Phase III Trial Comparing AC-T with AC-TH and with TCH in the Adjuvant Treatment of HER2 positive Early Breast Cancer Patients: Second Interim Efficacy Analysis


Study sponsored by Sanofi-Aventis
Support from Genentech
After the presentation these slides will be available at:

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

Global Project Coordinator

Valerie Bee
BCIRG 006

Her 2+
(Central FISH)

N+
or high
risk N-

N=3,222

Stratified by Nodes and Hormonal Receptor Status

4 x AC
60/600 mg/m²

4 x Docetaxel
100 mg/m²

4 x AC
60/600 mg/m²

4 x Docetaxel
100 mg/m²

6 x Docetaxel and Carboplatin
75 mg/m² AUC 6

1 Year Trastuzumab

1 Year Trastuzumab

Slamon D., SABCS 2006
Endpoints

Primary
→ Disease-free Survival

Secondary
→ Overall Survival
→ Toxicity
→ Pathologic & Molecular Markers
## Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>AC-T</th>
<th>AC-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>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>63%</td>
<td>61%</td>
<td>63%</td>
</tr>
<tr>
<td>Hormonotherapy</td>
<td>50%</td>
<td>51%</td>
<td>51%</td>
</tr>
</tbody>
</table>

Enrollment: April 2001 to March 2004
## Tumor Characteristics

<table>
<thead>
<tr>
<th></th>
<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>Number of nodes +</strong></td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>0</td>
<td>29</td>
<td>29</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>1 – 3</td>
<td>38</td>
<td>38</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>4 – 10</td>
<td>22</td>
<td>24</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>&gt; 10</td>
<td>11</td>
<td>9</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td><strong>Tumor Size (cm)</strong></td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>≤ 2</td>
<td>41</td>
<td>38</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>&gt; 2 and ≤ 5</td>
<td>53</td>
<td>55</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>&gt; 5</td>
<td>6</td>
<td>7</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td><strong>ER and/or PR +</strong></td>
<td>54</td>
<td>54</td>
<td>54</td>
<td></td>
</tr>
</tbody>
</table>
Crossover

After the trastuzumab efficacy results were announced in April ’05, to date:

✓ A total of 17 patients (1.6%) of 1,073 randomized to the ITT control arm (AC-T) crossed-over to receive trastuzumab

✓ Leaving 98.4% of the control arm enrollment intact for subsequent DFS, OS and safety comparison analyses
First/Second Interim Efficacy Analysis
(cutoff date June 30, 2005/November 01, 2006)

- Median follow-up time = 23/36 months
- 322/462 DFS Events
  - ✓ Breast Cancer Relapse
  - ✓ Second Primary Malignancy
  - ✓ Death
- 84/185 Deaths
Disease Free Survival – 1st interim analysis

Patients Events
- 1073 147 AC->T
- 1074 77 AC->TH
- 1075 98 TCH

HR (AC->TH vs AC->T) = 0.49 [0.37;0.65] P<0.0001
HR (TCH vs AC->T) = 0.61 [0.47;0.79] P=0.0002

BCIRG 006
Slamon D., SABCS 2006
Disease Free Survival - 2nd Interim Analysis

Absolute DFS benefits (from years 2 to 4):
AC→TH vs AC→T: 6%
TCH vs AC→T: 5%

HR (AC→TH vs AC→T) = 0.61 [0.48;0.76]  P<0.0001
HR (TCH vs AC→T) = 0.67 [0.54;0.83]  P=0.0003
### p-values at Interim Efficacy Analyses

<table>
<thead>
<tr>
<th></th>
<th>AC-T</th>
<th>AC-TH</th>
<th>TCH</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=1,073</td>
<td></td>
<td>n=1,074</td>
<td>n=1,075</td>
</tr>
<tr>
<td>Patients with event</td>
<td>147 / 192</td>
<td>77 / 128</td>
<td>98 / 142</td>
</tr>
<tr>
<td>at 1\textsuperscript{st} interim analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at 2\textsuperscript{nd} interim analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR at 1\textsuperscript{st} interim analysis</td>
<td>TCH 0.61</td>
<td>AC-TH 0.49</td>
<td>TCH 0.67</td>
</tr>
<tr>
<td>Metastatic events</td>
<td>113 / 143</td>
<td>52 / 93</td>
<td>67 / 98</td>
</tr>
</tbody>
</table>

BCIRG 006
Slamon D., SABCS 2006
Overall Survival – 2nd Interim Analysis

HR (AC→TH vs AC→T) = 0.59 [0.42;0.85]  P=0.004

HR (TCH vs AC→T) = 0.66 [0.47;0.93]  P=0.017

Patients Events
1073 80 AC→T
1074 49 AC→TH
1075 56 TCH

BCIRG 006
Slamon D., SABCS 2006
## Deaths at Interim Efficacy Analyses

<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</td>
<td>20 / 49</td>
<td>28 / 56</td>
</tr>
<tr>
<td>at 1&lt;sup&gt;st&lt;/sup&gt; interim analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at 2&lt;sup&gt;nd&lt;/sup&gt; interim analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast Cancer Deaths</td>
<td>33 / 69</td>
<td>19 / 44</td>
<td>21 / 47</td>
</tr>
</tbody>
</table>

**p-values:**
- P=0.004
- P=0.017
- P=0.58
DFS Lymph Node Negative
2nd Interim Analysis

% Disease Free

Year from randomization

Patients Events

309 35 AC->T
310 12 AC->TH
309 17 TCH

HR (AC->TH vs AC->T) = 0.32 [0.17;0.62] P=0.0007
HR (TCH vs AC->T) = 0.47 [0.26;0.83] P=0.0096

BCIRG 006
Slamon D., SABCS 2006
Overall Survival Lymph Node Negative

2nd Interim Analysis

% Survival

0.5 0.6 0.7 0.8 0.9 1.0

Patients
Events

- 307 12 AC->T
- 309 2 AC->TH
- 307 5 TCH

HR (AC->TH vs AC->T) = 0.16 [0.04;0.73]  P=0.018
HR (TCH vs AC->T) = 0.42 [0.15;1.2]  P=0.106

Year from randomization

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Slamon D., SABCS 2006
DFS Subpopulations

**AC-TH vs AC-T**

- Subgroup
  - Node neg
  - Node pos
  - HR -
  - HR +
  - Tsize < 2cm
  - Tsize = 2cm

**TCH vs AC-T**

- Subgroup
  - Node neg
  - Node pos
  - HR -
  - HR +
  - Tsize < 2cm
  - Tsize = 2cm
Overall Survival Subpopulations

AC-TH vs AC-T

Subgroup
- Node neg
- Node pos
- HR -
- HR +
- Tsize<2cm
- Tsize=2cm

TCH vs AC-T

Subgroup
- Node neg
- Node pos
- HR -
- HR +
- Tsize<2cm
- Tsize=2cm
Safety Results
## 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>7.0%</td>
<td>7.3%</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>3.6%</td>
<td>3.1%</td>
<td>1.4%*</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.0%</td>
<td>5.7%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Nausea</td>
<td>6.0%</td>
<td>5.7%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6.1%</td>
<td>6.8%</td>
<td>3.4%*</td>
</tr>
<tr>
<td>Irregular menses</td>
<td>27.1%</td>
<td>24.2%</td>
<td>26.4%</td>
</tr>
</tbody>
</table>

Yellow = numerically less events AC-TH or TCH
*Statistically significant AC-TH or TCH
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>Neuropathy-sensory</td>
<td>48.3%</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>49.2%</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>0.2%</td>
</tr>
</tbody>
</table>

Yellow = numerically less events AC-TH or TCH
*Statistically significant AC-TH or TCH
<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>63.3%</td>
<td>71.3%</td>
<td>66.2%*</td>
</tr>
<tr>
<td>Leucopenia</td>
<td>51.5%</td>
<td>60.2%</td>
<td>48.2%*</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>9.1%</td>
<td>11.0%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Neutropenic infection</td>
<td>11.3%</td>
<td>12.0%</td>
<td>11.0%</td>
</tr>
<tr>
<td>Anemia</td>
<td>2.5%</td>
<td>3.1%*</td>
<td>5.8%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>1.0%</td>
<td>1.2%*</td>
<td>5.4%</td>
</tr>
<tr>
<td><strong>Leukemia (%)</strong></td>
<td>3 pts (0.3)</td>
<td>1 pt (0.1)</td>
<td>0 pts</td>
</tr>
</tbody>
</table>

Yellow = numerically less events AC-TH or TCH

*Statistically significant AC-TH or TCH
# Cardiovascular risk factors

<table>
<thead>
<tr>
<th>Risk factors († of Pts)</th>
<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>
<td></td>
</tr>
<tr>
<td>Median</td>
<td></td>
<td>49 yrs</td>
<td>49 yrs</td>
<td>49 yrs</td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td>(23 - 74 yrs)</td>
<td>(22 - 74 yrs)</td>
<td>(23 - 73 yrs)</td>
</tr>
<tr>
<td><strong>Risk factors († of Pts)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>38</td>
<td>36</td>
<td>28</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td></td>
<td>54</td>
<td>47</td>
<td>43</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td></td>
<td>20</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Obesity (BMI ≥ 30)</td>
<td></td>
<td>214</td>
<td>242</td>
<td>234</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td>177</td>
<td>177</td>
<td>190</td>
</tr>
<tr>
<td><strong>Radiotherapy († of Pts)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After chemotherapy</td>
<td></td>
<td>662</td>
<td>656</td>
<td>671</td>
</tr>
<tr>
<td>To left chest</td>
<td></td>
<td>346</td>
<td>320</td>
<td>333</td>
</tr>
</tbody>
</table>
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</td>
<td>0 / 0</td>
<td>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</td>
<td>17 / 20</td>
<td>4 / 4</td>
</tr>
</tbody>
</table>

P = 0.0015

first interim analysis

second interim analysis
Patients with >10% relative LVEF decline

<table>
<thead>
<tr>
<th></th>
<th>AC-T (n = 1012/1014)</th>
<th>AC-TH (n = 1040/1042)</th>
<th>TCH (n = 1029/1030)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>91/102</td>
<td>180/189</td>
<td>82/89</td>
</tr>
<tr>
<td>%</td>
<td>9/10</td>
<td>17.3/18</td>
<td>8/8.6</td>
</tr>
</tbody>
</table>

**first interim analysis**

- AC-T vs. AC-TH: P = 0.002
- AC-TH vs. TCH: P < 0.0001

**second interim analysis**

- AC-T vs. AC-TH: P < 0.0001
- AC-TH vs. TCH: P < 0.0001
- AC-T vs. TCH: P = 0.5

P = 0.5
Mean LVEF - All Observations
1st Interim Analysis

Days

LVEF

AC->T (N=1012)
AC->TH (N=1040)
TCH (N=1029)

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Mean LVEF - All Observations
2nd Interim Analysis

Time since randomization (days)

LVEF points %

AC->T (N=1014)

AC->TH (N=1042)

TCH (N=1030)

BCIRG 006
Slamon D., SABCS 2006
HER2 and TOPO II in BCIRG 006

2120 of 3222 patients analyzed
2990 of 3222 patients analyzed

<table>
<thead>
<tr>
<th>Region</th>
<th>Core region</th>
<th>TOPO II region</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 q 12</td>
<td>1285 pts (60%)</td>
<td>744 pts (35%)</td>
</tr>
<tr>
<td>17 q 21.1</td>
<td>1788 pts (60%)</td>
<td>1057 pts (35%)</td>
</tr>
<tr>
<td>17 q 21.2</td>
<td>91 pts (4%)</td>
<td>145 pts (5%)</td>
</tr>
</tbody>
</table>

N=2120 N=2990

Topo II
Non
Co-Amplified

145 pts (5%)
1057 pts (35%)

first interim analysis
second interim analysis

Normal | Amplified | Deletion
Since 2002, at least 6 studies have been published demonstrating the association between topo II alpha amplification and improved anthracycline response.

<table>
<thead>
<tr>
<th>Study</th>
<th>Yr</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Park et al.</td>
<td>2006</td>
<td>284</td>
</tr>
<tr>
<td>Tanner et al.</td>
<td>2006</td>
<td>525</td>
</tr>
<tr>
<td>Knoop et al.</td>
<td>2005</td>
<td>805</td>
</tr>
<tr>
<td>Park et al.</td>
<td>2003</td>
<td>188</td>
</tr>
<tr>
<td>Coon et al.</td>
<td>2002</td>
<td>35</td>
</tr>
<tr>
<td>Di Leo et al.</td>
<td>2002</td>
<td>354</td>
</tr>
</tbody>
</table>
DFS Topo II Co-Amplified vs Non Co-Amplified All Patients (1st interim analysis)

- Patients: 744 Co-Amplified, 1376 Non Co-amplified
- Events: 57 Co-Amplified, 191 Non Co-amplified

Logrank P<0.001
DFS Topo II Co-Amplified vs Non Co-Amplified
All Patients (2nd interim analysis)

% Disease Free

Year from randomization

Patients Events Topo II

Co-Amplified: 1044 119
Non Co-amplified: 1904 325

HR (Co-Amp vs Non Co-Amp) = 1.44 [1.16;1.78] P<0.001
DFS Co-Amplified Topo II by Arm (1st Interim Analysis)

% Disease Free

Patients | Events | Arm
---|---|---
227 | 23 | AC->T
265 | 13 | AC->TH
252 | 21 | TCH

Logrank P = 0.24
DFS Co-Amplified Topo II by Arm
(2nd Interim Analysis)

% Disease Free

Patients Events
- 328 42 AC->T
- 357 35 AC->TH P=0.336
- 359 42 TCH P=0.648

Year from randomization

P=0.336
P=0.648
DFS Non Co-Amplified Topo II by Arm
(1st Interim Analysis)

Patients: 458, 472, 446
Events: 92, 45, 54

Logrank P = <0.001

Year from randomization
DFS Non Co-Amplified Topo II by Arm

(2nd Interim Analysis)

% Disease Free

0.5 0.6 0.7 0.8 0.9 1.0

Year from randomization

P<0.001

BCIRG 006
Slamon D., SABCS 2006
Therapeutic Index – Most Recent Data

- Difference in DFS, OS and BC death events (ITT) between the 2 Herceptin-containing arms
  - DFS
    - AC-TH - 128
    - TCH – 142
  - OS
    - AC-TH - 49
    - TCH – 56
  - Br Ca Deaths
    - AC-TH - 44
    - TCH – 47

- Difference in critical adverse events between anthracycline and non-anthracycline containing arms
  - Grade 3/4 CHF
    - AC-T - 5
    - AC-TH - 20
    - TCH - 4
  - Leukemia
    - Anthracycline-Based Arms - 4
    - TCH – 0

- Global safety TCH > AC-TH

- In addition, 23 pts with bona fide HER2 amplification who were randomized to the AC-TH arm never got trastuzumab due to unacceptable declines in LVEF before receiving the antibody
Critical Question

✓ Considering:

✓ The recently published data from US Oncology showing a highly statistically significant superiority of docetaxel-cyclophosphamide (TC) over adriamycin-cyclophosphamide (AC) in terms of breast cancer efficacy (Jones, S. JCO 24:5381, 2006).

✓ The 006 update for HER2 positive malignancies shows the difference in number of DFS events and breast cancer deaths in favor of AC-TH, neither of which are statistically significant, is now exceeded by the number of critical adverse events. These include grade III/IV CHF and AC-related leukemia as well as a small AND sustained loss of LVEF for 18% (189 pts) both of which are highly statistically significant...

What is the role of anthracyclines in the adjuvant treatment of breast cancer?
Acknowledgements

- All participating Investigators and Patients
- IDMC (Chair, S Swain) and Independent Cardiac Panel
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- NBCC: Fran Visco and Carolina Hinestrosa
- BCIRG Central Team:
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  L Lallaoui, H Taupin, K Afenjar, P Drevot, L Andersen,
  H Fung, J Mortimer, A Riva, MA Lindsay
Principal Investigators involved in the study (I)

ARGENTINA
Fein
Giacomi
Martinez
Mickiewicz

AUSTRALIA/NZ
Abdbi
Begbie
Beith
Byard
Chan*
Chirgwin
Clingan
Craft
Dalley
Dewar
Ganju
Green
Grimes
Harvey
Isaacs
Jameson
Kannourakis
Koczwar
Kotasek
Lewis
Links
Ransom
Richardson

BRAZIL
Beslija
Bosch

EIRELAND
Crown*

FRANCE
Achille
Bonner
e

IRELAND
Crown*
Grogan
Keane
Kennedy*
McCaffrey

ISRAEL
Barak
Ben Baruch
Geffen
Goldberg
Kaufman
Rizel
Steiner

ITALY
Barone
Bonetti
Gamucci
Gasparini
Geminiani
Iaffaioli
Marangolo
Nardi
Pollera
Ravaloli

ARGENTINA
Beslija

BELGIUM
Cocquyt
Demol
Dirix
Verhoeven

BOSNIA
Beslija
Bosch

BULGARIA
Basileva

Bulgaria
Tzeka

BOSNIA
Beslija

CZECH REPUBLIC
Petruzela

CYPRUS
Adamou

DENMARK
Bloom

EGYPT
Azim

FINLAND
Kallioniemi

FRANCE
Achille

GREAT BRITAIN
Bjorklund

GREECE
Georgoulas

HONG KONG
Chow

IRELAND
Crown*

INDIA
Advani

ISRAEL
Barak

ITALY
Barone

IRELAND
Crown*

* Highest recruiters

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Principal Investigators involved in the study (II)

**POLAND**  
Borowska  
Karnicka  
**Pawlicki**  
**Pienkowski**  
Wojtkiewicz  
Zaluski  
**ROMANIA**  
Badulescu  
Ghilezan  
Roman  
**RUSSIA**  
Garin  
Gorbunova  
Semiglazov  
**SLOVAKIA**  
Koza  
Spanik  
**SLOVENIA**  
Cufer  
Takac  
**SOUTH AFRICA**  
Moodley  
Pienaar  
Rapoport  
Slabber  
**SOUTH KOREA**  
Bang  
Im  
Kim  
Ro  
**SPAIN**  
Adrover  
Alba Conejo  
Alonso Romero  
Alvarez  
Ales Martinez  
Aranda  
Arqua  
Baena Canada  
Calvo Martinez  
Crespo  
Dominguez  
Garcia Estevez  
Florian Gerico  
Jara  
Margeli  
**Martin**  
Martin Lorente  
Mel Lorenzo  
Olta Ferrando  
Pelegrin  
**SWEDEN**  
Forfander  
**SWITZERLAND**  
Aapro  
**TAIWAN**  
Chao  
**Liu**  
**TUNISIA**  
Mezlini  
Frikha  
**TURKEY**  
Akdener  
Baltali  
**UK**  
Chan  
sherwin  
Wardley  
**URUGUAY**  
Rodriguez  
Krygier  
**USA**  
Abubakr  
Adler  
Appelbaum  
Ansari  
Aren  
Beall  
Berdeaux  
Beattie  
Bianco  
Boros  
Bruksky  
Burris  
Carroll  
Chakrabarti  
Chitneni  
Chowhan  
Chuu  
Cobb  
Dreisbach  
**Falkson**  
Fesen  
Goodman  
Greenwald  
Grosbach  
Hajdenberg  
Houston  
Jhangiani  
Jones  
Justice  
Juturi  
Kalman  
Kennedy  
Kerr  
Kincaid  
Koneky  
Laufman  
Lemon  
Lewis  
Limentani  
Link  
Lower  
Mac Andrew  
Malamud  
Mc Croskey  
McKeen  
Mena  
Mills  
Modiano  
Moore  
Moroose  
Moss  
Nair  
Neel  
Nicholls  
Olopade  
Orlowski  
Osborn  
Page  
Patel  
Patton  
Petruska  
Philip  
Polikoff  
Polikoff (network)  
Posada  
Rahman  
Rangineni  
Reich  
Reiling  
Rinaldi  
**Robert (USO)**  
Rodriguez  
Rubin  
Russell  
Schwatzberg  
Shafter  
**Shiftan**  
Silvermann  
**Slamon**  
Sparano  
Sylvester  
Tang  
Tansino  
Tchekmedyian  
Tezcan  
Touroutouglou  
**Valero**  
Vaughn  
Vogel  
Waintraub  
Waisman  
Walker  
Wallmark  
Yost  
Young  
Yunus  
**VENEZUELA**  
De Joghn  
Vera  

*Highest recruiters*  

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