BCIRG 006 Phase III Trial Comparing AC $\rightarrow$ T with AC $\rightarrow$ H and with TCH in the Adjuvant Treatment of HER2-Amplified Early Breast Cancer Patients: Third Planned Efficacy Analysis

- Dr. Buyse has no relevant financial relationships to disclose.
- Dr. Chan has no relevant financial relationships to disclose.
- Dr. Crown has disclosed that he is the recipient of research grants from sanofi-aventis, GSK and Roche. He has also disclosed that he is on the speaker’s bureau for sanofi-aventis, GSK, BMS and Roche.
- Dr. Eiermann has disclosed that he is on the speaker’s bureau for Novartis, Roche, AZ and Sanofi-Aventis. He has also disclosed that he is a consultant for AZ and Sanofi.
- Dr. Falkson has no relevant financial relationships to disclose.
- Dr. Fornander has no relevant financial relationships to disclose.
- Dr. Kiskartalyi has no relevant financial relationships to disclose.
- Dr. Landreau has no relevant financial relationships to disclose.
- Dr. Liu has no relevant financial relationships to disclose.
- Dr. Mackey has disclosed that he is on the speaker’s bureau for Amgen and Roche.
- Dr. Martin has disclosed that he is on the speaker’s bureau for BMS, Sanofi-Aventis, Roche, Pharmamam, Pfizer and Novartis. He has also disclosed that he is a consultant for Sanofi, Lilly, Glaxo and Pfizer.
BCIRG 006 Phase III Trial Comparing AC \( \rightarrow T \) with AC \( \rightarrow TH \) and with TCH in the Adjuvant Treatment of HER2-Amplified Early Breast Cancer Patients: Third Planned Efficacy Analysis

- Dr. Olsen has disclosed that he is an employee of sanofi-aventis.
- Dr. on Behalf of BCIRG006 Investigators has no relevant financial relationships to disclose.
- Dr. Pienkowski has disclosed that he is the recipient of a research grant from Roche. He has also disclosed that he is on the speaker’s bureau for Roche and Sanofi. He has also disclosed that he is a consultant for Roche.
- Dr. Pinter has no relevant financial relationships to disclose.
- Dr. Press has no relevant financial relationships to disclose.
- Dr. Robert has no relevant financial relationships to disclose.
- Dr. Rolski has no relevant financial relationships to disclose.
- Dr. Shifman has no relevant financial relationships to disclose.
- Dr. Slamon has disclosed that he is the recipient of a research grant from Amgen. He has also disclosed that he is on the speaker’s bureau for Genentech and Sanofi-Aventis. He has also disclosed that he is a consultant for Pfizer.
- Dr. Valero has no relevant financial relationships to disclose.
- Dr. Wilson has no relevant financial relationships to disclose.
BCIRG 006
Phase III Trial Comparing
AC\rightarrow T with AC\rightarrow TH and with TCH
in the Adjuvant Treatment of
HER2-Amplified Early Breast Cancer Patients:

Third Planned Efficacy Analysis


Study sponsored by sanofi-aventis
Support from Genentech

BCIRG 006
Slamon D., SABCS 2009
After the presentation, these slides will be available at:

www.sabcs.org
www.cirg.org
The HER2 Alteration

Southern
Northern
Western
IHC


BCIRG 006
Slamon D., SABCS 2009
BCIRG 006 Trial Design

Her 2+ (Central FISH)

N+ or high risk N-

N=3,222

Stratified by Nodes and Hormonal Receptor Status

AC→T

4 x AC
60/600 mg/m²
4 x Docetaxel
100 mg/m²

AC→TH

4 x AC
60/600 mg/m²
4 x Docetaxel
100 mg/m²

TCH

6 x Docetaxel and Carboplatin
75 mg/m²
AUC 6

1 Year Trastuzumab

1 Year Trastuzumab

BCIRG 006
Slamon D., SABCS 2009
Global Project Coordinator

Valerie Bee
BCIRG 006 Endpoints

Primary
- Disease-free Survival

Secondary
- Overall Survival
- Safety
- Pathologic & Molecular Markers
### BCIRG 006 Patient Characteristics

<table>
<thead>
<tr>
<th>Randomized (n=3,222)</th>
<th>AC→T n=1,073</th>
<th>AC→TH n=1,074</th>
<th>TCH n=1,075</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Age &lt; 50 years</td>
<td>52</td>
<td>52</td>
<td>54</td>
</tr>
<tr>
<td>KPS = 100</td>
<td>80</td>
<td>79</td>
<td>80</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>60</td>
<td>63</td>
<td>60</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>68</td>
<td>67</td>
<td>69</td>
</tr>
<tr>
<td>Hormonotherapy</td>
<td>51</td>
<td>51</td>
<td>51</td>
</tr>
</tbody>
</table>

Enrollment: April 2001 to March 2004
## BCIRG 006 Tumor Characteristics

<table>
<thead>
<tr>
<th></th>
<th>AC(\rightarrow)T</th>
<th>AC(\rightarrow)TH</th>
<th>TCH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=1,073</td>
<td>n=1,074</td>
<td>n=1,075</td>
</tr>
<tr>
<td><strong>Number of nodes +</strong></td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>0</td>
<td>29</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>1 – 3</td>
<td>38</td>
<td>38</td>
<td>39</td>
</tr>
<tr>
<td>4 – 10</td>
<td>22</td>
<td>24</td>
<td>23</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>11</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td><strong>Tumor Size (cm)</strong></td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>(\leq 2)</td>
<td>41</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>&gt; 2 and (\leq 5)</td>
<td>53</td>
<td>55</td>
<td>54</td>
</tr>
<tr>
<td>&gt; 5</td>
<td>6</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td><strong>ER and/or PR +</strong></td>
<td>54</td>
<td>54</td>
<td>54</td>
</tr>
</tbody>
</table>
After the trastuzumab efficacy results were announced in April 2005, to date:

- 23 patients (2.1%) of 1,073 randomized to the control arm (AC→T) crossed-over to receive trastuzumab
- leaving 97.9 % of the control arm enrollment intact for subsequent DFS, OS and safety comparisons
Efficacy

BCIRG 006
Slamon D., SABCS 2009
BCIRG 006 DFS Events

First/Second/Third Planned Efficacy Analyses
(cutoff dates 30Jun2005 / 01Nov2006 / 16Oct2009)

- Median follow-up time = 23/36/65 mths
- 322/462/656 DFS Events
  (42% additional events)
  - Breast Cancer Relapse
  - Second Primary Malignancy
  - Death
- 84/185/348 Deaths
  (88% additional deaths)
Initial Disease Free Survival from 1st Analysis – June 2005

Patients Events
- 1073 147 AC->T
- 1074 77 AC->TH HR (AC->TH vs AC->T) = 0.49 [0.37;0.65] P<0.0001
- 1075 98 TCH HR (TCH vs AC->T) = 0.61 [0.47;0.79] P=0.0002

BCIRG 006
Slamon D., SABCS 2009
Current BCIRG 006

Disease Free Survival – 3rd Planned Analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients</th>
<th>Events</th>
<th>HR (95% C.I.)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC-T</td>
<td>1073</td>
<td>257</td>
<td>1 (reference)</td>
<td></td>
</tr>
<tr>
<td>AC-TH</td>
<td>1074</td>
<td>185</td>
<td>0.64 (0.53 - 0.78)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TCH</td>
<td>1075</td>
<td>214</td>
<td>0.75 (0.63 - 0.90)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

BCIRG 006
Slamon D., SABCS 2009
## BCIRG 006 Events by Arm

<table>
<thead>
<tr>
<th></th>
<th>AC→T n=1,073</th>
<th>AC→TH n=1,074</th>
<th>TCH n=1,075</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of DFS events</td>
<td>147/192/257</td>
<td>77/128/185</td>
<td>98/142/214</td>
</tr>
<tr>
<td>at 1st planned analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at 2nd analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at 3rd analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastatic events</td>
<td>113/143/188</td>
<td>52/93/124</td>
<td>67/98/144</td>
</tr>
</tbody>
</table>

P < 0.001

P = 0.002

P = 0.21

---

BCIRG 006
Slamon D., SABCS 2009
# BCIRG 006 Deaths

<table>
<thead>
<tr>
<th></th>
<th>AC→T n=1,073</th>
<th>AC→TH n=1,074</th>
<th>TCH n=1,075</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of deaths from any cause</td>
<td>36/80/141</td>
<td>20/49/94</td>
<td>28/56/113</td>
</tr>
<tr>
<td>at 1st planned analysis</td>
<td>P &lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>at 2nd analysis</td>
<td></td>
<td>P=0.038</td>
<td></td>
</tr>
<tr>
<td>at 3rd analysis</td>
<td></td>
<td></td>
<td>P=0.14</td>
</tr>
<tr>
<td>Breast cancer deaths</td>
<td>33/69/122</td>
<td>19/44/83</td>
<td>21/47/97</td>
</tr>
</tbody>
</table>

Slamon D., SABCS 2009
BCIRG 006
DFS Lymph Node Negative

<table>
<thead>
<tr>
<th>Patients</th>
<th>Events</th>
<th>HR (95% C.I.)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACT</td>
<td>309</td>
<td>46</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>ACTH</td>
<td>310</td>
<td>23</td>
<td>0.47 (0.28 - 0.77)</td>
</tr>
<tr>
<td>TCH</td>
<td>309</td>
<td>32</td>
<td>0.64 (0.41 - 1.01)</td>
</tr>
</tbody>
</table>

% alive and disease-free

Time (months)

Slamon D., SABCS 2009
BCIRG 006
OS Lymph Node Negative

% alive

0 0.4 0.6 0.8 1

Time (months)
0 12 24 36 48 60 72

Patients
AC-T 309
AC-TH 310
TCH 309

Events
12

HR (95% C.I.)
0.56 (0.27 - 1.13)
0.38 (0.17 - 0.87)
1 (reference)

P
0.11
0.02
0.11

BCIRG 006
Slamon D., SABCS 2009
Do Higher Risk HER2-positive Breast Cancers Require Anthracycline-based Rx
BCIRG 006
DFS Lymph Node Positive

% alive and disease-free

| Time (months) | 0  12  24  36  48  60  72 |
|---------------|---------|---------|---------|---------|---------|---------|---------|
| AC-T          | 764     | 211     | 1 (reference) |
| AC-TH         | 764     | 162     | 0.68 (0.56 - 0.84) |
| TCH           | 766     | 182     | 0.78 (0.64 - 0.95) |

P-value

BCIRG 006
Slamon D., SABCS 2009
BCIRG 006
DFS Lymph Node ≥4

% alive and disease-free

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>AC-T</th>
<th>AC-TH</th>
<th>TCH</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>350</td>
<td>350</td>
<td>352</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>72</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patients | Events | HR (95% C.I.) | P |
----------|--------|---------------|---|
350       | 133    | 1 (reference) |   |
350       | 99     | 0.66 (0.51 - 0.86) | 0.002 |
352       | 101    | 0.66 (0.51 - 0.86) | 0.002 |

BCIRG 006
Slamon D., SABCS 2009
General Safety
### BCIRG 006

**Grade 3/4 Non-Hematological toxicity**

<table>
<thead>
<tr>
<th>Condition</th>
<th>AC→T n=1,050</th>
<th>AC→TH n=1,068</th>
<th>TCH n=1,056</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>3.2%</td>
<td>3.3%</td>
<td>1.4%*</td>
</tr>
<tr>
<td>Myalgia</td>
<td>5.2%</td>
<td>5.2%</td>
<td>1.8%*</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7%</td>
<td>7.2%</td>
<td>7.2%</td>
</tr>
<tr>
<td>Hand-foot syndrome</td>
<td>1.9%</td>
<td>1.4%</td>
<td>0.0%*</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>3.5%</td>
<td>2.9%</td>
<td>1.4%*</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.0%</td>
<td>5.6%</td>
<td>5.4%</td>
</tr>
<tr>
<td>Nausea</td>
<td>5.9%</td>
<td>5.7%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6.1%</td>
<td>6.7%</td>
<td>3.5%*</td>
</tr>
<tr>
<td>Irregular menses</td>
<td>27%</td>
<td>24.3%</td>
<td>26.5%</td>
</tr>
</tbody>
</table>

*Yellow=*Statistically significant less events
### BCIRG 006
Specific non-hematological toxicity (all grades)

<table>
<thead>
<tr>
<th></th>
<th>AC→T n=1,050</th>
<th>AC→TH n=1,068</th>
<th>TCH n=1,056</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Neuropathy-sensory</td>
<td>48.6</td>
<td>49.7</td>
<td>36.1*</td>
</tr>
<tr>
<td>Neuropathy-motor</td>
<td>5.2</td>
<td>6.3</td>
<td>4.2*</td>
</tr>
<tr>
<td>Nail changes</td>
<td>49.3</td>
<td>43.6</td>
<td>28.7*</td>
</tr>
<tr>
<td>Myalgia</td>
<td>52.8</td>
<td>55.5</td>
<td>38.6*</td>
</tr>
<tr>
<td>Renal failure</td>
<td>0.0</td>
<td>0.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Creatinine Grade 3/4</td>
<td>0.6</td>
<td>0.3</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Yellow=*Statistically significant less events

BCIRG 006
Slamon D., SABCS 2009
<table>
<thead>
<tr>
<th></th>
<th>AC→T n=1,050 (%)</th>
<th>AC→TH n=1,068 (%)</th>
<th>TCH n=1,056 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>63.5</td>
<td>71.6</td>
<td>66.2*</td>
</tr>
<tr>
<td>Leucopenia</td>
<td>51.9</td>
<td>60.4</td>
<td>48.4*</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>9.3</td>
<td>10.9</td>
<td>9.6</td>
</tr>
<tr>
<td>Neutropenic infection</td>
<td>11.5</td>
<td>12.1</td>
<td>11.2</td>
</tr>
<tr>
<td>Anemia</td>
<td>2.4</td>
<td>3.1*</td>
<td>5.8</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>1.6</td>
<td>2.1*</td>
<td>6.1</td>
</tr>
<tr>
<td>Acute Leukemias: #(%)</td>
<td>6 (0.6)</td>
<td>1 (0.1)</td>
<td>1 (0.1***)</td>
</tr>
</tbody>
</table>

*Statistically significant less events

**B-cell lymphoma developed 24 months after TCH in this pt and represented her ITT DFS event. This acute leukemia occurred 20 months after rx with CHOP for the B cell lymphoma.
Cardiac Safety
# Cardiovascular risk factors

<table>
<thead>
<tr>
<th>Randomized (n=3,222)</th>
<th>AC→T n=1,073</th>
<th>AC→TH n=1,074</th>
<th>TCH n=1,075</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>49 yrs</td>
<td>49 yrs</td>
<td>49 yrs</td>
</tr>
<tr>
<td>Range</td>
<td>(23 - 74 yrs)</td>
<td>(22 - 74 yrs)</td>
<td>(23 - 73 yrs)</td>
</tr>
<tr>
<td><strong>Risk factors (# of patients)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>38</td>
<td>36</td>
<td>28</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>54</td>
<td>47</td>
<td>43</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>20</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Obesity (BMI &gt; 30)</td>
<td>214</td>
<td>242</td>
<td>234</td>
</tr>
<tr>
<td>Hypertension</td>
<td>178</td>
<td>178</td>
<td>190</td>
</tr>
<tr>
<td><strong>Radiotherapy (# of patients)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After chemotherapy</td>
<td>718</td>
<td>723</td>
<td>729</td>
</tr>
<tr>
<td>To left chest</td>
<td>378</td>
<td>349</td>
<td>364</td>
</tr>
</tbody>
</table>

Slamon D., SABCS 2009
BCIRG 006
Cardiac Deaths and CHF as per Independent Review Panel

<table>
<thead>
<tr>
<th></th>
<th>AC→T n=1,050</th>
<th>AC→TH n=1,068</th>
<th>TCH n=1,056</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac related death</td>
<td>0 / 0 / 0</td>
<td>0 / 0 / 0</td>
<td>0 / 0 / 0</td>
</tr>
<tr>
<td>Cardiac left ventricular function (CHF)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 / 4</td>
<td>3 / 4 / 7</td>
<td>17 / 20 / 21</td>
<td>4 / 4 / 4</td>
</tr>
</tbody>
</table>

First planned analysis
Second analysis
**Third analysis**

P = 0.0121
P < 0.001
P = 0.3852

BCIRG 006
Slamon D., SABCS 2009
Patients with >10% relative LVEF decline

<table>
<thead>
<tr>
<th></th>
<th>AC→T n=1,018</th>
<th>AC→TH n=1,042</th>
<th>TCH n=1,031</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>91/102/114</td>
<td>180/189/194</td>
<td>82/89/97</td>
</tr>
<tr>
<td>% of Pts</td>
<td>9/10/11</td>
<td>17/18/19</td>
<td>8/9/9</td>
</tr>
</tbody>
</table>

First interim analysis  
P <0.001  
Second analysis       
P <0.001  
Third analysis        
P = 0.19

Slamon D., SABCS 2009
BCIRG 006
Topo IIa Amplification
HER2 and TOPO IIa in BCIRG 006

2990 of 3222 patients tested

Topo II

N = 2948

Non Co-Amplified

1761 (60%)
143 (5%)

Co-Amplified

1044 (35%)

Nolan et al., 2009
### BCIRG 006

**Disease Free Survival – 3rd Planned Analysis**

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>% alive and disease-free</th>
<th>Patients</th>
<th>Events</th>
<th>HR (95% C.I.)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td>1 (reference)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td>0.64 (0.53 - 0.78)</td>
<td>0.04</td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td>0.75 (0.63 - 0.90)</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>48</td>
<td></td>
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<tr>
<td>60</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>72</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Patients:**
- AC-T: 1073
- AC-TH: 1074
- TCH: 1075

**Events:**
- AC-T: 257
- AC-TH: 185
- TCH: 214
DFS by Arm: Topo IIa Non Co-Amplified

<table>
<thead>
<tr>
<th>Arm</th>
<th>Patients</th>
<th>Events</th>
<th>HR (95% C.I.)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC-T</td>
<td>643</td>
<td>191</td>
<td>1 (reference)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>AC-TH</td>
<td>643</td>
<td>119</td>
<td>0.53 (0.42 - 0.67)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TCH</td>
<td>618</td>
<td>130</td>
<td>0.61 (0.49 - 0.77)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

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DFS by Arm: Co-Amplified for Topo IIa

Patients | Events | HR (95% C.I.) | P
---|---|---|---
AC-T | 328 | 55 | 0.90 (0.62 - 1.32) | 0.60
AC-TH | 357 | 52 | 1.20 (0.85 - 1.71) | 0.30
TCH | 359 | 72 | 1 (reference) | 0.0

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<table>
<thead>
<tr>
<th></th>
<th>AC-TH</th>
<th>TCH</th>
</tr>
</thead>
<tbody>
<tr>
<td>DFS Events</td>
<td>185</td>
<td>214</td>
</tr>
<tr>
<td>Grade 3 / 4 CHF</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>206</td>
<td>218</td>
</tr>
<tr>
<td>Rx-Related Leukemias</td>
<td>7(8)*</td>
<td>0(1)**</td>
</tr>
<tr>
<td></td>
<td>*Only in AC-Rx patients</td>
<td>**Leukemia developed after CHOP Rx</td>
</tr>
<tr>
<td>Sustained LVEF Loss &gt;10%</td>
<td>194</td>
<td>97</td>
</tr>
</tbody>
</table>

*BCIRG 006*
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Conclusions: BCIRG-006

- Trastuzumab provides a similar and significant advantage for both DFS and OS when used with either anthracycline-based (ACTH) or non-anthracycline (TCH) chemotherapy. This advantage is seen in both low and high-risk patients.

- The acute and chronic toxicity profiles of TCH are better than those seen with the ACTH regimen in almost all parameters measured.

- There is no statistical advantage of ACTH over TCH but there is a 29 event numerical advantage in DFS events in the ACTH treatment arm.

- This numeric advantage comes at the cost of 21 CHFs (5X more than in TCH) and to date, there are 8 acute leukemias in BCIRG-006.....all occurring in patients receiving AC as part of their treatment.

- BCIRG-006 demonstrates that the incremental benefit conferred by AC that is known for HER2-positive breast cancers is restricted to TOP2A co-amplified malignancies which constitute a subset (35%) of these cancers.

- This same incremental benefit (found in the TOP2A subset) can also be achieved by trastuzumab used in a non-anthracycline regimen, avoiding the long-term and life-altering toxicities (CHF or acute leukemia) seen with the anthracycline-based regimens.
Acknowledgements

- All participating Patients and Investigators
- IDMC (Chair, S Swain) and Independent Cardiac Panel
- Central laboratories: M Press (USC), G Sauter (Basel)
- IDDI: M Buyse, F Piette
- NBCC: Fran Visco and Carolina Hinestrosa
- CIRG Central Team: L Andersen, V Bee, D Cabaribere, P Drevot, H Fung, T Kiskartalyi, V Landreau, M Lindsay, T Manella, E Mekercke, T Smith, V Wilson

**The Group of 20**
Principal Investigators involved in the study (I)

ARGENTINA
- Fein
- Giacomi
- Martinez / Korbenfeld
- Mickiewicz
- Xynos / Cassanello

AUSTRALIA / NZ
- Abdbi
- Bayliss
- Begbie
- Beith
- Chan
- Chirgwin
- Claringbold
- Clingan
- Craft
- Dalley
- Dewar
- Ganju
- Gauden / Byard
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- Lewis
- Links

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- Cocquyt
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- Mebis / Vanstraelen
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BOSNIA
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- O'Reilly
- Breathnach

ISRAEL
- Barak
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- Fried / Goldberg
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- Kaufman / Weitzen

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- Fried / Goldberg
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- Kaufman / Weitzen
- Rizel

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Principal Investigators involved in the study (II)

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- Safra / Wiegler / Inbar
- Steiner
- Barone
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- Marangolo
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- Klin
- Konuru
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- Lemon
- Limentani
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- Morose
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- Vera

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