dr. Wicha remains an active clinician, specializing in the treatment of breast cancer patients.

Hot Topic #1: Extended Adjuvant Endocrine Therapy

Because of the significant risk of recurrence of hormone receptor-positive breast cancer (HR+ BC), extended adjuvant endocrine therapy has been a very appealing topic of research.

Yesterday morning, Dr. Vivianne Tjan-Heijnen presented the multicenter, phase III DATA study, which randomized 1912 postmenopausal women with HR+ BC after 2-3 years of adjuvant tamoxifen (TAM) to either 3 or 6 years of anastrozole therapy.

Research concluded that the findings of the study do not support extended adjuvant AI use after 5 years of sequential endocrine therapy for all postmenopausal HR+ BC patients. However, the findings do suggest benefits for a selected group of patients, in particular those with both ER+ and PR+ disease, HER2- disease, large tumor load, and prior chemotherapy. A follow-up analysis when all patients have reached a minimum adapted follow-up of 9 years is to be expected.

For the IDEAL trial, 1824 postmenopausal patients were randomized between 2.5 and 5 years of letrozole (LET) therapy after initial therapy for 5 years of TAM and/or AI. Dr. Erik Blok and his co-investigators did not identify a subgroup that would benefit from the extended therapy of up to 10 years.

Interestingly, a hazard ratio of 0.37 was observed in 2nd primary BC in favor of the 5 year extended therapy. Much like the DATA study, toxicity caused a high frequency (70%) of adverse events, which had an effect on compliance. The IDEAL trial concludes that there is no benefit of extending AI-based adjuvant therapy longer than 2.5 years.

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Hot Topic #1: *continued*

Also looking into LET, Dr. Eleftherios P. Mamounas presented the results of NSABP B-42, which aimed to determine whether 5 years of LET vs. placebo improves disease-free survival (DFS) in patients who have already completed 5 years of hormonal therapy with either an AI or TAM followed by AI.

There was no statistical significance in the beneficial effect of extended LET therapy on DFS (15% reduction) and no significant difference in overall survival. However, LET provided a significant improvement in BC-free interval and distant recurrence. The study suggests that careful assessment of potential risks and benefits is required before recommending extended LET therapy to patients with early-stage BC.

Although these three trials have numerically negative primary end point analyses, as Dr. Michael Gnant said in his discussion of the three presentations, "at least there are some interesting signals about potential counseling strategies for individual patients in the clinic."

Hot Topic #2: Tumor-infiltrating Lymphocytes: Predictive and Prognostic Biomarker

On Wednesday morning, Stephen J. Luen (Australia) presented findings from a secondary analysis of the CLEOPATRA study. Luen and his group looked at the associations between stromal tumor-infiltrating lymphocytes (TILs) and progression-free survival (PFS) in patients with advanced HER2+ breast cancer (BC) who were treated with trastuzumab and pertuzumab.

Of the 808 patients enrolled in CLEOPATRA, the group evaluated TILs in prospectively collected pretreatment tumor samples of 678 patients.

Using a multivariate Cox analysis for PFS, Luen showed that there was a trend toward improved outcome with increasing stromal TILs, but this finding did not reach significance. However, for overall survival (OS), the association between an 11% reduction in risk for death and increasing stromal TIL levels was found to be significant. Luen showed that this prognostic effect was linear (per 10% incremental rise in TILs), consistent with prior studies.

Luen also stated that since patients benefited from pertuzumab irrespective of TIL level, TILs should not be used as a predictive biomarker of pertuzumab efficacy. "The positive influence of preexisting anti-tumor immunity persists in the advanced setting, and strategies to augment immunity may further improve survival," he concluded.

Next, Carsten Denkert (Germany), discussed the role of TILs as a predictive and prognostic biomarker in triple-negative BC (TNBC), HER2+ BC, and luminal HER2- BC.

As TILs appear strongly predictive of pathologic complete response (pCR) in these subtypes, Dr. Denkert explained that this pCR effect can be translated to survival benefit in TNBC and HER2+ BC, but not in luminal HER2- BC. This is because in luminal tumors, Dr. Denkert and his team found that low TIL levels were linked to better OS, even in patients without pCR.

Dr. Denkert suggested that subsequent endocrine therapies may be contributing to the effects in these types of luminal tumors, and concluded that the role of TILs in resistance to different types of hormone therapies should be investigated.