(Neo-) Adjuvant systemic therapy in Triple Negative Early Breast Carcinoma

Giuseppe Curigliano, MD, PhD
University of Milano and Istituto Europeo di Oncologia
Milano, Italia
Disclosures

- Board Member : Ellipses
- Consultant: Lilly, Novartis, Seattle Genetics, Roche-Genentech
- Research grants to my Institute : MSD, Astra Zeneca
- Speakers bureau: Pfizer, Lilly, Novartis, Roche-Genentech, Samsung, Celltrion
- Stock ownership: None
Outline

• Triple negative breast cancer
• Neo-Adjuvant treatment in triple negative disease
• Adjuvant treatment in triple negative disease
• Conclusions
Triple negative breast cancer

Immunohistochemistry

- ER and PR <1% nuclear
- HER2 “negative”: IHC 0 or 1+ staining or 2+ IHC staining with negative FISH

Histology

- High grade ductal
Triple negative breast cancer

TNBC: An heterogeneous disease

- Invasive Ductal Carcinoma high grade
- Invasive Lobular Carcinoma high grade, pleomorphic
- High grade neuroendocrine
- Metaplastic, high grade
- Myoepithelial carcinoma
- Medullary
- Apocrine
- Adenoid-cystic
- Metaplastic, low grade

Poor prognosis

Good prognosis
TNBC: An heterogeneous disease

- Invasive Ductal Carcinoma high grade
- Invasive Lobular Carcinoma high grade, pleomorphic
- High grade neuroendocrine
- Metaplastic, high grade
- Myoepithelial carcinoma
- Medullary
- Apocrine
- Adenoid-cystic
- Metaplastic, low grade

Prognosis:
- Poor prognosis
- Good prognosis
Triple negative disease

- PST should be used to reduce the extent of surgery in locally advanced and large operable cancers, in particular when mastectomy is required due to tumour size [I, A]. It should also be considered in all patients with tumours > 2 cm for which ChT is deemed necessary, in particular with triple-negative subtypes [I, B].

- Drugs and drug regimens used in preoperative setting should be selected according to rules identical to those in postoperative setting [I, A]. A sequential regimen of anthracyclines and taxanes is recommended for the vast majority of patients [I, B].
The addition of a platinum compound may be considered in triple-negative tumours and/or in patients with deleterious BRCA1/2 mutations [I, C].

In high-risk, triple-negative patients not achieving pCR after standard neoadjuvant ChT, the addition of 6-8 cycles of capecitabine post-operatively may be considered [I, C].
Neoadjuvant approach

Neoadjuvant approach

Symmans et al. J Clin Oncol 2017

<table>
<thead>
<tr>
<th>RCB Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCB-0 (pCR)</td>
<td>35%</td>
</tr>
<tr>
<td>RCB-1</td>
<td>16%</td>
</tr>
<tr>
<td>RCB-2</td>
<td>33%</td>
</tr>
<tr>
<td>RCB-3</td>
<td>17%</td>
</tr>
</tbody>
</table>
Immune-infiltration and response

Denkert, et al. Lancet Oncol 2018
Immune-infiltration and residual disease


Immune-infiltration and prognosis in untreated patients

5Y: 91%  3Y: 93%
84-96  89-96

5Y: 97%  3Y: 97%
95-100  95-99

5Y: 98%  3Y: 99%
95-100  97-100
Carboplatin in TN

<table>
<thead>
<tr>
<th>Trial</th>
<th>n</th>
<th>Drugs</th>
<th>Population</th>
<th>pCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEICAM</td>
<td>94</td>
<td>EC-D</td>
<td>Basal-like</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EC-D+carbo</td>
<td></td>
<td>30%</td>
</tr>
<tr>
<td>GeparSixto</td>
<td>165</td>
<td>PM/bev</td>
<td>TNBC (subset)</td>
<td>38%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PMCb/bev</td>
<td></td>
<td>59%*</td>
</tr>
<tr>
<td>CALGB 40603</td>
<td>455</td>
<td>T-AC(bev)</td>
<td>TNBC</td>
<td>46%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T/carbo-AC(bev)</td>
<td></td>
<td>60%*</td>
</tr>
<tr>
<td>ADAPT-TN</td>
<td>336</td>
<td>Nab-P/wkly Gem</td>
<td>TNBC</td>
<td>29%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nab-P/wkly Carbo</td>
<td></td>
<td>46%*</td>
</tr>
</tbody>
</table>

Alba, BCRT’12; von Minckwitz, Lancet Oncol’14; Sikov, JCO’14; Gluz, AACC-SABCS’15

Carboplatin augments pCR in TNBC
Carboplatin in TN

Study Objectives

Primary objectives:
- Pathologic complete response (pCR) in breast and ipsilateral axillary lymph nodes

Secondary objectives:
- EFS, OS, and rate of eligibility for breast conservation after therapy

AC, doxorubicin plus cyclophosphamide; Cb, carboplatin; EFS, event free survival; OS, overall survival; P, paclitaxel; V, veliparib

S. Loibl et al. The Lancet Oncology 2018
**Carboplatin in TN**

**Pathologic Complete Response**

ypT0/Tis ypN0

- **Clinical Response Rate**
  - V+Cb+P: 53.2%
  - Cb+P: 57.5%
  - P: 31.0%

- **Minimal Residual Disease**
  - Residual Cancer Burden Class 0 or I
  - V+Cb+P: 68.3%
  - Cb+P: 70.0%
  - P: 47.2%

**Intent to Perform a Breast Conserving Surgery**

- ypT0/Tis ypN0
  - V+Cb+P: 61.6%
  - Cb+P: 44.1%
  - P: 44.1%

- ypT0/Tis ypN0
  - Intent to Perform Breast Conserving Surgery
  - V+Cb+P: 68.3%
  - Cb+P: 70.0%
  - P: 47.2%

Error bars are 95% confidence intervals based on normal approximation. p-values were calculated from Cochran-Mantel-Haenszel test versus Arm A (V+Cb+P).

*Clinical response rate after paclitaxel based treatment on serial MRI assessment*
PARP inhibitors in TN

- PARP inhibitors and "synthetic lethality"
- Current available evidence that this concept is clinically actionable
PARP inhibitors in TN

- N = 17 BRCA1 mut
- N = 3 BRCA2 mut
- 17 TNBC/3HR+
- Clin st I -> III

Talazoparib 1 mg PO x 6 months

Side effects

Mostly hema-toxicity resulting in
- RBC transfusions (8/19)
- dose delays/reductions (9/10)

pCR 53%
95% CI: 32%-73%

Systemic therapy of
physician’s choice

Interim biopsy to predict « resistance » (not done)

- Validated « surrogate endpoint » in TNBC
- In the range of pCR rates seen w/chemo + PARPi in neoadj trials mixing TNBC/BRCA mut (I-SPY, Brightness,...)
- UNIQUE to Talazoparib given its higher trapping potency?

Is any further therapy needed?
If yes, can it be given « full dose »?

Litton JK, Breast NJP, 2018
PARP Inhibitors or cisplatin?

<table>
<thead>
<tr>
<th></th>
<th>Talazoparib</th>
<th>Cisplatin ¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>20</td>
<td>107</td>
</tr>
<tr>
<td>BRCA 1</td>
<td>85%</td>
<td>100%</td>
</tr>
<tr>
<td>BRCA 2</td>
<td>15%</td>
<td>N/A</td>
</tr>
<tr>
<td>Neoadjuvant treatment duration</td>
<td>6 months</td>
<td>75 mg/m2 q21 days, 4 cycles = 3 months</td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td>According to physician’s choice</td>
<td>Doxorubicin + Cyclophosphamide</td>
</tr>
<tr>
<td>Toxicities</td>
<td>Hematological</td>
<td>Emesis, neuropathy, nephrotoxicity</td>
</tr>
<tr>
<td>pCR rates</td>
<td>53%</td>
<td>61%</td>
</tr>
<tr>
<td>Estimated costs of the neoadjuvant treatment</td>
<td>$ 28.000*</td>
<td>$ 240**</td>
</tr>
</tbody>
</table>

(Neo)-Adjuvant Chemo + anti-PDL1 in TNBC

Keynote 522, IMpassion031

A-Brave
Neoadjuvant Chemo + anti-PDL1 in TNBC

KEYNOTE-173 phase 1/2 trial

**Chemotherapy + anti-PD1**

Pathological CR = ypT0 ypN0

Paclitaxel Q1W x12 ± carboplatin Q1W x12 + pembrolizumab Q3W x4 → AC Q3W x4 + pembrolizumab Q3W x4

Cohort A (no platinum)

60%

Cohort B (platinum)

80%

I-SPY 2 trial

**Chemotherapy+/- anti-PD1**

Pathological CR = ypT0/is ypN0

Paclitaxel Q1W x12 + pembrolizumab Q3W x4 → AC Q3W x4

Control (no immunotherapy)

20%

Immunotherapy (no platinum)

60%

AC, doxorubicin + cyclophosphamide; CR, complete response; PD-1, programmed death-1; PD-L1, programmed death-ligand 1; Q1W, every week; Q3W, every 3 weeks; ypT0/Tis ypN0, no invasive residual in breast or nodes - noninvasive breast residuals allowed; ypT0 ypN0, no invasive or noninvasive residual in breast or nodes

Neoadjuvant Chemo + anti-PDL1 in TNBC

GepardoNuevo Trial

Chemotherapy + anti-PDL1

Pathological CR = ypT0 ypN0

Control (no immunotherapy) 44.2%

Immunotherapy 53.4%

Chemotherapy + anti-PDL1

Control (no immunotherapy) 41.4%

Immunotherapy 61%

with window treatment

anti-PD1 for 2/52

Paclitaxel + carboplatin Q1W x12 + durvalumab Q2W x 6 → AC Q2W x4 + durvalumab Q2W x4

Loibl, et al. ASCO 2018;
Pembrolizumab showed antitumor activity and manageable safety in metastatic TNBC, especially the first-line setting.

Chemotherapy is a rational combination partner for anti–PD-1 therapy as it disrupts tumor architecture and may overcome immune exclusion, results in antigen shedding, and induces rapid disease control.

Dual primary endpoints: pCR defined as ypT0/Tis ypN0 and EFS
Pathological Complete Response

Primary Endpoint: ypT0/Tis ypN0
Statistically significant benefit for Pembro + Chemo

Δ 13.6 (5.4–21.8)$^a$
$P=0.00055$

64.8% 51.2%

260/401 103/201

$^a$Estimated treatment difference based on Miettinen & Nurminen method stratified by randomization stratification factors.
Data cutoff date: September 24, 2018.
Pathological Complete Response

**Primary Endpoint: ypT0/Tis ypN0**
Statistically significant benefit for Pembro + Chemo

- **Δ 13.6 (5.4–21.8)**
  - **P = 0.00055**
  - **64.8%** (Pembro + Chemo)
  - **51.2%** (Placebo + Chemo)

**PD-L1 Status**

**By PD-L1 Status**: ypT0/Tis ypN0
Benefit for Pembro + Chemo in both PD-L1–positive and PD-L1–negative

- **Δ 14.2 (5.3–23.1)**
  - **68.9%** (PD-L1–positive)
  - **54.9%** (PD-L1–negative)

- **Δ 18.3 (–3.3–36.8)**
  - **45.3%** (PD-L1–negative)
  - **30.3%**

**By PD-L1 Status**

- **pdT0/Tis pdN0**
- **Benefit for Pembro + Chemo**

Data cutoff date: September 24, 2018.

*Estimated treatment difference based on Miettinen & Nurminen method stratified by randomization stratification factors. The PD-L1 combined positive score was defined as number of PD-L1–positive cells (tumor cells, lymphocytes, and macrophages) divided by total number of tumor cells × 100. PD-L1 positivity was defined as CPS ≥1.*
Event-Free Survival at IA2

Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors.

Data cutoff April 24, 2019.

Event-Free Survival (%)

<table>
<thead>
<tr>
<th>Months</th>
<th>EFS, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
<td>91.3%</td>
</tr>
<tr>
<td>2</td>
<td>85.3%</td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th>Months</th>
<th>No. at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>784</td>
</tr>
<tr>
<td>1</td>
<td>780</td>
</tr>
<tr>
<td>2</td>
<td>765</td>
</tr>
<tr>
<td>3</td>
<td>666</td>
</tr>
<tr>
<td>6</td>
<td>519</td>
</tr>
<tr>
<td>9</td>
<td>376</td>
</tr>
<tr>
<td>12</td>
<td>242</td>
</tr>
<tr>
<td>15</td>
<td>73</td>
</tr>
<tr>
<td>18</td>
<td>2</td>
</tr>
<tr>
<td>21</td>
<td>0</td>
</tr>
</tbody>
</table>

Event-Free Survival (EFS, %) vs. Months

- **Pembro + Chemo**: 7.4% (HR 0.63, 95% CI 0.43-0.9)
- **Placebo + Chemo**: 11.8%

Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors.

Data cutoff April 24, 2019.
Treatment-Related AEs in Neoadjuvant Phase: IA2

<table>
<thead>
<tr>
<th>All Treatment-Related</th>
<th>Pembro + Chemo (N = 781)</th>
<th>Placebo + Chemo (N = 389)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any grade</td>
<td>99.0%</td>
<td>99.7%</td>
</tr>
<tr>
<td>Grade 3-5</td>
<td>76.8%</td>
<td>72.2%</td>
</tr>
<tr>
<td>Led to death</td>
<td>0.3%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.3%&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Led to discontinuation of any drug</td>
<td>24.5%</td>
<td>13.1%</td>
</tr>
</tbody>
</table>

*<sup>a</sup>1 patient from sepsis and multiple organ dysfunction syndrome; 1 patient from pneumonitis. <sup>b</sup>1 patient from septic shock. Data cutoff date: April 24, 2019.*
Treatment-Related AEs in Adjuvant Phase: IA2

<table>
<thead>
<tr>
<th>All Treatment-Related</th>
<th>Pembro + Chemo (N = 547)</th>
<th>Placebo + Chemo (N = 314)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any grade</td>
<td>48.1%</td>
<td>43.0%</td>
</tr>
<tr>
<td>Grade 3-5</td>
<td>5.7%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Led to death</td>
<td>0.2%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
</tr>
<tr>
<td>Led to discontinuation</td>
<td>3.3%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

*1 patient from pulmonary embolism.

Data cutoff date: April 24, 2019.
KEYNOTE-522: IMPLICATIONS AND FUTURE DIRECTIONS

• KEYNOTE-522 is the first prospective, randomized placebo controlled trial of pembrolizumab in early TNBC in the neoadjuvant setting

• Addition of pembrolizumab to platinum-containing neoadjuvant chemotherapy resulted in a statistically significant and clinically meaningful increase in pCR (ypT0/Tis ypN0), from 51.2% with chemotherapy to 64.8% with pembrolizumab plus chemotherapy (P=0.00055)

• Neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab showed a favorable trend for EFS compared with neoadjuvant placebo plus chemotherapy followed by adjuvant placebo

• Safety was consistent with the known profiles of each regimen

• Patients are continuing to be followed to assess survival and safety

• Pembrolizumab plus chemotherapy has been granted Breakthrough Therapy Designation by the U.S. FDA for the neoadjuvant treatment of patients with high-risk, early-stage TNBC
Post-Neoadjuvant setting TN

C. Liedtke JCO, 26, 8, 2008: pp. 1275-1281
Post-Neoadjuvant setting TN

- Preplanned interim analysis of a randomized, open-label phase III study[1]

  **Stratified by ER status, age, neoadjuvant chemotherapy, use of 5-FU, institution, node status**

  Pts 20-74 yrs of age with stage I-IIIB HER2- BC and residual disease (non-pCR, N+) after neoadjuvant chemotherapy* and surgery; ECOG PS 0 or 1; no previous oral fluoropyrimidines (N = 910)†

  - Primary endpoint: DFS
  - Secondary endpoints: OS, time from first day of preoperative chemotherapy to recurrence or death, safety, cost-effectiveness

  Capecitabine 2500 mg/m²/day PO Days 1-14 Q3W for 8 cycles‡
  Hormonal therapy if ER/PgR+ (n = 455)†

  - Wk 24

  Hormonal therapy if ER/PgR+
  No further therapy if ER/PgR- (n = 455)†

  *Anthracycline/taxane, anthracycline containing, or docetaxel/cyclophosphamide.

  †25 pts were removed from treatment (n = 10) and control (n = 15) arms due to failure to meet eligibility criteria.

  ‡IDMC recommended extension to 8 cycles following interim safety analysis of first 50 pts receiving 6 cycles.[2]
Post-Neoadjuvant setting TN
Triple negative BRCA mutated

Figure 1. OlympiA study design

- **Screening**
- **Randomization (1:1)**
  - Olaparib 300 mg bid (12 months’ duration)
  - Matched placebo (12 months’ duration)
- **Invasive disease-free survival assessment** (mammogram/breast MRI 6 months from randomization)
- **Follow-up for local and distant recurrence and survival status**
Triple negative IO

BRAVE Protocol

TNBC → Neoadj Chemo → Surgery

- pCR: 40%
- No pCR: 60%

1. Placebo
2. Radiotherapy
3. Avelumab

Principle Investigator: Pierfranco Conte
Adjuvant therapy in TN

- Sequential anthracycline, cyclophosphamide and taxane-based therapy
- An option ddAC → paclitaxel in high risk
- Alternative regimens
  - Preferred regimen without anthracyclines: TC
  - Preferred regimen without taxanes: AC or CMF
  - Neoadjuvant regimens = adjuvant regimens

St Gallen 2019
Adjuvant therapy in TN: When to start

- 24,843 patients diagnosed with BC stages I to III.
- TTC 91 or more days after surgery experienced worse overall survival and worse breast cancer-specific survival.

Subgroup analysis according to subtype

- Longer TTC caused patients with triple-negative breast cancer to have worse overall survival (HR, 1.53; 95% CI, 1.17-2.00) and worse breast cancer-specific survival (HR, 1.53; 95% CI 1.17-2.07).
Adjuvant therapy in TN: When to start

![Graph showing distant recurrence-free survival over time](graph.png)

**N=687 pts**

<table>
<thead>
<tr>
<th>TTC (days)</th>
<th>Total</th>
<th>Events</th>
<th>12mo</th>
<th>60mo</th>
<th>120mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤30</td>
<td>189</td>
<td>39</td>
<td>97.9%</td>
<td>85.7%</td>
<td>80.2%</td>
</tr>
<tr>
<td>31-60</td>
<td>329</td>
<td>112</td>
<td>94.5%</td>
<td>72.2%</td>
<td>64.9%</td>
</tr>
<tr>
<td>61-90</td>
<td>115</td>
<td>38</td>
<td>93%</td>
<td>68.7%</td>
<td>67.5%</td>
</tr>
<tr>
<td>≥91</td>
<td>54</td>
<td>24</td>
<td>87%</td>
<td>68.4%</td>
<td>58.6%</td>
</tr>
</tbody>
</table>

P <0.001

Morante Z, et al. SABCS 2018
Adjuvant therapy in TN: When to start

N=687 pts

<table>
<thead>
<tr>
<th>TTC (days)</th>
<th>Total</th>
<th>Events</th>
<th>12mo</th>
<th>60mo</th>
<th>120mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤30</td>
<td>189</td>
<td>39</td>
<td>97.9%</td>
<td>85.7%</td>
<td>80.2%</td>
</tr>
<tr>
<td>31-60</td>
<td>329</td>
<td>112</td>
<td>94.5%</td>
<td>72.2%</td>
<td>64.9%</td>
</tr>
<tr>
<td>61-90</td>
<td>115</td>
<td>38</td>
<td>93%</td>
<td>68.7%</td>
<td>67.5%</td>
</tr>
<tr>
<td>≥91</td>
<td>54</td>
<td>24</td>
<td>87%</td>
<td>68.4%</td>
<td>58.6%</td>
</tr>
</tbody>
</table>

Morante Z, et al. SABCS 2018
Adjuvant therapy in triple negative disease

**Early Breast Cancer**

- **ER-negative**
  - **HER2-positive**
    - Ductal
      - ChT¹ + anti-HER2<br>   [I, A]
  - **TNBC**
    - Special histological types², N₁<br>   no other risk factors
      - ChT<br>   [I, A]
      - Observation or ChT<br>   [III, B]

- **ER-positive**
  - **HER2-negative**
    - Luminal A
      - ET<br>   ChT only in selected cases with high-disease burden<br>   [I, A]
      - ET + ChT³<br>   [I, A]
  - **HER2-positive**
    - Luminal B
      - ChT¹ + anti-HER2<br>   + ET<br>   [I, A]

ESMO EBC Guidelines, Cardoso F et al, Annals of Oncology 2019
## Adjuvant therapy in triple negative disease

<table>
<thead>
<tr>
<th>Subtype</th>
<th>TNBC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage 1</strong></td>
<td></td>
</tr>
<tr>
<td>T1a</td>
<td>Chemo-Case by case</td>
</tr>
<tr>
<td>T1b</td>
<td>TC chemo or AC/T</td>
</tr>
<tr>
<td>T1c</td>
<td>AC/T chemo</td>
</tr>
<tr>
<td><strong>Stage 2</strong></td>
<td>Neoadjuvant Preferred</td>
</tr>
<tr>
<td>IIA</td>
<td>AC/T chemo +/- platinum</td>
</tr>
<tr>
<td>IIB (N+)</td>
<td></td>
</tr>
<tr>
<td><strong>Stage 3</strong></td>
<td></td>
</tr>
<tr>
<td>Residual invasive cancer after NST</td>
<td>Capecitabine</td>
</tr>
</tbody>
</table>

Subtype TNBC

- **Subtype TNBC**
- **Stage 1 T1a Chemo-Case by case**
- **Stage 2 IIA Neoadjuvant Preferred**
- **Stage 3 Residual invasive cancer after NST**
- **Neoadjuvant Preferred**
- **AC/T chemo +/- platinum**
- **Capecitabine**
## Considerations in triple negative breast cancer

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Opinion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platinum routine in neo-adjuvant Rx</td>
<td>No according to St Gallen 2019 (justifiable but no known EFS advantage)</td>
</tr>
<tr>
<td>Capecitabine in residual disease</td>
<td>An option - Stage II+ who has received anthracycline/taxane-based Rx</td>
</tr>
<tr>
<td></td>
<td>Uncertain in non adequately treated</td>
</tr>
<tr>
<td>Biological subsets to tailor escalating Rx</td>
<td>No</td>
</tr>
<tr>
<td>Immunotherapy/PARPi/anti androgens or other novel strategies</td>
<td>Not off-trial</td>
</tr>
</tbody>
</table>
Considerations in triple negative breast cancer

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Opinion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical low risk subsets can omit chemotherapy</td>
<td>Only in very small, node-negative (T1a pN0)</td>
</tr>
<tr>
<td>Biologic low risk subsets can omit / limit chemotherapy</td>
<td>No</td>
</tr>
<tr>
<td>Neoadjuvant Rx to reduce surgery</td>
<td>No stage I</td>
</tr>
<tr>
<td></td>
<td>Yes stage II+</td>
</tr>
<tr>
<td>Treating to pCR to de-escalate systemic therapy</td>
<td>No</td>
</tr>
<tr>
<td>Anthracyclines may be omitted</td>
<td>No (may consider in low risk)</td>
</tr>
</tbody>
</table>
Conclusions

• Existing clinical trials with carboplatin have not shown statistically valid improvement of EFS or OS

• PARPi role is unknown when platinum compounds are used
  – De-escalation strategy in gBRCA mutations?

• We don’t know how much of a pCR delta is needed to translate into DFS or OS advantage...
Conclusions

• Delayed adjuvant chemotherapy has a big negative impact in eTNBC

• Adjuvant capecitabine for high-risk patients (residual disease after neoadjuvant chemotherapy) should be considered
  – No data after platinum compounds

• Biology-driven clinical trials in residual tumors will be key to optimize new strategies in TNBC
Thank You

Giuseppe Curigliano MD, PhD

giuseppe.curgliano@ieo.it
ESMO BREAST CANCER
Annual Congress

BERLIN GERMANY
7-9 MAY 2020

Save the date!