Triple Negative and HER2+ Breast Cancer Highlights from SABCS 2015

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Texas Oncology
US Oncology
Subtypes of TNBC and targeted therapy selection

No TNBC subtyping approach is yet of proven clinical utility

Basal1
Basal2
Immune Module
Mesenchymal
Mesenchymal Stem-like
Luminal Apocrine

Cell cycle, DNA damage
GFR, glycolysis, p63
B/TCR, cytokines, JAK/STAT
ECM receptors
TGF-β
Rho
Wnt/β-Cat
EMT
Stem cell markers
Luminal CK’s
AR
FOXA1
XBP1

### Exceptional Responders to First-Line Platinum

**Isakoff S et al. J Clin Oncol 2015**

<table>
<thead>
<tr>
<th>Patient</th>
<th>BRCA</th>
<th>Subtype</th>
<th>PIK3CA</th>
<th>p53</th>
<th>p63/p73</th>
<th>OS (months)*</th>
<th>Adjuvant Therapy</th>
<th>Therapy</th>
<th>Best Response</th>
<th>Site of Disease</th>
<th>Therapy After Platinum</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>WT</td>
<td>B</td>
<td>Missense mutation</td>
<td>Missense mutation</td>
<td>&lt; 2</td>
<td>69</td>
<td>None</td>
<td>Cisplatin</td>
<td>CR</td>
<td>Breast, lymph nodes</td>
<td>Surgery, chemotherapy, and radiation</td>
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<tr>
<td>28</td>
<td>WT</td>
<td>N</td>
<td>WT</td>
<td>WT</td>
<td>&gt; 2</td>
<td>58</td>
<td>Anthracycline-taxane</td>
<td>Cisplatin</td>
<td>PR</td>
<td>Lymph nodes</td>
<td>None</td>
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<tr>
<td>45</td>
<td>WT</td>
<td>X</td>
<td>WT</td>
<td>WT</td>
<td>X</td>
<td>48</td>
<td>None</td>
<td>Cisplatin</td>
<td>CR</td>
<td>Lung, breast, lymph nodes</td>
<td>Surgery, chemotherapy, and radiation</td>
</tr>
<tr>
<td>53</td>
<td>WT</td>
<td>B</td>
<td>WT</td>
<td>Missense mutation</td>
<td>&lt; 2</td>
<td>40</td>
<td>Anthracycline-taxane</td>
<td>Cisplatin</td>
<td>PR</td>
<td>Lung</td>
<td>None</td>
</tr>
<tr>
<td>69</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>41</td>
<td>Anthracycline-taxane</td>
<td>Carboplatin</td>
<td>PR</td>
<td>Lung, lymph nodes</td>
<td>Radiation</td>
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<tr>
<td>77</td>
<td>WT</td>
<td>N</td>
<td>WT</td>
<td>Missense mutation</td>
<td>X</td>
<td>34</td>
<td>Anthracycline-taxane</td>
<td>Carboplatin</td>
<td>CR</td>
<td>Lymph nodes</td>
<td>Stereotactic radiosurgery to brain metastasis, chemotherapy</td>
</tr>
</tbody>
</table>

4/34 highly durable ORR 11.7 %  
2/35 highly durable ORR 5.7%  
First-line cisplatin (overall ORR 35%)  
First-line carboplatin (overall ORR 23%)
PFS – BRCA 1/2 status

% patients progression free

- Carboplatin + BRCA1/2 mutated
- Carboplatin + BRCA1/2 not mutated
- Docetaxel + BRCA1/2 mutated
- Docetaxel + BRCA1/2 not mutated

Median PFS:
- C + BRCA 1/2 mutated: 6.8 months (95% CI = 4.4 to 8.1)
- C + BRCA1/2 not mutated: 3.1 months (95% CI = 2.4 to 4.2)
- D + BRCA 1/2 mutated: 4.8 months (95% CI = 2.2 to 7.2)
- D + BRCA1/2 not mutated: 4.6 months (95% CI = 4.2 to 5.5)

Interaction: randomised treatment & BRCA 1/2 status (restricted mean survival): p = 0.03
Design for Patients with TNBC

N=315 patients with centrally confirmed TNBC

cT2, cT3, or cT4a-d, or cT1 and cN+ or pN_{SLN}+

PM

R

PMCb

Paclitaxel (P) 80 mg/m² q1w
Non-pegylated liposomal doxorubicin (M) 20 mg/m² q1w
Carboplatin (Cb) q1w
Dose of AUC 2 was reduced to AUC 1.5 after enrolment of 330 patients
Bevacizumab 15 mg/kg q3w

von Minckwitz et al. Lancet Oncology 2014
# Prediction of Carboplatin Effect on pCR in GeparSixto

<table>
<thead>
<tr>
<th>GROUP</th>
<th>PM (N=146)</th>
<th>PMCbOR (N=149)</th>
<th>HR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factor</td>
<td>34.5</td>
<td>46.0</td>
<td>1.61</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>Δ 11.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of BC/OC</td>
<td>30.8</td>
<td>57.5</td>
<td>3.04</td>
<td>0.02</td>
</tr>
<tr>
<td>without alteration</td>
<td></td>
<td></td>
<td>Δ 26.7</td>
<td></td>
</tr>
<tr>
<td>gBRCA/RAD alteration</td>
<td>43.5</td>
<td>66.7</td>
<td>2.60</td>
<td>0.13</td>
</tr>
<tr>
<td>with/without family history</td>
<td></td>
<td></td>
<td>Δ 23.2</td>
<td></td>
</tr>
</tbody>
</table>

von Minckwitz et al, ASCO 2014
DFS: Effect of Carboplatin in HER2-pos BC

Logrank $p=0.3698$

HR PMCb to PM = 1.33, 95% CI (0.71, 2.48), $p=0.3719$

PM 18/136 events
PMCb 22/137 events

3 yrs DFS 86.7%
3 yrs DFS 83.4%
DFS: Effect of Carboplatin in TNBC

Logrank p=0.0325
HR PMCb to PM = 0.56, 95% CI (0.33, 0.96), p=0.0350

PM 36/157 events
PMCb 21/158 events
DFS by gBRCA Status and Carboplatin in TNBC

Proportion disease-free

- BRCA wt PM 31/121 events
- BRCA wt PMCb 17/120 events
- BRCA mt PM 4/24 events
- BRCA mt PMCb 3/26 events

DFS, months

| BRCA wt PM | 121 | 104 | 88 | 43 | 0 |
| BRCA wt PMCb | 120 | 107 | 95 | 40 | 0 |
| BRCA mt PM | 24 | 23 | 19 | 6 | 0 |
| BRCA mt PMCb | 26 | 25 | 20 | 7 | 0 |
Carboplatin improved DFS substantially (HR=0.56, p=0.035) in patients with TNBC; but showed no effect in patients with HER2-positive BC (HR 1.33, p=0.372; test for interaction p=0.046).

DFS effect of carboplatin was correctly predicted by its extensive effect on pCR, supporting surrogacy of pCR (comparable to NOAH).

Unexpectedly, a strong positive effect of carboplatin on pCR and DFS was observed in patients with wt gBRCA.

Favorable prognosis after pCR was confirmed and is independent of gBRCA status.

In summary, GeparSixto supports the use of carboplatin as part of neoadjuvant treatments in all patients with TNBC.

Bottom line: Can’t extrapolate observed Cb benefit from this trial -where control arm does not have an alkylating agent (no cyclophosphamide)- to US pts who receive preop AC/T for TNBC
CALGB 40603: Schema – Randomized Phase II

Paclitaxel 80 mg/m² wkly x 12, ddAC x 4

Paclitaxel 80 mg/m² wkly x 12, ddAC x 4
Bevacizumab 10 mg/kg q2wks x 9

Paclitaxel 80 mg/m² wkly x 12, ddAC x 4
Carboplatin AUC 6 q3wks x 4

Paclitaxel 80 mg/m² wkly x 12, ddAC x 4
Carboplatin AUC 6 q3wks x 4
Bevacizumab 10 mg/kg q2wks x 9

2 X 2 Randomization

Research biopsies - frozen and fixed

Surgery & XRT*
No Adjuvant Systemic Treatment Planned*

*MD discretion

&Research biopsies if residual tumor

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### CALGB 40603 – pCR Results by factor

<table>
<thead>
<tr>
<th>pCR Breast ypT0/is (%, 95% CI)</th>
<th>Overall</th>
<th>Carbo</th>
<th>No Carbo</th>
<th>OR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>60 (54-66)</td>
<td>46 (40-53)</td>
<td>1.76</td>
<td>0.0018</td>
</tr>
<tr>
<td></td>
<td>53 (49-58)</td>
<td>59 (52-65)</td>
<td>48 (41-54)</td>
<td>1.58</td>
<td>0.0089</td>
</tr>
<tr>
<td>pCR Breast/Axilla ypT0/is ypN0 (%, 95% CI)</td>
<td>Overall</td>
<td>54 (48-61)</td>
<td>41 (35-48)</td>
<td>1.71</td>
<td>0.0029</td>
</tr>
<tr>
<td></td>
<td>48 (43-53)</td>
<td>52 (45-58)</td>
<td>44 (38-51)</td>
<td>1.29</td>
<td>0.0570</td>
</tr>
</tbody>
</table>

Sikov et al, J Clin Oncol 2015

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CALGB 40603 – OS by pCR Breast/Axilla

HR = 0.20 (0.11-0.36), p = <0.0001

- non-pCR 3-yr = 73%
- pCR 3-yr = 93%

Number at Risk
- non-pCR: 238, 210, 170, 99, 33, 4, 0
- pCR: 207, 202, 178, 122, 37, 0, 0

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CALGB 40603 – EFS for carboplatin vs. not

Proportion Event-Free

HR=0.84 (0.58-1.22), p=0.36

No Cb 3-yr=71%
Cb 3-yr=76%

Number at Risk

<table>
<thead>
<tr>
<th></th>
<th>No Cb</th>
<th>Cb</th>
</tr>
</thead>
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<tr>
<td></td>
<td>218</td>
<td>225</td>
</tr>
<tr>
<td>1</td>
<td>185</td>
<td>202</td>
</tr>
<tr>
<td>2</td>
<td>145</td>
<td>162</td>
</tr>
<tr>
<td>3</td>
<td>94</td>
<td>101</td>
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<td>4</td>
<td>31</td>
<td>37</td>
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<tr>
<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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CALGB 40603 – EFS for bevacizumab vs. not

HR=0.80 (0.55-1.17), p=0.25

No B 3-yr=72%
B 3-yr=75%

Number at Risk

<table>
<thead>
<tr>
<th></th>
<th>Years from Study Entry</th>
</tr>
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<tbody>
<tr>
<td>No B</td>
<td>221 189 145 90 32 2 0</td>
</tr>
<tr>
<td>B</td>
<td>222 198 162 105 36 2 0</td>
</tr>
</tbody>
</table>

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Note: a pCR is a pCR – no extra improvement in DFS with pCR obtained with Cb vs not
<table>
<thead>
<tr>
<th>Event type</th>
<th>Overall</th>
<th>Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>A: Control</td>
</tr>
<tr>
<td>EFS Events</td>
<td>109</td>
<td>29 (27%)</td>
</tr>
<tr>
<td>Ipsilateral Inv Br Rec</td>
<td>36</td>
<td>14</td>
</tr>
<tr>
<td>Other LRR</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>Distant Recurrence</td>
<td>80</td>
<td>19</td>
</tr>
<tr>
<td>OS Events</td>
<td>79</td>
<td>20</td>
</tr>
<tr>
<td>Breast Cancer Death</td>
<td>70</td>
<td>17</td>
</tr>
<tr>
<td>Non-BC, non-Rx Death</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Unknown Death</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>
Note: adding RCB1 to pCR did not diminish prognostic power of pCR in TNBC, ie, TNBC pts with RCB1 have excellent prognosis.
CALGB/Alliance 40603: Conclusions

- Results from other completed (GeparSixto) and ongoing (BrighTNeess, NRG-003) studies in the neoadjuvant and adjuvant settings should help to clarify whether the addition of carboplatin benefits patients with early stage TNBC.

- Despite the significantly higher pCR rates seen in CALGB 40603, neither carboplatin nor bevacizumab has yet been shown to improve RFS or OS when administered as part of neoadjuvant therapy in stage II-III TNBC.
NRG-BR003

Node-Positive or High-Risk Node-Negative Triple Negative Breast Cancer

Randomization

ACx4 → Paclitaxel qwk x 12

ACx4 → Paclitaxel qwk x 12 + Carboplatin beginning with WP

AC: 60 mg/m² /600 mg/m² (Std or DD AC); Paclitaxel: 80 mg/m² IV weekly; Carboplatin: N/A; DD AC: dose-dense AC
ADAPT HR-/-HER2-:
Trial Design

Standard chemotherapy (4xEC) recommended after surgery / 12-week biopsy (in case of clinical non-pCR)
Bottom line: 46% pCR rate with just 4 cycles preop nab paclitaxel/carboplatin in TNBC pts is interesting. Await DFS data from this study. May be useful to consider this regimen for TNBC pts who cannot receive anthracycline.
CREATE-X: Trial Design

HER2-
NAC  Surgery  Pathology Non-pCR or node +
       (n=900)

Control: Standard therapy
Standard therapy + Capecitabine

Stratification factors:
ER, Age, NAC, ypN, 5FU and institution

Standard therapy:
HR+: Hormone therapy
HR-: No further systemic treatment

Toi M et al. SABCS 2015
Capecitabine Therapy

Capecitabine (X): 2,500 mg/m²/day, po, day 1-14
Repeat every 3 weeks for 8 cycles

According to the safety interim analysis of the first 50 pts treated with 6 cycles of X, the IDMC recommended extending X to 8 cycles.
Key Inclusion Criteria

- Age: 20-74
- ECOG PS 0 or 1
- Stage I – IIIB
- HER2-negative (IHC 0 or 1 and/or FISH negative)
- Non-pCR and/or node-positive after NAC with anthracycline (A) and taxane (T), A-containing or TC (docetaxel, cyclophosphamide)
- No prior treatment with oral FU
- Adequate organ functions
- No toxicity reactions of grade 2 or higher carried over from NAC
- Written informed consent
## Patients & Tumor Characteristics (1)

<table>
<thead>
<tr>
<th></th>
<th>Capecitabine (N=440)</th>
<th>Control (N=445)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Median (range)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>48 (25-74)</td>
<td>48 (25-74)</td>
</tr>
<tr>
<td><strong>Menopausal status</strong></td>
<td>Pre (%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>261 (59.3)</td>
<td>249 (56.0)</td>
</tr>
<tr>
<td></td>
<td>Post (%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>179 (40.7)</td>
<td>196 (44.0)</td>
</tr>
<tr>
<td><strong>Stage</strong></td>
<td>I / IIA / IIB</td>
<td></td>
</tr>
<tr>
<td></td>
<td>259 (58.9)</td>
<td>276 (62.0)</td>
</tr>
<tr>
<td></td>
<td>IIIA / IIB</td>
<td></td>
</tr>
<tr>
<td></td>
<td>178 (40.5)</td>
<td>167 (37.5)</td>
</tr>
<tr>
<td><strong>ER &amp; PgR</strong></td>
<td>ER(+) or PgR(+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>281 (63.9)</td>
<td>280 (62.9)</td>
</tr>
<tr>
<td></td>
<td>ER(-) &amp; PgR(-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>147 (33.4)</td>
<td>149 (33.5)</td>
</tr>
<tr>
<td><strong>Nodal metastases</strong></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>173 (39.3)</td>
<td>172 (38.7)</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>165 (37.5)</td>
<td>174 (39.1)</td>
</tr>
<tr>
<td></td>
<td>4-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>100 (22.7)</td>
<td>99 (22.2)</td>
</tr>
<tr>
<td><strong>Histological effect grading by NAC</strong></td>
<td>0 / 1a / 1b</td>
<td>0 / 1a / 1b</td>
</tr>
<tr>
<td></td>
<td>248 (56.4)</td>
<td>234 (52.6)</td>
</tr>
<tr>
<td></td>
<td>2 / 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>183 (41.6)</td>
<td>202 (45.4)</td>
</tr>
</tbody>
</table>

*General Rules for Clinical and Pathological Recording of Breast Cancer, from The Japanese Breast Cancer Society*
## Patients & Tumor Characteristics (2)

<table>
<thead>
<tr>
<th></th>
<th>Capecitabine (N=440)</th>
<th>Control (N=445)</th>
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</thead>
<tbody>
<tr>
<td>Neoadjuvant chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A containing*</td>
<td>18 (4.1)</td>
<td>16 (3.6)</td>
</tr>
<tr>
<td>A-T (sequential)*</td>
<td>357 (81.1)</td>
<td>371 (83.4)</td>
</tr>
<tr>
<td>AT (concurrent)*</td>
<td>60 (13.6)</td>
<td>53 (11.9)</td>
</tr>
<tr>
<td>TC*</td>
<td>5 (1.1)</td>
<td>3 (0.7)</td>
</tr>
<tr>
<td>5FU containing regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>260 (59.1)</td>
<td>269 (60.4)</td>
</tr>
<tr>
<td>No</td>
<td>180 (40.9)</td>
<td>176 (39.6)</td>
</tr>
<tr>
<td>Adjuvant endocrine therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes for premenopausal</td>
<td>187 (42.5)</td>
<td>178 (40.0)</td>
</tr>
<tr>
<td>Yes for postmenopausal</td>
<td>108 (24.5)</td>
<td>127 (28.5)</td>
</tr>
<tr>
<td>No</td>
<td>145 (33.0)</td>
<td>140 (31.5)</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>318 (72.3)</td>
<td>327 (73.5)</td>
</tr>
<tr>
<td>No</td>
<td>122 (27.7)</td>
<td>118 (26.5)</td>
</tr>
</tbody>
</table>

*A: Anthracycline containing, T: Taxane (Docetaxel or Paclitaxel), TC: Docetaxel + Cyclophosphamide*
Disease Free Survival

5yr DFS
74.1% Capecitabine
67.7% Control

HR (95% CI) 0.70 (0.53-0.93)
One-sided p=0.00524 < 0.00671

Carcinobine 440 385 359 286 175 34
Non-capecitabine 445 367 329 256 158 19

Time from randomization (year)
Overall Survival

94.0%
89.2%

89.2% Capecitabine
83.9% Control

HR (95%CI) 0.60 (0.40-0.92)

One-sided p<0.01
Exploratory: Biological subtype and RFS

Joensuu H. J Clin Oncol, 2012

ER+ and/or PR+, HER2-

\[ P = 0.591 \]
\[ \text{HR} = 0.91 \]
\[ n = 1009 \]

ER+ and/or PR+, HER2+

\[ P = 0.845 \]
\[ \text{HR} = 1.11 \]
\[ n = 163 \]

ER- and PR-, HER2+

\[ P = 0.786 \]
\[ \text{HR} = 0.91 \]
\[ n = 122 \]

ER- and PR-, HER2-

\[ P = 0.0177 \]
\[ \text{HR} = 0.48 \]
\[ n = 202 \]
BCIRG 006 Overall Survival (10.3 yrs)

<table>
<thead>
<tr>
<th>Treatment</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>203</td>
<td>1 (reference)</td>
<td></td>
</tr>
<tr>
<td>AC-TH</td>
<td>1074</td>
<td>141</td>
<td>0.63 (0.51 - 0.79)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TCH</td>
<td>1075</td>
<td>167</td>
<td>0.76 (0.62 - 0.93)</td>
<td>0.0075</td>
</tr>
</tbody>
</table>

Time (months)
Therapeutic Index – Most Recent 006 Data

<table>
<thead>
<tr>
<th></th>
<th>AC→TH</th>
<th>TCH</th>
</tr>
</thead>
<tbody>
<tr>
<td>DFS Events</td>
<td>269</td>
<td>279</td>
</tr>
<tr>
<td>Grade 3 / 4 CHF</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>290</td>
<td>283</td>
</tr>
<tr>
<td>Rx-Related Leukemias</td>
<td>7(8)*</td>
<td>(0(1)**</td>
</tr>
<tr>
<td>*Only in AC-Rx patients</td>
<td></td>
<td><strong>Leukemia developed after CHOP Rx</strong></td>
</tr>
<tr>
<td>Sustained LVEF Loss &gt;10%</td>
<td>200</td>
<td>97</td>
</tr>
</tbody>
</table>

Bottom line: TCH very similar to AC- TH re: long term efficacy, with better safety
ExteNET: final study design

- HER2+ breast cancer (local)
- Prior adjuvant trastuzumab & chemotherapy
- Completed trastuzumab ≤1 year prior to study entry
- Lymph node positive or non-pCR after neoadjuvant therapy
- ER/PR status known

Primary analysis: invasive DFS (iDFS) in ITT population (n=2840)
- iDFS at 2 years: HR=0.67 (0.50–0.91); p=0.009
  - Hormone receptor-positive (n=1631; 57.4%); HR=0.51; p=0.001
  - Centrally-confirmed HER2-positive 60% (n=1463; 51%); HR=0.51; p=0.002

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3-year iDFS analysis (ITT: n=2840)

Two-sided *P-value = 0.023
HR [95% CI] = 0.74 (0.56–0.96)

No. at risk
Neratinib 1420 1302 1247 1196 1007 783 761 710 600
Placebo 1420 1350 1287 1223 1075 856 822 773 641

* p-value descriptive
3-year iDFS analysis: Hormone receptor status

Hormone receptor-positive

Hormone receptor-negative

No. at risk
Neratinib 816 746 730 682 581 454 445 418 353
Placebo 815 777 743 709 617 494 472 445 397

No. at risk
Neratinib 604 556 537 514 426 329 316 292 247
Placebo 605 573 542 521 458 362 350 328 274

Two-sided *P-value = 0.005
HR (95% CI) = 0.57 (0.39–0.82)

Two-sided *P-value = 0.938
HR (95% CI) = 0.98 (0.67–1.45)

Disease-free survival (%)
40% grade 3 diarrhea – prophylactic loperamide for first 30 days decreases grade 3 diarrhea rate to 8-17% in ongoing trials
**TH3RESA Study Schema**

**Stratification factors:** World region, number of prior regimens for advanced BC, presence of visceral disease

**Co-primary endpoints:** PFS by investigator and OS

**Key secondary endpoints:** ORR by investigator and safety

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*First patient in: Sept, 2011. Study amended: Sept, 2012 following EMILIA 2nd interim OS results to allow patients in the TPC arm to receive T-DM1 after documented PD.

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Bottom line: well tolerated TDM1 that generally doesn’t have treatment-limiting toxicities improves OS. Does TDM1 improve OS following taxane plus pertuzumab and trastuzumab?
ADAPT HER2+/HR+: Trial design

*TStandard chemotherapy recommended after surgery / 12-week biopsy (in case of clinical non-pCR); trastuzumab to be completed, for a total of one year.

Hofmann et al, Trials 2013

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Bottom line: TDM1 -- high pCR rate in ER+ HER2+ BC (not improved with addition of endocrine therapy. Await systemic outcome data from TDM1 adjuvant trials
Conclusions

• Cisplatin and carboplatin highly active in metastatic gBRCA1/2 TNBC. About 10% ExRx first line metTNBC
• No DFS benefit for carboplatin added to standard preop AC/weekly paclitaxel
• Adjuvant capecitabine improved DFS/OS in pts who did not have pCR with preop AC/T (especially TN and node + residual disease)
• Neratinib improves DFS in ER+ HER2+ pts following chemotherapy/trastuzumab
• T-DM1 improves OS in HER2+ MBC and has high single agent pCR rate as preop Rx in HER2+ ER+ breast cancer