Publication Number: S1-05

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

Piccart M, Rutgers E, van’t Veer L, Slaets L, Delaloge S, Viale G, Pierga J, Vuyykepeo P, Brain E, Vrijaldenhoven S, Neijenhuis P, Coudert B, Smilde T, Gil M, Thompson A, Rubio l, Passalaqua R, Matos E, Nitz U, Delorenzi M, Thomas G, Gaulioti T, Straehle C, Tryfonidis K, Bogaerts J, Cardoso F. Institute Jules Bordet Brussels, Belgium; Breast International Group- EB Chair Brussels, Belgium; EORTC Headquarters Brussels, Belgium; UCSF Helen Diller Family Comprehensive Cancer Center San Francisco, CA; Institute Gustave Roussy Villejuif, France; University of Milan, Instituto Europeo di Oncologia Milan, Italy; Institute Curie Paris, France; Clinique et Maternite Saint Elisabeth Namur, Belgium; Institute Curie-Hopital Rene Huguerin Saint Cloud, France; Med Centrum Alkmaar Netherlands; Rijnland Leiderdorp Netherlands; Centre G.F Lecerc, France; JBoss's Hertogenb Netherlands; ICO Barcelona, Spain; Champalimaud Clinical Center Lisbon, Portugal; The Netherlands Cancer Institute Amsterdam, Netherlands; MD Anderson Cancer Center Houston, TX; Hospital General Vall D’ Hebron Barcelona, Spain; Azienda Istituti Ospitalieri di Cremona Italy; The Institute of Oncology Slovenia; Evangelisches Krankenhaus Bethesda Mochengladbach Germany; Swiss Institute of Bioinformatics Switzerland; Imperial College London, United Kingdom; Breast International Group- Headquarters Brussels, Belgium

Body:

Background
The MINDACT trial investigates the clinical benefit of the 70-gene profile (MammaPrint), when added to the standard clinical pathological (CP) criteria, for the selection of patients for adjuvant chemotherapy (CT).

Methods
From Mar 2007 - Jul 2011, 11289 patients were screened (113 centers- 9 countries), of which 6694 (59%) were enrolled. Enrolled patients had undergone successful determination of their genomic risk G (with MammaPrint) and clinical risk C (based on a modified version Adjuvant! Online). Patients are evaluated as low clinical risk, if their 10-year disease specific survival (without CT or endocrine therapy (ET), as estimated by Adjuvant! Online, is greater than 88% for ER-positive patients, and greater than 92% for ER-negative patients. Patients characterized as low-risk in both assessments were spared from CT and those characterized as high-risk, CT was advised. Discordant ones were randomized to treatment based on either the C or G result. Additionally patients that were assigned to CT (either randomly or based on high-risk by both assessments) were proposed randomization between an anthracycline vs a non-anthracycline (taxane-based) CT regimen & those assigned to ET could be randomized between tamoxifen for 2 years, followed by letrozole for 5 years vs letrozole for 7 years. Primary objective was to demonstrate superiority of the G over the C in selecting patients for adjuvant CT. The CT &ET regimen randomization will not be part of the current presentation. 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 DFS. In the G-low/C-high risk group, patients who were randomized to use the MammaPrint prognosis (no CT), a null hypothesis of a 5-year DMFS of 92% was tested (one-sided at a 97.5% confidence level).

Results
Mean age of enrolled patients was 55 years. 80% were LN-negative & 20% LN-positive. 58% had tumor size between 1 & 2cm, 87% were ER-positive & 9% were HER2 positive. Enrolled patients were categorized in 4 risk groups; G-low/C-low [2743 patients (41%)], G-high/C-low [592 (9%)], G-low/C-high [1550 (23%)] & G-high/C-high [1807 (27%)]. In the G-low/C-high group, 51% of patients were randomized to CT (49% to no CT) & in the G-high/C-low group, 50% to CT (50% to no CT). There was an absolute 14% reduction in adjuvant CT administration when using the G versus C treatment strategy. Primary analysis on the outcome of discordant risk patients that were randomly treated according to either G or C, will be available at time of SABCS 2015.

Conclusion
This logistically complex trial, with a large number of participating sites & real-time genomic testing performed on fresh frozen material, was successfully completed. Study confirmed the previously reported 32% discordance between G/C. The reduction of adjuvant CT administration by 14% is in line with the initial hypothesis of reducing adjuvant CT by 10-20% based on MammaPrint assessment. Outcome results will be presented.