BREAST CANCER IN OLDER WOMEN, WHAT’S THE PROBLEM?

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MILANO
INCIDENCE

Most common shortcut in statistics
“1 in 8 women will develop BC in their lifetime”

Instead of
“If everyone lived beyond the age of 70, 1 in 8 of those women would get or have had BC”
Median age at diagnosis: 62 y
30% occurs >70 y
TUMOR BIOLOGY
> 70y compared to younger

**IHC studies:**
- More ER+
- Less HER2+
- Lower grade

**Intrinsic subtypes (PAM 50)**
- Less Basal-like
- Less Her2-E

**BIOLOGY SLIGHTLY MORE FAVORABLE**

Mol. Oncol 2014 de Kruijf
Oncologist 2014 Jenskins
TREATMENTS FOR STAGE I/II
LESS TREATMENT WITH INCREASING AGE

Loco-regional approach for stage II BC by age

Use of adjuvant CT in ER+ N+ stage I/II BC by age

SEER database 49616 women with stage I/II BC > 67 y
PROGNOSIS

More breast cancer deaths

Undertreatment
• A sizeable proportion of elderly with operable breast cancer die of NON-CANCER-related causes
• Absolute benefit of surgery and adjuvant treatment (chemo/radio)therapy is lower

PROGNOSIS

OVERTREATMENT! if treated identically to younger pts
SYSTEMIC TREATMENTS

ENDOCRINE THERAPY

WHO?

TUMOUR EXTENT
T (tumour size)
N (nodal status)

TUMOUR BIOLOGY
LUMINAL LIKE
TN
HER2 POS

PATIENT PREFERENCE

GENERAL HEALTH STATUS
Geriatric assessment

THERAPY CHOICE
SYSTEMIC TREATMENTS
ENDOCRINE THERAPY

- OS BENEFIT >70 Y
- BENEFIT OF AI VS TAMOXIFEN LARGELY INDEPENDENT OF AGE
- TOLERABILITY

Fig 1: Age-related mortality reduction (%) with adjuvant tamoxifen and polychemotherapy

- Hot flushes
- Thrombosis & embolism
- Uterus cancer
- Gynecological tractus
- Vaginal discharge
- Cataract

TAM
- Neurocognition
- Sexuality

AI
- Arthralgias & myalgias
- Osteoporosis
- Fractures
- Dryness
- Cardiovascular
- Lipid profile

COMPLIANCE is the issue!!!

derived from EBCTG 2005 (n=42000), numbers derived from Lancet Oncol 2007 Wildiers
SYSTEMIC TREATMENTS
CHEMOTHERAPY

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Geriatric assessment
### SYSTEMIC TREATMENTS

**CHEMOTHERAPY**

**ADJUVANT CT**

**ELDERLY SPECIFIC TRIALS IN HER2 neg BREAST CANCER**

<table>
<thead>
<tr>
<th>Study</th>
<th>Study arms</th>
<th>N</th>
<th>Outcome</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>French 08 a50y FUP 7y</td>
<td>Epirub. + Tam</td>
<td>174</td>
<td>DFS better with Epirub (HR 1.934 in multivariate analysis) OS idem</td>
<td>Mild, 97% received 6 cycles</td>
</tr>
<tr>
<td>Tam</td>
<td>164</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CALGB 49907 a50y FUP 2.4y</td>
<td>Capecit.</td>
<td>307</td>
<td>3y RFS 68%</td>
<td>2 R/ related deaths in Capex; but more gr III-IV toxicity with AC/CMF (84 vs 33%)</td>
</tr>
<tr>
<td>4AC or 6CMF</td>
<td>326</td>
<td>3y RFS 85%*</td>
<td>3y OS 91%*</td>
<td></td>
</tr>
<tr>
<td>ELDA 65-79y FUP 3,8y</td>
<td>Weekly docetaxel</td>
<td>147</td>
<td>5y DFS 65% OS idem</td>
<td>Worse QoL for nausea, anorexia, diarrhea, body image, alopecia</td>
</tr>
<tr>
<td>4 or 6 CMF</td>
<td>152</td>
<td>5y DFS 69%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICE GBG32 a60y FUP 5y</td>
<td>Capecit. + ibandronate</td>
<td>677</td>
<td>5y iDFS 78,8% OS 90,1%</td>
<td>More GI and skin toxicity</td>
</tr>
<tr>
<td>ibandronate</td>
<td>681</td>
<td>5y iDFS 75,0% OS 87,6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICE-II GBG52 a60y FUP 2y</td>
<td>6nab-paclit + Capecit.</td>
<td>193</td>
<td>iDFS and OS similar</td>
<td>much more R/ discontinuation (36 vs 7%) and non-haematol gr III-V toxicity (59 vs 19%)</td>
</tr>
<tr>
<td>4FC or 6CMF</td>
<td>198</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**REGIMEN VALIDATED**
- 4 AC OR 6 CMF
- OPTION 4 TC
- CAPECITABINE NO
- SEQUENTIAL REGIMEN NO DATA

**CHALLENGES:**
- Most frequently used regimens have been studied in younger fit population
- Over selection of older patients in clinical trials
- No data for unfit patients and for the oldest old i.e. >80 y
SYSTEMIC TREATMENTS
CHEMOTHERAPY
TOXICITY IN ELDERLY

% HOSPITALISATION FOR CHEMO-RELATED REasons

ANTHRACYCLINES:
• Heart failure clearly increased after anthracyclines
• More haematological and non-haematological toxicity, lower dose intensity

TAXANES REGIMENS higher risk of:
• dose delay, dose reduction, hospitalisation, therapy discontinuation
• haematological toxicity
• non haematological toxicity (fatigue, mucositis loss of appetite)

SHORT TERM MORTALITY
• in trials: CMF 1.3%, anthracyclines 1.5% died during chemo
• SEER 2.9% >65 y early BC died within 1 year
TARGETED TREATMENTS

LACK OF SPECIFIC DATA BUT EVIDENCE OF CLINICAL BENEFIT

• Anti-HER2 treatments

The prevalence of HER2-positive tumors in women aged 70 years and older ranges between 7% and 20%.

The efficacy and safety data on antiHER2 agents in elderly patients are still limited because older patients have been largely underrepresented in clinical trials.

• CDK 4-6 INHIBITORS
TARGETED TREATMENTS anti-HER2
PERTUZUMAB IN ELDERLY CLEOPATRA STUDY

15.7% of patients ≥ 65 y
2% of patients ≥ 75 y

< 65 y
Plac + T + D 12.5 months
Pert + T + D 17.2 months
HR 0.65

≥ 65 y
Plac + T + D 10.4 months
Pert + T + D 21.6 months
HR 0.52

Miles D et al., Breast Cancer Res Treat 2013
## TARGETED TREATMENTS anti-HER2
**PERTUZUMAB IN ELDERLY CLEOPATRA STUDY**

### Table 6 Ten most common grade ≥3 adverse events overall

<table>
<thead>
<tr>
<th></th>
<th>&lt;65 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td>Placebo + trastuzumab + docetaxel (n = 332)</td>
<td>Pertuzumab + trastuzumab + docetaxel (n = 346)</td>
</tr>
<tr>
<td><strong>Total number of patients with at least one grade ≥3 adverse event</strong></td>
<td>241 (72.6)</td>
<td>255 (73.7)</td>
</tr>
<tr>
<td><strong>Blood and lymphatic system disorders</strong></td>
<td>184 (55.4)</td>
<td>210 (60.7)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>156 (47.0)</td>
<td>174 (50.3)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>51 (15.4)</td>
<td>44 (12.7)</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>26 (7.8)</td>
<td>51 (14.7)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>16 (4.8)</td>
<td>23 (6.6)</td>
</tr>
<tr>
<td>Anemia</td>
<td>9 (2.7)</td>
<td>10 (2.9)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9 (2.7)</td>
<td>7 (2.0)</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>6 (1.8)</td>
<td>6 (1.7)</td>
</tr>
<tr>
<td>LVSD</td>
<td>8 (2.4)</td>
<td>4 (1.2)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>4 (1.2)</td>
<td>10 (2.9)</td>
</tr>
<tr>
<td>Granulocytopenia</td>
<td>9 (2.7)</td>
<td>4 (1.2)</td>
</tr>
</tbody>
</table>

*Miles D et al., Breast Cancer Res Treat 2013*
TARGETED TREATMENTS CDK4-6 INHIBITORS
FOCUS ON PALBOCICLIB IN ELDERLY
POOLED ANALYSIS OF PALOMA-1-2 AND 3 DATA

- CLINICALLY SIGNIFICANT IMPROVEMENT IN MEDIAN PFS WAS OBSERVED IN OLDER PATIENTS RECEIVING PALBO + LETROZOLO AND PALBO+ FULVESTRANT

- THE SAFETY PROFILE IN OLDER PATIENTS WAS CONSISTENT WITH PREVIOUS OBSERVATIONS
BALANCE OF GOALS ACCORDING TO AGE

YOUNG PATIENTS
• SOCIAL /FAMILY OBLIGATIONS
• QUANTITY OF LIFE

ELDERLY PATIENTS
• STAYING AT HOME/INDIPENDENCE
• QUANTITY OF LIFE

ONCOLOGY
• THERAPIES AND INNOVATION
• TOXICITY, RESPONSE, SURVIVAL
• FAST MOVING WORLD

GERIATRICS
• SYMPTOMS DIAGNOSIS
• QUALITY OF LIVE i.e. AMOUNT OF LIFE WITH GOOD QoL (cognition, funcional status, nutrition …)
• GLOBAL PORTRAIT OF PATIENTS & CGA
KEY MESSAGES

1. UNDER AND OVERTREATMENT ARE FREQUENT

2. ACCESS TO INNOVATION IS UNBALANCED

3. GERIATRIC PROBLEM ARE MORE FREQUENT THAN USUALLY BELIEVED (impaired G8, >50% functional dependence, >10% cognitive dysfunctions, 20% depression, >40% significant comorbidities, >50% risk of malnutrition, polypharmacy …

4. COMPREHENSIVE GERIATRIC ASSESSMENT CGA brings to clinicians new informations in > 2/3 cases, modified clinical decision in 20-25% cases

5. COMPETING RISK OF MORTALITY call for a certain degree of assessment of life expectancy to balance treatment decision

Caillet J Clin Oncol 2011
Kenis Ann Oncol 2013