SPECIAL PLENARY SESSION: Results of MINDACT clinical trial

S Delaloge, Gustave Roussy

On behalf of the European Commission-supported TRANSBIG consortium and MINDACT investigators
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

Martine Piccart, Emiel Rutgers, Laura van’t Veer, Leen Slaets, Suzette Delaloge, Giuseppe Viale, Jean Yves Pierga, Peter Vuylsteke, Etienne Brain, Suzan Vrijaldenhoven, Peter Neijenhuis, Bruno Coudert, Tineke Smilde, Miguel Gil, Alastair Thompson, Isabel T. Rubio, Rodolfo Passalaqua, Erika Matos, Urlike Nitz, Mauro Delorenzi, Geraldine Thomas, Theodora Goulioti, Carolyn Straehle, Konstantinos Tryfonidis, Jan Bogaerts & Fatima Cardoso

On behalf of the European Commission supported TRANSBIG consortium and MINDACT investigators

Presented at AACR, April 18, 2016
# Disclosures – S Delaloge

<table>
<thead>
<tr>
<th></th>
<th>Consulting/expert</th>
<th>Conferences/formations</th>
<th>Research grants/clinical trials</th>
<th>Stock options/patents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amgen</td>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Astra Zeneca</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Novartis</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Pfizer</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Puma</td>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Roche</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>
BREAST CANCER

Localized disease
Curable

Generalized disease
Very difficult to cure

« Adjuvant » medical therapies

But risk of:
- overtreatment
- undertreatment
- wrong treatment
- suboptimal treatment

Lung
Liver
Bone
Adjuvant chemotherapy in early breast cancer

Benefit / Risk Balance

Lessons learned from 3 decades of clinical trials

**BENEFIT**

\[ \uparrow \text{Survival (2 to 12\%)} \]

**LONG-TERM RISKS**

- Secondary cancers
- Cardiac toxicity
- Early menopause
- \[ \downarrow \text{Cognitive function} \]

... AND SOCIO-ECONOMIC BURDEN
Low

Intermediate

High

Node –, HER2+ or LVI absent
Node –, HER2+ or LVI present
Node + (1-3) and HER2 -
Node + (1-3) and HER2 +
Node + ≥ 4

G1
T≤2

AGE < 35
G2-3
T>2

ST. GALLEN DEFINITIONS OF RISK

Only 20% of patients!

Most difficult group for CT decision!

Other similar guidelines exist: NCCN, ESMO,…
**Patient Information**

<table>
<thead>
<tr>
<th>Age</th>
<th>50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidity</td>
<td>Average for Age</td>
</tr>
<tr>
<td>ER Status</td>
<td>Positive</td>
</tr>
<tr>
<td>Tumor Grade</td>
<td>Grade 3</td>
</tr>
<tr>
<td>Tumor Size</td>
<td>2.1 - 3.0 cm</td>
</tr>
<tr>
<td>Positive Nodes</td>
<td>0</td>
</tr>
<tr>
<td>Calculate For</td>
<td>Mortality</td>
</tr>
<tr>
<td>10 Year Risk</td>
<td>24</td>
</tr>
</tbody>
</table>

**Adjuvant Therapy Effectiveness**

<table>
<thead>
<tr>
<th>Hormonal Therapy</th>
<th>Overview 98 (Tamoxifen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemo</td>
<td>Overview 98 (CMF-Like)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hormonal Therapy</th>
<th>28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>11</td>
</tr>
<tr>
<td>Combined Therapy</td>
<td>36</td>
</tr>
</tbody>
</table>

**No additional therapy:**

- **72.2 alive in 10 years.**
- **23.5 die of cancer.**
- **4.3 die of other causes.**

---

P. Ravdin
IMPROVED RISK ASSESSMENT OF EARLY BREAST CANCER THROUGH GENE EXPRESSION PROFILING

78 untreated N− primary tumors

44 w/o relapse at 8 y follow-up

34 with a relapse within 5 y

5000 genes

231 genes

295 partially treated N− / N+ tumors

microarray

Gene-expression profile

van ‘t Veer L., Nature 2002; 415 (31): 530-536
B.C. CLINICAL OUTCOME PREDICTION
70-gene profiler outperforms St Gallen criteria
Amsterdam gene-expression prognostic signature
N=78 / 151

Independent validation study on archive material
• Other populations
• Internal + external quality assurance

High powered clinical trial specifically addressing the gene signature’s utility: MINDACT

Levels of evidence for biomarker studies

E.U. GRANT, 6th Framework Programme
Coordination: F. Cardoso, M. Piccart
Important milestones along the development pathway of MINDACT
The development pathway of MINDACT

Two important milestones before the launch of the trial

2004

- TRANSBIG
  Independent validation of the 70-gene (MammaPrint®) signature

2005

- Clinical validity proven

2006

- Analytical validity proven

2007

- MINDACT recruitment

N= 302 pts (no CT)
Median fup: 13y / 92 events
O.S. H.R. High vs Low
MammaPrint® risk = 2.66
(19% absolute survival difference at 10 years)

Buyse, JNCI, 2006

Ach, BMC Genomics, 2007
Hypothesis: the Genomic assay will outperform the Clinical criteria by reducing the prescription of adjuvant chemotherapy WITHOUT IMPAIRING OUTCOME
Why a 92% threshold for 10y OS w/o adjuvant chemotherapy using Adjuvant! Online?

Consensus reached within the TRANSBIG consortium, including EuropaDonna patient advocates

Gain in survival counterbalanced by treatment associated risks

**Predicted OS without chemotherapy**

![Bar chart showing predicted OS for ER- and ER+ patients.]

- **ER-**
  - 92% survival
  - Adj. Endocrine Therapy: 4%
  - Pred. OS: 88%

- **ER+**
  - 92% survival
  - Pred. OS: 92%

**Predicted benefit versus harm of adjuvant CT in this population**

- Adj. CTX + 2% gain
- 2% risk of CHF leukemia
The MINDACT study design

Diagnosis of breast cancer
Screening informed consent

Surgery

Local pathology
(T1-3, 0 to 3 positive nodes, ER status, HER2 status)

Agendia
(frozen tumor sample shipment, RNA extraction, microarray analysis)

Enrollment

Clinical risk (c)
Adjuvant Online!

Genomic risk (g)
70-gene signature or MammaPrint®

Discordant

c-Low/g-Low

R-T

No Chemotherapy

If HR+

Chemotherapy

R-C

R-E

If HR+

c-High/g-High

R-T

No Chemotherapy

R-E

If HR+

c-High/g-Low
The development pathway of MINDACT
Three important milestones after the launch of the trial

- MammaPrint is strongly prognostic in 241 pts with 1-3 N+ (Med Fup ≈ 8y; 53% had CTX)
- HR for distant mets 4.13 (1.72-9.96) 76% vs 91% at 10y DMFS

- Study logistically feasible
- Discordant risk populations: 34%
- > 92% compliance with randomisation

- High concordance between locally and centrally assessed
  ER ≈ 98%
  PgR ≈ 90%
  HER2 ≈ 96%

Breast Canc Res Treat, 2009
EJC, 2011
Annals of Oncology, 2014

MINDACT OPENED TO women with 1-3 N+
MINDACT in line with expectations
MINDACT « clinical » strategy based on local pathology is a solid clinical trial arm
MINDACT recruitment

- 9 European countries
- 112 centers
- EORTC (Sponsor) and
- 6 additional Cooperative Groups
  - BOOG
  - GOIRC
  - NCRI-UK
  - SOLTI
  - UNICANCER
  - WSG
Key eligibility criteria

- Women with histologically proven operable invasive breast cancer (clinical stage T1, T2 or operable T3) & 0-3 positive lymph nodes and of any subtype (post-surgery)

- Mandatory Shipment of tumor tissue (in liquid nitrogen) to Central Lab for 70-gene signature assay (Amsterdam) and central pathology evaluation (Milan)

- A frozen tumor sample should have been taken from the excised primary tumor (a core punch biopsy)

- Confirmation of 70-gene signature performance & clinical risk assessment by Adjuvant! Online (8.0 including HER2 status)

- And 10 ml blood sample plus 1 paraffin block

Max. 56 days

Enrollment & Randomization

EORTC

The future of cancer therapy

BIG

Breast International Group

TRANSBIG
The MINDACT study: Patient screening and enrollment

Diagnosis of BC
Informed consent for screening 70-gene array

N = 11,288

Surgery

Local pathology evaluation

Tissue sample not appropriate for Genomic analysis: 26%
Patient/investigator decision: 20%
Higher nr. of nodes positive: 17%
Inadequate sample: 17%
Ineligible: 10%
Other: 11%

[40% «drop out» rate]

Enrolled N = 6,693

Agendia microarray analysis (frozen sample)
The MINDACT study: Patient enrollment

Enrolled
N = 6,693

Clinical risk (c)
Adjuvant Online!

Genomic risk (g)
70-gene signature or MammaPrint®

- c-Low/g-Low
  - N=2745
  - No Chemotherapy

- c-Low/g-High
  - N=592

- c-High/g-Low
  - N=1,550
  - Chemotherapy

- c-High/g-High
  - N=1,806
  - No Chemotherapy
The primary analysis population

- **Enrolled**
  - N = 6,693

- Clinical risk (c)
  - Adjuvant Online!

- Genomic risk (g)
  - 70-gene signature or MammaPrint®

- c-Low/g-Low
  - N = 2,745
  - No Chemotherapy

- c-Low/g-High
  - N = 592
  - Discordant
  - N = 1550

- c-High/g-High
  - N = 1,806
  - Chemotherapy

- c-High/g-Low
  - N = 644
  - R-T
Primary endpoint: Distant metastasis free survival (DMFS) at 5 years

Null hypothesis: 5-year DMFS rate in PT population = 92%

Alpha: 2.5% (1-sided)

Power: 80% when true 5-year DMFS rate=95%

Primary test:

95% 2-sided Confidence interval (CI) for the 5-year DMFS rate will be compared to 92%

significant if CI exceeds 92%
Primary test

- **Distant metastasis free survival (DMFS)**
  
  Events: distant metastatic recurrences and deaths (for any cause)

- **Timing of primary analysis when two conditions are met:**
  
  - The standard error of DMFS rate at 5 years is 0.01 or less
  
  - At least one third of the patients in the above dataset have been followed for five years.
Patients «as enrolled» and subsequently randomized (if discordant)

Discordant $N = 2,187$

Patients with a corrected risk post-enrollment $\rightarrow$ slightly fewer discordant patients

Concordant $\rightarrow$ Discordant 1.7%
Discordant $\rightarrow$ Concordant 2.3%

$N = 6,693$

= Intention-to-treat populations

= Corrected risk (per protocol) populations
Patient demographics and Compliance with assigned treatment (YES or NO chemotherapy)

A. CONCORDANT RISK GROUPS
B. DISCORDANT RISK GROUPS
The MINDACT study: Patient demographics

\[N = 6,693\]

Median age = 55y
Node - 79%
Node + 21%
T1 tumours 72%
Grade 2 49%
HR positive 88%
HER2+ 10%

Discordant

N=2745
clinical Low/ genomic Low

N=592
clinical Low/ genomic High

N=1550
clinical High/ genomic Low

N=1806
clinical High/ genomic High
MINDACT: patient demographics and compliance with assigned therapy

**Risk group**
- **clinical Low / genomic Low**
  - N = 2745
  - med. age = 55y
  - T size < 2cm: 96%
  - Node negative: 94%
  - Luminal: 96%
  - HER2+: 4%
  - Grade 1 or 2: 98%

**Assigned:**
- NO CHEMOTHERAPY

**Compliance:** 99%

**Received Endocrine therapy:** 79%

**Risk group**
- **clinical High / genomic High**
  - N = 1806
  - med. age = 53y
  - T size > 2cm: 48%
  - Node positive: 26%
  - Luminal: 50%
  - Triple –: 31%
  - HER2+: 19%
  - Grade 3: 76%

**Assigned:**
- CHEMOTHERAPY

**Compliance:** 96%

**Received Endocrine therapy:** 59%

**Received trastuzumab:** 15%
MINDACT: patient demographics and compliance with assigned therapy

**Risk group clinical Low / genomic High**

- N = 592
- med. age = 55y
- T size < 2cm 98%
- Node negative 97%
- Grade 1 or 2 85%
- Luminal 79%
- HER2+ 12%
- [triple – 9%]

**Randomization**
- No chemotherapy
  - Compliance = 88%
  - Received E.T.: 82%
  - Received Trastuzumab: 7%
- Chemotherapy
  - Compliance = 80%

**Risk group clinical High / genomic Low**

- N = 1550
- med. age = 55y
- T size > 2cm 58%
- Node positive 48%
- Grade 3 29%
- Luminal 90%
- HER2+ 8%
- [triple - 1%]

**Randomization**
- No chemotherapy
  - Compliance = 89%
  - Received E.T.: 94%
  - Received Trastuzumab: 5%
- Chemotherapy
  - Compliance = 85%
EFFICACY RESULTS

N = 6,693 patients randomized
The MINDACT population: CT assignment according to a “Clinical” vs a “Genomic” strategy

Whole population N = 6,693

- N=2745
  - clinical Low/
    genomic Low

- Discordant
  - N=592
    - clinical Low/
      genomic High
  - N=1550
    - clinical High/
      genomic Low

- N=1806
  - clinical High/
    genomic High

«Clinical» strategy
CT to 1550 + 1806 = 3,356 pts
= 50 %

«Genomic» strategy
CT to 592 + 1806 = 2,398 pts
= 36 %

14% reduction
Events across the entire MINDACT population
Median follow-up = 5 years

<table>
<thead>
<tr>
<th>DMFS</th>
<th>DFS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Distant relapses</td>
<td>• Distant relapses</td>
<td>• Deaths (all causes)</td>
</tr>
<tr>
<td>• Deaths (all causes)</td>
<td>• Deaths</td>
<td></td>
</tr>
<tr>
<td><strong>N = 362</strong></td>
<td><strong>N = 672</strong></td>
<td><strong>N = 208</strong></td>
</tr>
<tr>
<td><strong>Relapses 73%</strong>&lt;br&gt;<strong>Deaths 27%</strong></td>
<td><strong>Distant relapses 36%</strong>&lt;br&gt;<strong>Locoreg relapses 16%</strong>&lt;br&gt;<strong>2nd prim. 42%</strong>&lt;br&gt;<strong>Deaths 6%</strong></td>
<td><strong>Deaths (all causes)</strong></td>
</tr>
</tbody>
</table>

Outcome results per corrected risks
Randomization outcome: per intent-to-treat
Clinical outcome of the MINDACT population at 5y median follow-up

A) CONCORDANT RISK GROUPS (using corrected risk)

DMFS

% at 5y (95% CI)
cL/gL  97.6 (96.9 – 98.1)
cH/gH  90.6 (89.0 – 92.0)

DFS

% at 5y
92.8 (91.7 – 93.7)

OS

% at 5y
98.4 (97.8 – 98.9)

Clinical outcome of the MINDACT population at 5y median follow-up

B) DISCORDANT RISK GROUPS: PRIMARY TEST

The primary analysis population

Discordant risks

c-Low / g-High

The primary statistical test (DMFS at 5Y)

No change in risk post enrolment and no CT received

N = 644

NEW

c-High / g-Low

RANDOMIZATION

No chemotherapy

N = 748

Null Hypothesis: set at 92%

Observed 5Y DMFS = 94.7%

95% CI ≈ 92.5 – 96.2% excludes 92% !!!
Clinical outcome of the MINDACT population at 5y median follow-up
DMFS in all 4 risk groups

Distant Metastasis Free Survival

% at 5 year
- cL/gL: 97.6 (96.9, 98.1)
- cL/gH: 94.8 (92.4, 96.4)
- cH/gL: 95.1 (93.8, 96.2)
- cH/gH: 90.6 (89.0, 92.0)

Number of patients at risk:
- cL/gL: 2628, 2331, 735
- cL/gH: 550, 484, 136
- cH/gL: 1457, 1317, 311
- cH/gH: 1689, 1462, 395

Corrected risk:
- cL/gL: 33
- cL/gH: 2
- cH/gL: 9
- cH/gH: 11

Discordant risk groups
Clinical outcome of the MINDACT population at 5y median follow-up

Discordant groups: outcome in relation with adjuvant chemotherapy

Yes or NO?
Discordant groups: Impact of adjuvant CT?

Intent-to-treat analysis

Discordant
N=2,187

Reason for exclusion from intent-to-treat population:
- Ineligible: 31 (1.4%)
- Risk Change: 154 (7.0%)
- CT non-compliance: 286 (13%)
- CT unknown: 10 (0.5%)

Per protocol analysis

Discordant
N=1,706

Trial not powered for the comparisons of yes or no chemotherapy
Efficacy: CT vs no CT in discordant risk groups

Intent-to-treat analysis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% at 5 Year(s) (95% CI)</th>
<th>Hazard Ratio (adjusted Cox model) (95% CI)</th>
<th>p-value (adjusted logrank)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>95.9 (94.0, 97.2)</td>
<td>0.78 (0.50, 1.21)</td>
<td>0.267</td>
</tr>
<tr>
<td>no CT</td>
<td>94.4 (92.3, 95.9)</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% at 5 Year(s) (95% CI)</th>
<th>Hazard Ratio (adjusted Cox model) (95% CI)</th>
<th>p-value (adjusted logrank)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>95.8 (92.9, 97.6)</td>
<td>1.17 (0.59, 2.28)</td>
<td>0.657</td>
</tr>
<tr>
<td>no CT</td>
<td>95.0 (91.8, 97.0)</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>
Efficacy: CT vs no CT in discordant risk group c-Low/g-High

Per protocol analysis

<table>
<thead>
<tr>
<th>c-Low/g-High</th>
<th>CT vs no CT per protocol population</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DMFS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CT</strong></td>
<td>Treatment received</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT</td>
</tr>
<tr>
<td></td>
<td>no CT</td>
</tr>
<tr>
<td><strong>DFS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CT</strong></td>
<td>Treatment received</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT</td>
</tr>
<tr>
<td></td>
<td>no CT</td>
</tr>
<tr>
<td><strong>OS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CT</strong></td>
<td>Treatment received</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT</td>
</tr>
<tr>
<td></td>
<td>no CT</td>
</tr>
</tbody>
</table>
## Efficacy: CT vs no CT in discordant risk group c-High/g-Low

**Per protocol analysis**

<table>
<thead>
<tr>
<th>c-High/g-Low</th>
<th>CT vs no CT per protocol population</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DMFS</strong></td>
<td><strong>Treatment received</strong></td>
<td><strong>Patients</strong></td>
<td><strong>Observed Events</strong></td>
<td><strong>% at 5 Year(s) (95% CI)</strong></td>
<td><strong>Hazard Ratio (adjusted Cox model) (95% CI)</strong></td>
</tr>
<tr>
<td>CT</td>
<td>592</td>
<td>22</td>
<td>96.7 (94.7, 98.0)</td>
<td>0.65 (0.38,1.10)</td>
<td>0.106</td>
</tr>
<tr>
<td>no CT</td>
<td>636</td>
<td>37</td>
<td>94.8 (92.6, 96.3)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td><strong>DFS</strong></td>
<td><strong>Treatment received</strong></td>
<td><strong>Patients</strong></td>
<td><strong>Observed Events</strong></td>
<td><strong>% at 5 Year(s) (95% CI)</strong></td>
<td><strong>Hazard Ratio (adjusted Cox model) (95% CI)</strong></td>
</tr>
<tr>
<td>CT</td>
<td>592</td>
<td>39</td>
<td>93.3 (90.7, 95.2)</td>
<td>0.64 (0.43,0.95)</td>
<td>0.026</td>
</tr>
<tr>
<td>no CT</td>
<td>636</td>
<td>66</td>
<td>90.3 (87.6, 92.4)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td><strong>OS</strong></td>
<td><strong>Treatment received</strong></td>
<td><strong>Patients</strong></td>
<td><strong>Observed Events</strong></td>
<td><strong>% at 5 Year(s) (95% CI)</strong></td>
<td><strong>Hazard Ratio (adjusted Cox model) (95% CI)</strong></td>
</tr>
<tr>
<td>CT</td>
<td>592</td>
<td>10</td>
<td>98.8 (97.4, 99.5)</td>
<td>0.63 (0.29,1.37)</td>
<td>0.245</td>
</tr>
<tr>
<td>no CT</td>
<td>636</td>
<td>18</td>
<td>97.3 (95.6, 98.4)</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>
Proposed future clinical use of MammaPrint®

Clinical risk (c) Adjuvant Online!

Genomic risk (g) 70-gene signature or MammaPrint®

- c-Low/g-Low
- c-Low/g-High
- c-High/g-Low
- c-High/g-High

R-T
N=1550

Clinical «Low risk» patients

No proven added value of MammaPrint®

R-T
N=1806

Clinical «High risk» patients

Proven added value of MammaPrint® with a 46%[1550/(1550+1806)] reduction in CT prescription
The MINDACT Trial

• has played a major educational role in Europe, mobilized hundreds of professionals and popularized the concept of biology-driven treatment

• demonstrated that genomics can provide important information in order to treat patients with early breast cancer

• implemented the logistics to collect and freeze tumour materials in a quality-controlled fashion and built an invaluable biobank for future research in B.C (including full gene-array bank).
Conclusions (2)

- Mindact results provide level 1A evidence of the clinical utility of MammaPrint® for assessing the lack of a clinically relevant chemotherapy benefit in the clinically high risk (c-High) population.

- c-High/g-Low patients, including 48% Node positive, had a 5-year DMFS rate in excess of 94%, whether randomized to adjuvant CT or no CT.

- In the entire MINDACT population, the trial confirmed the hypothesis that the «genomic» strategy leads to a 14% reduction in CT prescription versus the «clinical» strategy.

- Among the c-High risk patients, the clinical use of MammaPrint® is associated with a 46% reduction in chemotherapy prescription.
ALL THE MANY MINDACT PATIENTS!

We are most grateful to you for your significant contribution to our research endeavour and for your faith in our work!
Acknowledgements

All National Teams and Participating Cooperative Groups

<table>
<thead>
<tr>
<th>Country</th>
<th>Enrolled pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Netherlands (NKI)</td>
<td>2092</td>
</tr>
<tr>
<td>France (UCBG)</td>
<td>2065</td>
</tr>
<tr>
<td>Germany (WSG)</td>
<td>835</td>
</tr>
<tr>
<td>Belgium (EORTC)</td>
<td>828</td>
</tr>
<tr>
<td>Spain (SOLTI)</td>
<td>546</td>
</tr>
<tr>
<td>Italy (GOIRC)</td>
<td>199</td>
</tr>
<tr>
<td>UK (NCRI-BCG)</td>
<td>66</td>
</tr>
<tr>
<td>Slovenia (IOL)</td>
<td>37</td>
</tr>
<tr>
<td>Switzerland (EORTC)</td>
<td>25</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>6693</strong></td>
</tr>
</tbody>
</table>

L-R, from top: Emiel Rutgers (NL), Suzette Delaloge (FR), Mahasti Saghatrchan (FR), Ulrike Nitz (DE), Isabel T. Rubio (ES), Rodolfo Passalacqua (IT), Alastair Thompson (UK), Erika Matos (SL), Khalil Zaman (CH)
# Acknowledgements - Funding

## Research Grants

<table>
<thead>
<tr>
<th>European Commission Framework Program VI (FP6-LSHC-CT-2004-503426)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Novartis</strong></td>
<td><strong>F. Hoffmann-La Roche</strong></td>
</tr>
<tr>
<td><strong>Sanofi-Aventis</strong></td>
<td><strong>Eli Lilly</strong></td>
</tr>
<tr>
<td><strong>Veridex LLC</strong></td>
<td><strong>Agendia</strong></td>
</tr>
<tr>
<td><strong>the Breast Cancer Research Foundation</strong></td>
<td><strong>EBCC-Breast Cancer Working Group – asbl</strong></td>
</tr>
<tr>
<td><strong>Susan G. Komen for the Cure</strong></td>
<td><strong>Jacqueline Seroussi Memorial Foundation</strong></td>
</tr>
<tr>
<td><strong>Fondation Contre le Cancer / Stichting tegen Kanker</strong> (Belgian Cancer Society)</td>
<td><strong>Cancer Research UK</strong></td>
</tr>
<tr>
<td><strong>KWF Kankerbestrijding</strong> (Dutch Cancer Society)</td>
<td><strong>Association Le cancer du sein, parlons-en!</strong></td>
</tr>
<tr>
<td><strong>Deutsche Krebshilfe</strong> (German Cancer Aid)</td>
<td><strong>Grant Simpson Trust</strong></td>
</tr>
<tr>
<td><strong>Prix Mois du Cancer du Sein</strong></td>
<td><strong>the (U.S.) National Cancer Institute</strong></td>
</tr>
<tr>
<td><strong>NIF Trust</strong></td>
<td><strong>EORTC Charitable Trust</strong></td>
</tr>
<tr>
<td><strong>Brussels Breast Cancer Walk-Run &amp; American Women’s Club of Brussels</strong></td>
<td></td>
</tr>
</tbody>
</table>
Acknowledgements

TRANSBIG Partners
Acknowledgements

And the great many others who contributed to MINDACT:

- The **MINDACT Steering and Executive Committee** members
- **EUROPA Donna** – the European Breast Cancer Coalition, and **ECCO**, the European CanCer Organization
- **BIG-TRANSBIG-MINDACT fellows**: Kim Aalders (NL), Jacques Bines (BR), Philippe Bedard (CA), Sofia Braga (PT), Ivana Bozovic (RS), Carlos Castaneda (PE), Aleksandar Celebic (RS), Camelia Colichi (RO), Carmen Criscitiello (IT), Lissandra Dal Lago (BR/BE), Gaston Demonty (AR/BE), Fei Fei (CN), Michela Lia (IT), Sherene Loi (AU), Stella Mook (NL), Camilo Moulin (BR), Roman Sreseli (GE), Gustavo Werutsky (BR)
- The **headquarters teams** from the EORTC and BIG
- The many **academic medico-scientific institutions / individual scientists** involved over the life of TRANSBIG and MINDACT
- The **entities providing scientific / logistical support**: Adjuvant!Online, Agendia, Fundazione IEO, IBBL, IDDI, Novartis, Roche, Sanofi, SIB