Optimizing treatment of triple negative breast cancer in the older woman.

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Triple negative BC: occurrence

- Slightly less frequent? Still ~15-18%
- Is TN different in elderly?

![Table 1: Relationship between patient age and tumor histology.](image)
Age and histological subtype (Triple neg)
Prognosis of Triple negative BC

- BETTER DFS in elderly!
- DFS **IDC-NOS** with primary surgery and outcome data (n=308)
  - DFS ↓ with age
  - But use of chemo and RT ↓ with age
    - age <50, 50-69, 70+
      - no chemo in 2/135 25/126 39/44
      - no RT in 14/135 22/126 12/44
  - ⇒ multivariate analysis DFS
    - increasing age +10y: HR 0.68 (0.52-0.89)
    - LN+ HR 2.17 (1.24-3.77)
    - chemo HR 0.28 (0.12-0.67)
    - RT HR 0.39 (0.20-0.73)

Dreyer, ..., Wildiers. SABCS 2010
Cheung K et al. J Clin Oncol 2011; 29:(suppl; abstr 1057).
Adjuvant chemotherapy

• SEER database
  – 70+, chemo vs no chemo
  – In hormone insensitive tumors: OS 15%-28% ↑

In hormone sensitive tumors: less clear (mainly if node negative)

(JCO vol 18 p2750/2757)
Adjuvant chemotherapy

CALGB 49907

Invasive breast cancer
Age ≥65y
ER pos 66%
ER neg 34%

R

6 CMF or 4 AC (n=226)

6 capecitabine (n=307)

DFS

Overall survival

• capecitabine: 2 toxic deaths (2500 mg/m²)
• Significant benefit in OS and DFS (mainly in HR negative)

H.B. Muss et al. (NEJM 360 2055)
Adjuvant chemotherapy

- **Anthracyclines** in elderly:
  - Anthracyclines superior to CMF: no age trend
  - 10-year cardiac failure rate in women 66-70 y *(JCO 25 3308)*
    - 38% if adjuvant anthracyclines; 33% if CMF; 29% if no adj CT

- **Taxanes**
  - US Oncology Research Trial 9735 *(JCO 27 1177)*
    - AC: Doxorubicin 60 mg/m² IV Day 1, Cyclophosphamide 600 mg/m² IV Day 1, Every 21 days X 4 Cycles
    - TC: Docetaxel 75 mg/m² IV Day 1, Cyclophosphamide 600 mg/m² IV Day 1, Every 21 days X 4 Cycles
Adjuvant chemotherapy

DFS ≥65y

A

Disease-Free Survival (proportion)

TC
AC

95% CI: 0.56 to 0.96

P = .033
HR = 0.74

B

Disease-Free Survival (proportion)

< 65 TC
< 65 AC
65 + TC
65 + AC

C

Overall Survival (proportion)

TC
AC

95% CI: 0.50 to 0.97

P = .017
HR = 0.69

D

Overall Survival (proportion)

< 65 TC
< 65 AC
65 + TC
65 + AC

No. at risk
TC
AC

DFS vs AC

TC
AC

≥65y
### Adjuvant chemotherapy

#### Toxicity gr III-IV haematological

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>TC n=506</th>
<th>AC n=501</th>
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<tbody>
<tr>
<td></td>
<td>&lt; 65 (n=428)</td>
<td>≥ 65 (n=78)</td>
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<tr>
<td>Anemia</td>
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<td>&lt;1%</td>
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<tr>
<td>Neutropenia</td>
<td>60%</td>
<td>52%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
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<tr>
<td>Febrile neutropenia</td>
<td>4%</td>
<td>8%</td>
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</table>

#### Toxicity gr III-IV non-haematological

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>TC n=506</th>
<th>AC n=501</th>
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<tbody>
<tr>
<td></td>
<td>&lt; 65 (n=428)</td>
<td>≥ 65 (n=78)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>3%</td>
<td>6%</td>
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<tr>
<td>Fever</td>
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<td>6%</td>
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<tr>
<td>Infection</td>
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<td>6%</td>
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<tr>
<td>Myalgia</td>
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<tr>
<td>Arthralgia</td>
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<td>&lt;1%</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>1%</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2%</td>
<td>5%</td>
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<tr>
<td>Nausea</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1%</td>
<td>0</td>
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</table>
Metastatic BC

- Epirubicine weekly (35 mg/m² 3w/4) or other (liposomal) anthracycline
- Paclitaxel weekly (+/- bevacizumab)
- Capecitabine
- Carboplatin
- Metronomic chemo
- ...
Metronomic chemotherapy (in elderly)

• Phase II (Ann Oncol. 2002 p73-80).
  – MTX 2.5 mg bid 2x/w ; CycloP 50 mg/d
  – 64 pts; 2\textsuperscript{nd} or 3\textsuperscript{rd} line Chemo
  – RR 19.0% ; CBR 32%

• In elderly? (JCO 2006 Bottoni et al)
  – Neoadjuvant letrozole + oral CycloP
  – RR 88% (vs 72% for letrozole alone)
Pts in Leuven with triple neg BC, treated with metronomic CT

• Case 1: 85y
  – Osteoporosis, depression, hip fracture, CVA 2006
  – 2006: surgery for triple neg BC pT2N0
  – 1-2008: lung mets and small brain mets.
    • Initially refusal of any therapy
    • After discussion start metronomic CT
Other Pts in Leuven

- **Case 2: 77y**
  - 1-2008: cT4N3Mx Triple neg BC; Neoadj FEC-taxol weekly -> surgery and RT
  - 2-2010: lung mets -> metronomic CT, **SD after 3 Mo**, **PD after 5 Mo**.

- **Case 3: 81y**
  - 7-2010: triple neg inoperable LABC, metronomic CT, hospitalisation after 5d for confusion, deterioration, discharged after 2w, lost of FUP.

- **Case 4: 83y**
  - 6-2009: Surgery + RT for triple neg BC, pT1bN3a
  - 3-2010: liver and other mets, metronomic CT, hospitalisation for pneumonia after 10d, stop CT
Conclusion Triple neg BC in elderly

• common problem

• Differences with younger pts:
  – More apocrine and lobular tumors
  – Better outcome if appropriately treated

• Adjuvant: Benefit of adjuvant chemotherapy!

• Metastatic: QoL dictates treatment choice