



**Embargoed for Release:** 8:30 a.m. CT, April 18, 2016

To interview Martine Piccart, contact Julia Gunther at [julia.gunther@aacr.org](mailto:julia.gunther@aacr.org), 215-446-6896, or 267-250-5441. For a photo of Piccart, click [here](#). Visit our [newsroom](#).

## **MammaPrint Genetic Test Can Reduce Use of Post-surgery Chemotherapy Among Early-stage Breast Cancer Patients**

NEW ORLEANS — Among patients with early-stage breast cancer who were considered at high risk for disease recurrence based on clinical and biological criteria, the [MammaPrint](#) genetic test identified a large group of patients for whom five-year distant metastasis-free survival was equally good whether or not they received adjuvant chemotherapy (chemotherapy given post-surgery), according to results from the randomized, phase III [microarray in node negative disease may avoid chemotherapy](#) (MINDACT) clinical trial to be presented here at the [AACR Annual Meeting 2016](#), April 16-20.

“At present, most oncologists make recommendations for adjuvant chemotherapy after considering common clinical and biological criteria such as patient’s age, and the stage and grade, as well as the hormonal receptor and HER2 status of his or her tumor,” said Martine Piccart, MD, PhD, head of the Medicine Department at the [Jules Bordet Institute](#) in Brussels, Belgium, and co-founder and chair of the [Breast International Group](#) (BIG). “The MINDACT trial results provide level 1A evidence that using MammaPrint could change clinical practice by substantially de-escalating the use of adjuvant chemotherapy and sparing many patients an aggressive treatment they will not benefit from.”

Among the 3,356 patients enrolled in the MINDACT trial who were categorized as having a high risk of breast cancer recurrence based on common clinical and pathological criteria (C-high), treatment according to MammaPrint reduced the chemotherapy prescription by 46 percent. Five-year distant metastasis-free survival for the discordant G-low/C-high group is in excess of 94 percent, whether patients received CT or not.

Piccart explained that when considering all the patients enrolled in the MINDACT trial, 14 percent could avoid chemotherapy by using the 70-gene signature MammaPrint genetic test to assess risk compared with using traditional clinical assessments.

From 2007 to 2011, Piccart and colleagues at 111 centers in nine countries enrolled in the trial 6,693 women who had undergone surgery for early-stage breast cancer (out of 11,288 women screened). All participants were categorized as low or high risk for tumor recurrence in two ways: first, through analysis of tumor tissue using MammaPrint at a central location in Amsterdam; and second, using [Adjuvant! Online](#), a tool that calculates risk of breast cancer recurrence based on common clinical and biological criteria.

The participants were then divided into four groups: 2,745 were categorized as having low risk of recurrence by both risk-assessment methods (G-low/C-low), 1,806 were categorized as having high risk of recurrence by both risk-assessment methods (G-high/C-high), 592 were categorized as having high risk of recurrence by MammaPrint and low risk of recurrence by Adjuvant! Online (G-high/C-low), and 1,550 were categorized as having low risk of recurrence by MammaPrint and high risk of recurrence by Adjuvant! Online (G-low/C-high).

Patients categorized as G-low/C-low were assigned to no adjuvant chemotherapy while those categorized as G-high/C-high were assigned to adjuvant chemotherapy. Patients categorized as G-high/C-low or G-low/C-high were randomly assigned adjuvant chemotherapy or no adjuvant chemotherapy.

According to Piccart, the MINDACT trial is the first prospective randomized controlled clinical trial of a breast cancer recurrence genomic assay with level 1A clinical evidence and the first prospective translational research study of this magnitude in breast cancer to report the results of its primary objective. She added that the trial has also created a huge resource for future research, because research using the participants' tumor samples, blood samples, and clinical outcomes data could allow us to gain a substantially better understanding of the biology of breast cancer.

The MINDACT trial is managed and sponsored by the European Organisation of Research and Treatment of Cancer (EORTC) as part of an extensive and complex partnership in collaboration with the BIG, Agendia, and a great many other academic and commercial partners, as well as patient advocates. The study was supported by grants from the European Commission Framework Programme VI (FP6-LSHC-CT-2004-503426, "TRANSBIG Network of Excellence"), the Breast Cancer Research Foundation, Novartis, F. Hoffman La Roche, Sanofi-Aventis, Eli Lilly, Veridex, the U.S. National Cancer Institute, the European Breast Cancer Council-Breast Cancer Working Group (BCWG grant for the MINDACT biobank), the Jacqueline Seroussi Memorial Foundation (2006 JSMF award), Prix Mois du Cancer du Sein (2004 award), Susan G. Komen for the Cure (SG05-0922-02), Fondation Belge Contre le Cancer (SCIE 2005-27), Dutch Cancer Society (KWF), Association Le Cancer du Sein, Parlons-en!, the Brussels Breast Cancer Walk-Run and the American Women's Club of Brussels, NIF Trust, Deutsche Krebshilfe, the Grant Simpson Trust and Cancer Research UK. This trial was also supported by the EORTC Charitable Trust. Whole genome analysis was provided in kind by Agendia. Total funding: approx. EUR 47 million. Piccart declares no conflicts of interest.

Press registration for the AACR Annual Meeting 2016 is free to qualified journalists and public information officers. Click [here](#) for more information.

Follow the AACR Annual Meeting 2016 on Twitter: [#AACR16](#)

###

Follow us: *Cancer Research Catalyst* <http://blog.aacr.org>; Twitter [@AACR](#); and Facebook <http://www.facebook.com/aacr.org>

For AACR information, visit [Fast Facts](#).

### **About the American Association for Cancer Research**

Founded in 1907, the American Association for Cancer Research (AACR) is the world's first and largest professional organization dedicated to advancing cancer research and its mission to prevent and cure cancer. AACR membership includes more than 35,000 laboratory, translational, and clinical researchers; population scientists; other health care professionals; and patient advocates residing in 104 countries. The AACR marshals the full spectrum of expertise of the cancer community to accelerate progress in the prevention, biology, diagnosis, and treatment of cancer by annually convening more than 30 conferences and educational workshops, the largest of which is the AACR Annual Meeting with nearly 19,300 attendees. In addition, the AACR publishes eight prestigious, peer-reviewed scientific journals and a magazine for cancer survivors, patients, and their caregivers. The AACR funds meritorious research directly as well as in cooperation with numerous cancer organizations. As the Scientific Partner of Stand Up To Cancer, the AACR provides expert peer review, grants administration, and scientific oversight of team science and individual investigator grants in cancer research that have the potential for near-term patient benefit. The AACR actively communicates with legislators and other policymakers about the value of cancer research and related biomedical science in saving lives from cancer. For more information about the AACR, visit [www.AACR.org](http://www.AACR.org).

Abstract: CT039

Presentation Session: Clinical Trials Plenary Session, Monday, April 18, 10:30 a.m.-12:30 p.m. CT, La Nouvelle Orleans Ballroom

Title: Primary analysis of the EORTC 10041/ BIG 3-04 MINDACT study: a prospective, randomized study evaluating the clinical utility of the 70-gene signature (MammaPrint) combined with common clinical-pathological criteria for selection of patients for adjuvant chemotherapy in breast cancer with 0 to 3 positive nodes

Authors: M. Piccart<sup>1</sup>, E. Rutgers<sup>2</sup>, L. van't Veer<sup>3</sup>, Leen Slaets<sup>4</sup>, S. Delaloge<sup>5</sup>, G. Viale<sup>6</sup>, JY. Pierga<sup>7</sup>, P. Vuylsteke<sup>8</sup>, E. Brain<sup>9</sup>, Suzan Vrijaldenhoven<sup>10</sup>, P. Neijenhuis<sup>11</sup>, B. Coudert<sup>12</sup>, T. Smilde<sup>13</sup>, M. Gil<sup>14</sup>, Alastair Thompson<sup>15</sup>, Isabel Rubio<sup>16</sup>, Rodolfo Passalacqua<sup>17</sup>, Erika Matos<sup>18</sup>, Urlike Nitz<sup>19</sup>, Mauro Delorenzi<sup>20</sup>, Geraldine Thomas<sup>21</sup>, Theodora Goulioti<sup>22</sup>, Carolyn Straehle<sup>22</sup>, K. Tryfonidis<sup>4</sup>, J. Bogaerts<sup>4</sup> & F. Cardoso<sup>23</sup> on behalf of TRANSBIG consortium and MINDACT investigators

1. Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium 2. The Netherlands Cancer Institute, Amsterdam, Netherlands, 3. UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, USA 4. EORTC Headquarters, Brussels, Belgium 5. Institute Gustave Roussy, Villejuif, France 6. University of Milan, Instituto Europeo di Oncologia, Milan, Italy 7. Institute Curie, Paris, France 8. Clinique et Maternité Saint Elisabeth, Namur, Belgium 9. Institute Curie- Hopital Rene Huguerin, Saint Cloud, France, 10. Med Centrum Alkmaar, Netherlands 11. Rijnland Leiderdorp, 12. Centre G.F, Leclerc, France, 13. J.Bosch'S Hertogenb, Netherlands, 14. ICO Barcelona, Spain 15. MD Anderson Cancer Center, Houston, Texas, USA 16. Hospital General Vall d'Hebron, Spain 17. Azienda Istituti Ospitalieri di Cremona, Italy, 18. The Institute of Oncology, Slovenia 19. Evangelisches Krankenhaus Bethesda Monchengladbach, Germany, 20. Swiss Institute of Bioinformatics, Switzerland, 21. Imperial College London, UK, 22. Breast International Group, Brussels, Belgium 23. Champalimaud Clinical Center, Lisbon, Portugal

**Background:** The MINDACT TRIAL investigated the clinical utility of the 70-gene profile (MammaPrint®), when confronted to the standard clinical pathological (CP) criteria, for the selection of patients unlikely to benefit from adjuvant chemotherapy (CT).

**Methods:** From 2007 to 2011, 11288 patients were screened in 112 centers from 9 countries, of whom 6693 were enrolled. Enrolled patients had undergone successful determination of their genomic risk G (with MammaPrint®) and clinical risk C (modified version Adjuvant! Online). Patients were evaluated as “low clinical risk”, if their 10-year disease specific survival (without CT or endocrine therapy (ET)), as estimated by Adjuvant! Online, was greater than 88% for ER-positive patients, and greater than 92% for ER-negative patients. Patients characterized in both assessments as “low- risk” were spared CT while for those “high- risk”, CT was advised. Those with discordant results were randomized to use either C or G risk evaluation to decide on CT. The main hypothesis was that G-assay would outperform the C-criteria by reducing the administration of adjuvant CT without impairing outcome. The CT and ET regimen randomization will not be part of the current presentation. The primary endpoint for the CT (yes/no) decision was distant metastasis free survival (DMFS). Secondary endpoints were the proportion of women treated per C over G, the overall survival (OS) and disease free survival (DFS). In the G-low/C-high risk group, a null hypothesis of a 5-year DMFS of 92% was tested (one-sided  $\alpha = 2.5\%$ ) in the patients who were randomized to use the 70-gene signature prognosis (no CT), and who complied with this “no CT” assignment.

**Results:** Median age of enrolled patients was 55 years. Eighty percent were LN- negative. 58% had tumor size between 1 and 2cm, 88% were HR-positive and 10% were HER2 positive. The enrolled patients were categorized in 4 risk groups; G-low/C-low [2745 patients (41%)], G-high/C-low [592 (9%)], G-low/C-high [1550 (23%)] and G-high/C-high [1806 (27%)]. In the G-low/C-high group, 51% of patients were randomized to CT (49% to no CT) and in the G-high/C-low group 50% to CT. At 5- years, DMFS was 94.7% (95%CI, 92.5-96.2%) for patients who were C- high/ G- low and randomized to use G and received no CT. This CI exceeds 92%, thereby rejecting the primary null hypothesis of MINDACT. There was an absolute 14% reduction in adjuvant CT administration when using the G versus C treatment strategy.

**Conclusion:** C-high/G-low patients had a 5-year DMFS rate in excess of 94%, whether they were randomized to adjuvant CT or no CT. Using the G assay for CT treatment decision led to a 14% reduction in adjuvant CT administration in MINDACT. When using the G assay MammaPrint® among the C-high patients, there was a 46% (1550/3356) reduction in CT prescription, providing level 1A evidence for the clinical utility of MammaPrint® for assessing the lack of a clinically relevant chemotherapy benefit in the clinically high risk (C-high) population.