

COMBATing Breast Cancer Conference 2013 – Chances for Cure

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On November 15th–16th 2013 160 physicians, scientists, and students interested in breast cancer research, followed the invitation of the three chairs Nadia Harbeck (Munich), Achim Rody (Lübeck) and Michael Gnant (Vienna) to join this year's 6th COMBATing (Conference On Molecular Basics And Therapeutic Implications in Breast Cancer) in Lübeck.

Recently established possibilities to gain extensive insights into tumor biology and genetics identify an enormous amount of potential targets in breast cancer therapy whose particular significance has to be proven in future. Therefore, this year's congress focused on those new 'Chances for Cure' provided by new diagnostic techniques, e.g. next-generation sequencing.

As usual, national and international pioneers in breast cancer research shared their findings and gave an overview over recent topics. This unique meeting in combination with the AGO TraFo pre-symposium offered an outstanding platform for translational networking, interdisciplinary crosstalk and scientific exchange for ambitious researchers, clinicians, pharmaceutical industry and students.

AGO TraFo Pre-Symposium

For the third year in a row, the main conference was enriched by a pre-symposium of the AGO TraFo (Arbeitsgruppe Gynäkologische Onkologie, Kommission Translationale Forschung), chaired by Tanja Fehm (Düsseldorf). The first session was set up to be a start-up aid for young researchers to gain ground in science. Therefore, experienced scientists gave tips on project planning, financing, and statistics. In addition, strategies for how to write a publication and how to give a good presentation were shown.

Afterwards, Martin Wildschwendtner (London) held the TraFo keynote lecture, presenting the development of research on breast cancer and gynecology in Europe. By analyzing statistics on morbidity and mortality, he highlighted the importance of basic and translational research to gain holistic insights in cancerogenesis in order to improve prevention and

therapy. To obtain valuable data, international cooperation is needed. This excellent lecture was followed by comprehensive overviews over the German research landscape regarding translational research in gyneco-oncology and senology.

The award winners of the AGO TraFo meeting in May 2013 were given time to present their latest findings during an oral presentation (Anna-Lena Krause (Heidelberg), best lecture; Melanie Kürschner (Hamburg), best poster). The pre-symposium then finished with a poster presentation; the 3 best contributions were rewarded with prizes during the evening's festivities (1st prize Carolin Hülsewig (Münster), 2nd prize Florian Bitterer (Regensburg) and 3rd prize Benjamin Ley (Halle)).

COMBATing Meeting

The main meeting started with an update on recent developments since the last COMBATing in 2012. Rita Schmutzler (Cologne) presented the latest findings in hereditary breast cancer. Today's knowledge hypothesizes the presence of several not yet discovered moderate breast cancer susceptibility risk genes. Some promising candidates are currently under closer inspection, one of them might be the first known recessive breast cancer susceptibility gene. An update on the intrinsic subtypes and their particular diagnostics and therapy was given by Cornelia Liedtke (Lübeck), focusing on the significance of different predictive assays. Subsequently, Alexander Katalinic (Lübeck) showed current epidemiological data where a relevant decline in mortality in young breast cancer patients could be observed.

The next session focused on tumor biology and formation. Hans Kreipe (Hanover) gave spectacular insights into the biology of B3 lesions, whose genetic information does not differ much from that of invasive cancers. He demonstrated a sequence from B3 lesion to DCIS to invasive cancer, showing the high impact of this pathological finding on clinical routine. With the following presentation, Anette Lebeau (Lübeck)

tied in perfectly, highlighting the role of stroma invasion in DCIS. Michael Knauer (Linz) and Marcus Schmidt (Mainz) discussed the common problems in clinical routine: on one hand 'bad stage but good biology' and on the other hand 'low stage but adverse biology'. Both speakers reasoned that only a combination of clinical and genetic aspects can lead to an appropriate prognostic estimate and therapy recommendation. Marcus Schmidt, this year's winner of the 'Henner Graeff COMBAT Award', concluded his talk with the wise citation of Karl Valentin: 'predictions are difficult, especially those concerning the future'.

The pharmaceutical industry was given the opportunity to present recent targets in breast cancer research. While Roche has products with HER3, Ang-2 and macrophages as targets in its pipeline, Novartis deepens its research in the mTOR/PI3K pathway and in CDk4/6 antibodies. With these compounds, phase III trials are already under way in breast cancer.

The first day concluded with a roundtable of the most important German (GBG, AGO-B, WSG, SUCCESS, DETECT), Austrian (ABCSG) and Swiss (SAKK) study groups. Leaders of each group presented the studies presently recruiting and demonstrated first results.

During the evening's get-together, 10 travel grants were awarded to ambitious young researchers and the winners of the poster prizes were congratulated by the 3 chairs of COMBATing, Nadia Harbeck, Achim Rody, and Michael Gnant. The Henner Graeff COMBAT award 2013 was given to Markus Schmidt (Mainz) for his role in the development of several prognostic markers, such as uPA/PAI-1 or the Endo-predict assay (fig. 1).



Fig. 1. The chairs Achim Rody, Michael Gnant and Nadia Harbeck (from left to right) award the Henner Graeff-COMBAT award to Martin Schmidt (3rd from left) accompanied by his laudator Christoph Thomssen (Halle) and Sigrid Welte (Novartis, sponsor of the award).

The second day of the meeting began with the keynote lecture of Martin Widschwendtner giving insights in the clinical significance of epigenetics and DNA methylation. Many life style factors can lead to epigenetic misprogramming leading to cancerogenesis. Especially methylation of CpG-islands and the repression of polycomb group proteins in stem cells may play a crucial role. Epigenetic methylation in *BRCA1/2*-mutation carriers causes elevated progesterone serum levels and an up-regulation of RANK-ligand leading to a higher individual risk in developing cancer. This knowledge may be used in prevention in the future.

The next session gave insight into the biology of the tumor cell. Illuminating the mTOR/PI3K pathway Friedrich Overkamp (Recklinghausen) showed the main reasons for endocrine resistance (PTEN loss, PI3K mutation or amplification) and ways to overcome them. Unfortunately, there are no validated biomarkers for products in the pipeline yet. A new drug, BKM 120, a pan-class PI3K inhibitor, is a promising substance with the ability to pass the blood-brain barrier. But a new spectrum of adverse effects may be problematic and require proactive management and patient education. Oleg Gluz (Mönchengladbach) highlighted the special role of HER2 in cancerogenesis and metastasis of breast cancer in an engaging speech. He pointed out that a prognostic differentiation between HER2-positive, hormone receptor-negative and triple-positive breast cancer is essential. In his presentation about tumor-stromal interactions, Thomas Karn (Frankfurt/Main) focused on tumor infiltrating lymphocytes, which may play a role in chemo-response of triple negative breast cancer (TNBC). He demonstrated the wide complexity of the immune response in cancer and outlined possible therapeutic approaches.

Subtype-specific patterns of metastasis in breast cancer were the focus of Rachel Würstlein (Munich), showing that a better prediction of the location of metastases will be possible in future, which may help to establish better detection and even prevention. The best approach for therapy recommendation is still to consider the biology of primary and metastatic disease and the observed response to prior treatment. Volker Müller (Hamburg) concentrated on brain metastases, whose incidence is increasing. As data are largely lacking, a special data and tissue register will be established (www.germanbreastgroup.de). The aim is to identify patients with a high risk of developing brain metastases who may benefit from special early detection programs or even from preventive irradiation. Actinotherapeutic aspects of breast cancer research were shown by Jochen Fleckstein (Homburg/Saar). Hypofractionation of irradiation is a budding therapy option; also the parallel use of substances affecting DNA repair, such as platinum derivatives and PARP-inhibitors is promising.

In his brilliant lecture Peter Fasching (Erlangen) showed the enormous amount of data which is obtained by gene profiling of breast cancer tissue. At the moment, the biggest

challenge for the clinician is the confrontation with this huge amount of information and a lack of specific therapy. The impact of metformin and statins as therapeutic approaches in breast cancer was discussed by Brigitte Rack (Munich), showing that especially biguanide has a positive effect on risk reduction in cancer in general. However, it might be hypothesized that a lifestyle intervention may lead to the same effect. Afterwards, an update on the role of vitamin D in breast cancer therapy was presented by Marc Till (Frankfurt/Main). He revealed that there is still no evidence of a benefit from vitamin D therapy. Therefore, a strict recommendation does not exist.

In the next session, special clinical constellations were reviewed. Dorothea Fischer (Lübeck) presented the case of young breast cancer patients. Here, a more aggressive biology is observed and the clinician is disproportionally often confronted with hereditary or pregnancy associated breast cancer. Breast cancer in elderly patients was discussed by Hans-Joachim Lück (Hanover). In spite of a better biology, a poorer prognosis is observed due to non-standard therapy. Finally, Sibylle Loibl (Neu-Isenburg) gave an exciting update on pregnancy associated breast cancer and fertility after breast cancer. To gain better insights into this special issue, all participants were encouraged to introduce pregnant breast cancer patients in the recruiting GBG register study (www.germanbreastgroup.de).

Conclusion

This 6th COMBATing meeting with AGO TraFo pre-symposium in Lübeck was an outstanding success. The excellent choice of national and international speakers discussing recent topics made this event unique. Researchers and clinicians from Germany, Austria, and Switzerland were given a possibility for networking and scientific exchange without comparison.

This year's meeting showed the advancement in breast cancer from an unselective 'one size fits all' approach to identification of the right individualized therapy for the right patient. We are all looking forward to learn more about these developments and happily accept the invitation of the chairpersons Michael Gnant, Achim Rody, and Nadia Harbeck to the 7th COMBATing in Düsseldorf, November 21–22, 2014.

More information about the meeting can be found at www.combating.de.

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