PRESS RELEASE

"New England Journal of Medicine" publishes results of MINDACT clinical trial

The 70-gene test (Mammaprint®) can significantly reduce use of chemotherapy among breast cancer patients and has the potential to change clinical practice:

46% of early stage breast cancer patients classified as high-risk by traditional methods can avoid chemotherapy

Brussels, 26 July 2016 - T**he prestigious "New England Journal of Medicine" published the primary outcome results of the MINDACT study. This breakthrough clinical trial is an example of international, academic, and multi-disciplinary leadership and achievement in breast cancer research. It is also a clear illustration of an integrated public, private and patient group collaboration.**

The MINDACT trial results provide the highest level of evidence that using the 70-gene test (Mammaprint®) could change clinical practice by substantially de-escalating the use of adjuvant chemotherapy and sparing many patients a treatment that may cause toxicities, and will offer no to very little benefit.

What is MINDACT?

MINDACT stands for "**M**icroarray **I**n **N**ode negative and 1 to 3 positive lymph node **D**isease may **A**void **C**hemo**T**herapy".

In summary, MINDACT provides evidence from a large-scale, prospective, randomised, controlled phase III international clinical trial for the value of integrating the 70-gene test (MammaPrint®) into clinical practice, which can now be considered in early breast cancer.

The results of the MINDACT clinical trial were presented for the first time by Dr Martine Piccart at the AACR Annual Meeting 2016 (American Association for Cancer Research, New Orleans, USA, April 2016). The aim of MINDACT – which enrolled 6693 breast cancer patients from 112 hospitals across 9 European countries – was to evaluate the added value of a test of 70 gene test (Mammaprint®) to the traditional method of assessing the likelihood of breast cancer recurrence for women with node-negative or 1-to-3 node positive breast cancer. The study results can help oncologists decide which of these patients will be able to safely avoid chemotherapy and the side effects that come with it.

Future research using the study's biological sample collection can also contribute to a much deeper understanding of breast cancer and how to continue to improve treatment in the future.

MINDACT, an extensive and complex academically-driven international partnership

Sponsored by the European Organisation for Research and Treatment of Cancer (EORTC) as part of an extensive and complex academically-driven international partnership in collaboration with the Breast International Group (BIG), Europa Donna – the European Breast Cancer Coalition, Agendia (the company behind MammaPrint®, the 70-gene test), as well as many other academic and commercial partners, MINDACT is the first prospective translational research study of this magnitude in breast cancer to report the results of its primary objective.

MINDACT is an international, prospective, randomised, phase III study investigating the clinical utility of the 70-gene test, in addition to standard clinical-pathological criteria in selecting patients for adjuvant chemotherapy (CT). It was designed to compare the ability of the 70-gene signature MammaPrint® with the clinical risk assessment tool Adjuvant!Online in identifying those patients with node-negative or 1-to-3 node positive early-stage breast cancer who can be safely spared adjuvant chemotherapy without affecting their long term outcome (i.e. Distant Metastasis-Free Survival, DMFS).

The hypothesis that a considerable proportion of patients with LN0 or 1-3 LN+ early breast cancer can be safely spared adjuvant CT based on the biology of their disease was proven. The assay is useful in the group of patients characterised as high-risk per traditional clinical-pathological characteristics (clinical-high, or C-high), in which 46% are low-risk according to MammaPrint® (genomic-low or G-low) and can thus forego adjuvant CT. C-high/G-low patients had a 5-year DMFS above 94%, independently of receiving or not CT. The study set-up was challenging because of the numerous statistical, ethical, legal and intellectual property rights issues to be addressed at a time when genomic risk assessment assays were still new territory. Furthermore, the need to perform the test on fresh frozen material at the time of the trial (it can now be done on FFPE) led to complex logistics for the real-time collection and analysis of tumour tissue from 112 hospitals across 9 different countries. Notwithstanding these hurdles, the study successfully enrolled and treated 6693 early breast cancer patients, proving the feasibility of large, prospective, randomised, biomarker-focused trials, in a multinational setting.

Quotes from the Principal Investigators of the MINDACT trial (Dr. Fatima Cardoso, Dr. Emiel Rutgers, Dr. Martine Piccart), Europa Donna, and MINDACT's lead scientist (Laura van 't Veer)

Dr. Fatima Cardoso, MD, Director of the Breast Unit of the Champalimaud Clinical Centre in Lisbon (Portugal), EORTC – Breast Group Chair and member of the EORTC Board of Directors, and co-principal investigator of the MINDACT trial: "When MINDACT was developed, it was on the forefront of a new generation of trials in breast cancer since it was the first to evaluate a genomic-based biomarker in the clinical setting. MINDACT has contributed substantially to showing the role that genomics can play in helping us treat breast cancer. In other words, through MINDACT and by using new technologies, we are able to make substantially more progress in tailoring treatment to individual women."

Dr. Emiel Rutgers, MD, PhD, FRCS, Surgical Oncologist at Netherlands Cancer Institute in Amsterdam, Chair of the Institutes of Breast Cancer Working Group, Professor at the medical faculty of the University of Amsterdam, Chair of the European Breast Cancer Council and co-principal investigator of the MINDACT trial: "MINDACT is a multi-centre, multi-group collaboration which acts as a great example of public-private partnership with the involvement of academic research groups, industry, patient organisations and European funding. The role of academic infrastructure like that of EORTC and the facilitating capability of BIG has made this extensive and international trial feasible. EORTC and BIG trials and research programmes always incorporate translational research within them. Translational research provides the link between the discoveries in the laboratory (basic science research) and their application for the benefit of patients (clinical research)."

Dr. Martine Piccart, MD, PhD, co-founder and chair of the Breast International Group (BIG), head of the Medicine Department at the Jules Bordet Institute in Brussels, Belgium, and co-principal investigator of the trial: "MINDACT can be qualified as a landmark study. Not only has the MINDACT trial the potential to change the way doctors treat patients with breast cancer, it has also created a huge resource for future research, because research using the participants' tumour samples, blood samples, and clinical outcomes data could allow us to gain a substantially better understanding of the biology of breast cancer."

Susan Knox, Chief Executive Officer at Europa Donna - the European Breast Cancer Coalition since 1999. Susan Knox, who is a two-time breast cancer survivor, is responsible for all on-going European advocacy initiatives in the areas of information, education and policy: "As part of the MINDACT Steering Committee, Legal/Ethics Committee and the Spreading of Excellence Committee, Europa Donna has been involved in the MINDACT trial since the beginning. We feel it is our responsibility to provide input from a patient's perspective and to help disseminate information about the trial to the public. Given that there are now concrete results from MINDACT demonstrating that chemotherapy can safely be avoided for a substantial group of patients, we will disseminate information about the trial to the general public, and in particular to those women affected."

Dr. Laura van 't Veer, MD, PhD, Molecular Biologist, Chief Research Officer at Agendia, Leader of the Breast Oncology Programme, Director Applied Genomics at UCSF Helen Diller Family Comprehensive Cancer Centre, former Head of Diagnostic Oncology at the Netherlands Cancer Institute, and inventor of MammaPrint®: "Our ability to profile the gene expression of a tumour is transforming the way we characterise cancers and how we can more effectively treat patients. MINDACT has proved with the highest level of evidence that, by evaluating the expression of 70 key genes, MammaPrint® provides an accurate, definitive assessment of the risk of breast cancer recurrence, empowering physicians to make confident, informed treatment decisions with their patients. MammaPrint® is already enabling thousands of patients with early stage breast cancer to safely forego the rigours of chemotherapy across the world."

MINDACT ABSTRACT

Background

The 70-gene signature test (MammaPrint) has been shown to improve prediction of clinical outcome in women with early-stage breast cancer. We sought to provide prospective evidence of the clinical utility of the addition of the 70-gene signature to standard clinical–pathological criteria in selecting patients for adjuvant chemotherapy.

Methods

In this randomized, phase 3 study, we enrolled 6693 women with early-stage breast cancer and determined their genomic risk (using the 70-gene signature) and their clinical risk (using a modified version of Adjuvant! Online). Women at low clinical and genomic risk did not receive chemotherapy, whereas those at high clinical and genomic risk did receive such therapy. In patients with discordant risk results, either the genomic risk or the clinical risk was used to determine the use of chemotherapy. The primary goal was to assess whether, among patients with high-risk clinical features and a low-risk gene-expression profile who did not receive chemotherapy, the lower boundary of the 95% confidence interval for the rate of 5-year survival without distant metastasis would be 92% (i.e., the noninferiority boundary) or higher.

Results

A total of 1550 patients (23.2%) were deemed to be at high clinical risk and low genomic risk. At 5 years, the rate of survival without distant metastasis in this group was 94.7% (95% confidence interval, 92.5 to 96.2) among those not receiving chemotherapy. The absolute difference in this survival rate between these patients and those who received chemotherapy was 1.5 percentage points, with the rate being lower without chemotherapy. Similar rates of survival without distant metastasis were reported in the subgroup of patients who had estrogen-receptor–positive, human epidermal growth factor receptor 2–negative, and either node-negative or node-positive disease.

Conclusion

Among women with early-stage breast cancer who were at high clinical risk and low genomic risk for recurrence, the receipt of no chemotherapy on the basis of the 70-gene signature led to a 5-year rate of survival without distant metastasis that was 1.5 percentage points lower than the rate with chemotherapy. Given these findings, approximately 46% of women with breast cancer who are at high clinical risk might not require chemotherapy. (Funded by the European Commission Sixth Framework Program and others; ClinicalTrials.gov number, NCT00433589; EudraCT number, 2005-002625-31.)

About EORTC (European Organisation for Research and Treatment of Cancer)

The EORTC is a unique organisation – a vibrant example of the fact that academic science and research know no national boundaries. Established in 1962, the EORTC is a non-profit European research organisation operating as an international association under Belgian law. The EORTC currently links a network of more than 4,000 pre-clinical scientists and oncologists in more than 600 hospitals in over 30 countries. It encompasses all aspects of cancer research, from translational research and new drug development to large phase III clinical trials and meta-analyses. The 180 members of the EORTC Headquarters staff handle some several thousand new patients enrolled each year in cancer clinical trials, approximately 50 protocols that are permanently open to patient entry, over 20,000 patients who are in follow-up, and a database of more than 190,000 patients. The ultimate goal of the EORTC is to improve the future of cancer therapy by developing new agents and innovative approaches and to test more effective treatment strategies using commercially available drugs, or surgery and radiotherapy.
For more information, visit www.eortc.org.

About Breast International Group (BIG)

The Breast International Group (BIG) is an international not-for-profit organisation for academic breast cancer research groups from around the world, based in Brussels, Belgium.

Global collaboration is crucial to make significant advances in breast cancer research, reduce unnecessary duplication of effort, share data, contribute to the faster development of better treatments, and increase the likelihood of cures for patients. Therefore, BIG facilitates breast cancer research at international level, by stimulating cooperation between its members and other academic networks, and collaborating with, but working independently from, the pharmaceutical industry.

Founded by leading European opinion leaders in 1999, BIG now constitutes a network of 56 collaborative groups from Europe, Canada, Latin America, Asia and Australasia. These entities are tied to several thousand specialised hospitals and research centres worldwide. More than 30 clinical trials are run or are under development under the BIG umbrella at any one time. BIG also works closely with the US National Cancer Institute (NCI) and the North American Breast Cancer Groups (NABCG), so that together they act as a strong integrating force in the breast cancer research arena.
For more information, visit www.BIGagainstbreastcancer.org.

About Europa Donna

EUROPA DONNA - The European Breast Cancer Coalition – is an independent, non-profit organisation whose members are affiliated groups from countries throughout Europe. EUROPA DONNA works to raise public awareness of breast cancer and to mobilise the support of European women in pressing for improved breast cancer education, appropriate screening, optimal treatment and care and increased funding for research. Member countries currently number 47.
For more information: www.europadonna.org.

About Agendia

Agendia is a privately held, leading molecular diagnostics company that develops and markets FFPE-based genomic diagnostic products, which help support physicians with their complex treatment decisions. Agendia's breast cancer and colorectal cancer tests were developed using an unbiased gene selection by analysing the complete human genome. Our offerings include the FDA-cleared MammaPrint® FFPE as well as BluePrint®, a molecular subtyping assay that provides deeper insight leading to more clinically actionable breast cancer biology, and TargetPrint®, a breast cancer ER/PR/HER2 expression assay. These tests can help physicians assess a patient's individual risk for metastasis – that is, which patients are more sensitive to chemo, hormonal, or combination therapy, and which patients may not require these treatments and which patients may be treated with other, less arduous and costly methods.

In addition, Agendia has a pipeline of other genomic products in development. The company collaborates with pharmaceutical companies, leading cancer centres and academic groups to develop companion diagnostic tests in the area of oncology. It is also a critical partner in the ISPY-2, NBRST and the MINDACT trials. For more information, visit www.agendia.com.

Note to the editor – not for publication:

Should you wish to receive more information on this release, please contact the MINDACT communications team:

Valerie Van der Veeken
BIG (Breast International Group)
Phone: +32 2 541 3524
Valerie.VanderVeeken@BIGagainstbc.org

Caroline De Bie
EORTC (European Organisation for Research and Cancer Treatment)
Phone: +32 2 774 1651
caroline.debie@eortc.be