Management of BC in specific populations

MANAGEMENT OF BREAST CANCER IN MALES

F. Cardoso, MD
EORTC Secretary General
ESO Breast Cancer Program Coordinator
Director Breast Unit, Champalimauad Cancer Center
Lisbon, Portugal
Multidisciplinary Meeting on Male Breast Cancer: Summary and Research Recommendations


Sept 2008: NCI-sponsored BIG-NABCG meeting
MALE BC: EPIDEMIOLOGY

- Rare disease (less than 1% of all male cancers; ~ 1% of all BC; about 2000 cases/year in US); African countries with high incidence (Uganda 5% and Zambia 15%)

- Literature: mainly of case-control and retrospective studies with small numbers of pts; few prospective data collected. But NO RANDOMIZED DATA! All clinical trials to date closed for lack of accrual...

- Treatment strategies largely extrapolated from female BC
MALE BC: EPIDEMIOLOGY

0.86/100,000 to 1.08/100,000 ($P<0.001$) (26% increase)

FIGURE 2. Male breast carcinoma incidence (with 95% confidence interval) by year of diagnosis.

BC-specific survival

Anderson et al, JCO 2009; 28:232-239

- **Incidence:**
  - U. S. incidence climbed through 2000, now steady
  - Nordic Cancer Registries: Stable rates

- **Mortality:** down by 28% (vs. 52% for women)
Comparison of age at diagnosis for male and female breast cancer: Surveillance, Epidemiology, and End Results registry, 1973 to 2005.

Bimodal distribution for FBC
One peak (+/- 75 y for MaleBC

Korde L A et al. JCO 2010;28:2114-2122
©2010 by American Society of Clinical Oncology
Male Breast Cancer: 5-Year Survival

Observed Survival
(but males have more comorbidities, older at dx, lower life expectancy)

Relative Survival
(adjusts for age, gender, stage at dx, comorbidities)

SEER 1973-1998, N = 2537

MALE BC: RISK FACTORS

• **Klinefelter’s (XXY) Syndrome** (Estimated 50-fold increase risk of BC & higher breast cancer mortality)

• **Age & Race**

• **Radiation exposure** (Study on Japanese atomic bomb survivors showed dose response & overall rate 1.8 vs 0.5 per 100,000 PY)

• **Family history**

• **Obesity**

• **Hormonal factors** (Testicular abnormalities OR = 2.2 (1.5-3.3); Cirrhosis: 3-fold to 4-fold increase in risk; estradiol levels inconclusive data)

• **Previous breast disease** (Previous breast pathology OR = 2.7 (1.7-4.2); Gynecomastia: Meta-analysis showed OR = 6.2 [3.4-11.4])

• **Environmental exposures** (Inconclusive evidence)
• **BRCA1**
  - Mutations reported in male patients; increase in risk (lifetime risk probably around 2%, corresponding to a 11-fold increase in risk)

• **BRCA2**
  Prevalence: 4%-11% affected men have BRCA2 mutations; 40% of Icelandic men with breast cancer have founder mutation (999del5)
  
  *Marker for “at-risk” families (60%-76% breast cancer families with men have BRCA 2 mutations)*
  
  *Men with mutations have 8% lifetime risk of breast cancer corresponding to a 22-fold increase in risk*

**OFFER GENETIC COUNSELING AND TESTING TO ALL MALE BREAST CANCER PATIENTS**

MALE BC: GENETICS

- Genetic counseling and consideration of BRCA testing recommended
- NCCN recommends that men with BRCA 1 or 2 mutations do self-exams and twice yearly clinical exams
- If BRCA+, baseline mammogram and annual mammograms if gynecomastia or glandular breast density on baseline study
- ~6% of male BRCA2 carriers with family history of breast cancer eventually develop breast cancer
- Other genetic associations are weaker and data are limited

MALE BC: TUMOR CHARACTERISTICS

- >90% invasive ductal carcinoma
- Grade I: 12%-20%; Grade II: 54%-58%; Grade III: 17-33%
- More likely ER+ PR+ (90%) (ER+: 75%-92% PgR: 54%-77%)
- Less likely HER2 positive (12%-16%)
- LN +: 52%-60%, 33%-46% 4 or more nodes involved

Males with breast cancer have more advanced cancers; 42% stage III/IV

LATE DIAGNOSIS!

Do we know anything else about the biology of BC in male patients?


2. Maria Grazia Daidone, PhD & Maurizio Callari, PhD, Istituto Nazionale dei Tumori, Milan, Italy

Molecular characterization of male breast cancer by standardized quantitative RT-PCR analysis: First large genomic study of 347 male breast cancers compared to 82,434 female breast cancers. S Shak et al, ASCO 2009, poster

- All ER+ tumor successfully examined in the Genomic Health from June-2004 to Dec-2008
- 347 male and 82,434 female BCs
- Males were older (mean age 63.8 vs 57.4 yrs)
- Standard histopathology was similar, although slightly more male BCs were ductal (83% vs 78%)
Like in female BC, wide variation in gene expression in male BC

The distribution of RS in males and females was similar - RS mean (±SD) 18.1 (±11.2) in males and 19.1 (±10.2) in females (p = NS)

Patterns of expression of the Oncotype DX genes were more similar than different but some differences were notable.
• Mean expression of ER, PR, and SCUBE2 were 0.5 units higher in males.

• Mean expression of the proliferation genes, Ki-67, MYBL2, Survivin, Cyclin B1, and STK15, were 0.5 units higher in males.

• Mean expression of STMY3 was 0.9 units higher in males.

• The level of quantitative ER significantly increased with increasing patient age in females (0.4 units per decade), little increase was observed in males (<0.1 units per decade).

• Conclusions: heterogeneous biology, similar to that observed in female BC. Some differences, which may reflect the differences in hormone biology between males and females, were noted and deserve further study.

S Shak et al, ASCO 2009

BUT

NO OUTCOME DATA.

SO NO DATA ON THE PROGNOSTIC VALUE OF ONCOTYPE DX IN MALE BC PTS
Gene expression profile study comparing breast cancer samples from male and female patients

- 37 ER+ primary tumors from male patients
- 53 ER+ primary tumors from female patients with comparable clinical and patho-biological features
- Gene expression profile using a two-channel cDNA platform (reference design)

<table>
<thead>
<tr>
<th></th>
<th>MBC</th>
<th>FBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range (years)</td>
<td>32–87</td>
<td>45–81</td>
</tr>
<tr>
<td>Median (years)</td>
<td>66</td>
<td>66</td>
</tr>
<tr>
<td>≤50 years</td>
<td>4 (11%)</td>
<td>5 (9%)</td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>33 (89%)</td>
<td>48 (91%)</td>
</tr>
<tr>
<td>Size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range (cm)</td>
<td>1–5</td>
<td>1–7</td>
</tr>
<tr>
<td>Median (cm)</td>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>≤2 cm</td>
<td>12 (32%)</td>
<td>17 (32%)</td>
</tr>
<tr>
<td>&gt;2 cm</td>
<td>25 (68%)</td>
<td>36 (68%)</td>
</tr>
<tr>
<td>ER</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pos</td>
<td>37 (100%)</td>
<td>53 (100%)</td>
</tr>
<tr>
<td>Neg</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>PgR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pos</td>
<td>29 (78%)</td>
<td>41 (77%)</td>
</tr>
<tr>
<td>Neg</td>
<td>8 (22%)</td>
<td>12 (23%)</td>
</tr>
<tr>
<td>Positive lymph nodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3</td>
<td>10 (27%)</td>
<td>15 (28%)</td>
</tr>
<tr>
<td>0–3</td>
<td>27 (73%)</td>
<td>38 (72%)</td>
</tr>
</tbody>
</table>

Callari, Daidone et al. 2010
Gender specific signature

- 920 differentially expressed genes (FDR<1%)

- Functional interpretation by Gene Ontology analysis (TopGo, Alexa et al. 2006)

Callari, Daidone et al. 2010
### Differentially expressed biological functions

<table>
<thead>
<tr>
<th>Biological categories</th>
<th>MBC</th>
<th>FBC</th>
<th>Key genes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OXPHOS and ATP metabolism</strong></td>
<td>↑</td>
<td>↓</td>
<td>Cytochrome C, ATP synthase, Peroxiredoxins</td>
</tr>
<tr>
<td><strong>Redox homeostasis</strong></td>
<td>↑</td>
<td>↓</td>
<td>Ribosomal proteins, Eukaryotic translation initiation factor</td>
</tr>
<tr>
<td><strong>Translation</strong></td>
<td>↑</td>
<td>↓</td>
<td>Tubulin σ/β, Microtubule-associated proteins, ARFs</td>
</tr>
<tr>
<td><strong>Cytoskeleton and cell motility</strong></td>
<td>↑↓</td>
<td>↑</td>
<td>LAMC1, TNC, MMP11, MMP7, TIMP3, SERPINs, FN1, ADAMTSs, CCL25, CXCLs, CXCL10, IL23A, MHC II, LCK, CD3</td>
</tr>
<tr>
<td><strong>ECM composition and remodeling</strong></td>
<td>↑↓</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td><strong>Immune response</strong></td>
<td>↓</td>
<td>↑</td>
<td>ABCC2, ABCC5, SLC2A1, SLC2A3, SLC16A3, FGFR2, ERBB2, MET</td>
</tr>
<tr>
<td><strong>Membrane transport</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC transporters</td>
<td>↓</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td>Solute carrier family</td>
<td>↑↓</td>
<td>↑↓</td>
<td></td>
</tr>
<tr>
<td>Growth factors response and apoptosis</td>
<td>↑↓</td>
<td>↑↓</td>
<td></td>
</tr>
</tbody>
</table>

Genes which are underlined are up-regulated in MBC and rest of the genes are down-regulated in MBC.

### Energy metabolism

Tubulin/microtubule system | target therapy

Tumor microenvironment | association with prognosis

Callari, Daidone et al. 2010
Genes in red were found up-regulated in Male BC compared to FBC, including mTOR.

**EIF4E:** downstream effector of PI3K/AKT/mTOR mediated signals; often overexpressed in solid tumors and specifically promotes translation of cancer associated genes

*Callari, Daidone et al. 2010*
HER-2, PgR and AR in Male BC

Correlation of all genes with ERBB2, PGR and AR separately for MBC and FBC

We assumed the total number of genes correlated with each biomarker might be an index of its biological relevance

<table>
<thead>
<tr>
<th>Correlated clones</th>
<th>Gene</th>
<th>MBC</th>
<th>FBC</th>
<th>Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERBB2</td>
<td>243</td>
<td>2288</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>PGR</td>
<td>159</td>
<td>582</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>AR</td>
<td>441</td>
<td>86</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

Less genes are correlated with HER-2 and PgR in Male BC than FBC

More genes are correlated with AR in Male BC than FBC

Callari, Daidone et al. 2010
Conclusion

- First genome-wide characterization of Male Breast Cancer
- Many cancer related biological functions are differentially expressed between the two genders
- Different tumorigenesis?
- Different response to target therapy?
  - Inhibition of translation targeting EIF4E or mTOR
  - Targeting of tubulin/microtubules (vinca alkaloids, taxanes...)
  - Endocrine therapy
  - Targeting of HER-2 (Trastuzumab, Lapatinib)
- Need for multicenter studies to validate our results and identify a gender specific treatment strategy

( NOTE: ONLY 37 MALE BC PTS)

Callari, Daidone et al. 2010
EARLY BC in MALES:
SUMMARY TREATMENT RECOMMENDATIONS

- **Surgery**: modified radical mastectomy with either an axillary LN dissection or SLNB; discuss oncoplastic surgical techniques
- **Radiation therapy**: limited data but use similar guidelines to women with EBC
- **Chemotherapy**: limited data but use similar guidelines to women with EBC
- **Endocrine therapy**:
  - Tamoxifen is ET of choice
  - efficacy of aromatase inhibitors is not clear; should not be used alone in the adjuvant setting

Sentinel Node Dissection

- Retrospective review of the 78 male pts who underwent SLND at MSKCC 9/96-7/05
- 76 mapped
- 2 (3%) failed, and ALND revealed positive nodes in both
- 51% SLN negative
  - 8% of total had only a palpable non-sentinel node positive
- 49% SLN positive
  - 59% of these were found intraoperatively → immediate ALND
  - 41% of these were found postop → 60% had delayed ALND
- No axillary recurrences at 28 months median follow-up

Courtesy K. Ruddy (Flynn et al., J Am Coll Surg, 2008)
**ADJUVANT AROMATASE INHIBITORS**

- **SEER Pattern of Care study (n=512):**
  - 63% of men with ER+ LN- tumors received hormonal therapy (n=124)
  - 22% received an aromatase inhibitor (n=19)
  - Survival improved with tamoxifen; not with AI

**TAMOXIFEN REMAINS STANDARD OF CARE IN THE ADJUVANT SETTING**

- 257 patients with HR+ disease and adjuvant hormonal therapy
- Tamoxifen (n=207), AI (n=50)
- 18% pts treated with tamoxifen died vs. 32% treated with AI (p=0.007).
- Adjusted HR=1.55 (95% CI 1.13-2.13)

**Courtesy S. Giordano**

Harlan et al, Cancer, 2010;
Eggemann, Breast Cancer Res Treat, 2013
AROMATASE INHIBITORS IN MEN

- Estrogen production in men (80% peripheral aromatization + 20% direct testicular production)

- Animal models: AIs cause increase in testosterone, no change in estradiol

- Healthy male volunteers: Increase in testosterone (58%), decrease in estradiol, but not complete estrogen suppression (50%)

- AIs cause significant increase in LH, FSH
  - Potential feedback loop
  - Case reports of response to combination AI and LNRH analog

Tamoxifen: Different Side Effects in Male Patients?

- Decreased libido
- Erectile dysfunction
- Hot flashes
- Changes in vision
- Cognitive changes

Overall less well tolerated than in female BC pts
20% to 25% discontinue TAM due to side effects
(Importance of education/discussion with pts)

SURVIVORSHIP CARE

• 30-90 fold greater risk of **contralateral breast cancer** than men with no history of breast ca
  – Absolute risk is still <2% in male breast ca pts overall

• **Elevated risk** of melanoma and prostate cancer in all men with breast cancer

• **BRCA2** mutation associated with increased risk of prostate cancer (RR>4), pancreatic cancer (RR>3), gallbladder/bile duct cancer (RR>4), gastric cancer (RR>2), and malignant melanoma (RR>2) (JNCI 1999, 91(15), 1310-6)

• Some male survivors opt for contralateral annual mammogram or mastectomy

• Should continue routine age-appropriate screening for hypercholesterolemia, HTN, colon/prostate cancer

Courtesy K. Ruddy
SPECIFIC ISSUES AND CONCERNS

- Delay in diagnosis
- Shock
- Stigma
- Altered body image
- Lack of support
- Inappropriate information

Courtesy S. Giordano
For **ER+ Male MBC**, which represents the majority of cases, **ET is the preferred option**, unless there is concern or proof of endocrine resistance or rapidly progressive disease needing a fast response. (LoE: Expert opinion) (100%).

For **ER+ Male MBC**, **tamoxifen** is the preferred option (LoE: Expert opinion).
For male patients with MBC who need to receive an AI, a concomitant LHRH agonist or orchiectomy is the preferred option. AI monotherapy may also be considered, with close monitoring of response. Clinical trials are needed in this patient population.

(LoE: Expert opinion) (86%)
Aromatase Inhibitors: Metastatic Male Breast Cancer

- Case reports of activity in metastatic or LABC
- Series of 15 cases
  - 2 (13%) CR; 4 (27%) PR; 2(13%) SD; 7 (47%) PD
  - Median PFS 4.4 months
  - Estradiol levels in 6 pts: all below normal and 4 undetectable (3 PR, 1 SD, 2 PD)
  - One patient had increase in estradiol, LSH, FSH at progression

Fulvestrant: Metastatic Male Breast Cancer

- Series of 5 cases\(^1\) of progressive visceral MBC in males
  - loading dose of 500 mg i.m. day 1, followed by 250 mg i.m. monthly thereafter, until PD
  - 1 PR lasting 12 mos; 2 SD for 22 & 6 mos (in HER2+ pts); 2 PD

- Case report\(^2\) of fulvestrant after TAM in HER2-neg BC with PR

- Case report: 2 cases\(^3\) with HER2-neg, fulvestrant as 1\(^{st}\)-line therapy; 1 PR & 1 SD

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When metastatic BC in males becomes endocrine-unresponsive and/or significantly symptomatic, chemotherapy should be offered following similar guidelines used for female patients (similar agents, doses, regimens, preferably sequential use of monotherapy,...)
Male BC QUALITY OF LIFE Pilot Study

- Online survey of 42 male breast cancer survivors
- Recruited through 3 websites:
  - www.malebreastcancer.org,
  - www.malebreastcancer.ca,
  - www.outoftheshadowofpink.com
- Validated measures: HADS, FACT-B, EPIC Hormonal, EPIC Sexual
- Additional items: demographics, tumor characteristics, genetic counseling, fertility counseling

Ruddy et al., Breast 2013; 22(2):197-9

Courtesy K. Ruddy
Male BC QUALITY OF LIFE Pilot Study: Genetic Testing Results

<table>
<thead>
<tr>
<th>Genetic Testing</th>
<th></th>
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<tbody>
<tr>
<td>Referred for genetic counseling</td>
<td>74%</td>
</tr>
<tr>
<td>Had genetic testing</td>
<td>60%</td>
</tr>
<tr>
<td>Found to carry BRCA mutation</td>
<td>12%</td>
</tr>
</tbody>
</table>

**Fertility Concerns Results**

<table>
<thead>
<tr>
<th>Fertility Issues</th>
<th></th>
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<tbody>
<tr>
<td>Have no biological children</td>
<td>24%</td>
</tr>
<tr>
<td>Desire future biological children</td>
<td>5%</td>
</tr>
<tr>
<td>Told that treatment could impact fertility</td>
<td>7%</td>
</tr>
<tr>
<td>Stored sperm prior to treatment</td>
<td>2%</td>
</tr>
</tbody>
</table>

Ruddy t al., Breast Apr 2013; 22(2):197-9

Courtesy K. Ruddy
Male BC QUALITY OF LIFE Pilot Study: ANXIETY & DEPRESSION

<table>
<thead>
<tr>
<th></th>
<th>HADS Anxiety Scale</th>
<th>HADS Depression Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients responding</td>
<td>38 (90%)</td>
<td>38 (90%)</td>
</tr>
<tr>
<td>Mean (S.D.)</td>
<td>5.6 (3.7)</td>
<td>4.2 (3.9)</td>
</tr>
<tr>
<td>Median score</td>
<td>5.5</td>
<td>3</td>
</tr>
<tr>
<td>Observed range</td>
<td>0 to 14</td>
<td>0 to 15</td>
</tr>
<tr>
<td>Grouped results:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (0-7)</td>
<td>26 (68%)</td>
<td>30 (79%)</td>
</tr>
<tr>
<td>Borderline (8-10)</td>
<td>9 (24%)</td>
<td>6 (16%)</td>
</tr>
<tr>
<td>Abnormal (11-21)</td>
<td>3 (8%)</td>
<td>2 (5%)</td>
</tr>
</tbody>
</table>

Ruddy t al., Breast Apr 2013; 22(2):197-9

Courtesy K. Ruddy
Male breast cancer is a rare disease, accounting for less than 1% of all breast cancers worldwide. According to the American Cancer Society, last year it was estimated that around 1,910 men would be diagnosed with breast cancer in the US, with around 440 deaths, compared with around 192,370 expected new cases and 40,170 deaths among women.

Male breast cancer patients go through a difficult fight with very little support, while having to cope with the additional stigma of having a ‘female disease’. They also suffer from a lack of evidence on how best to manage their disease. Not a single randomised phase III trial has ever been concluded on male breast cancer. As a consequence, management of male breast cancer is mainly driven by extrapolation from its female counterpart.

The Breast International Group and the North American Breast Cancer Group have now joined forces to launch a three-part international research programme for male breast cancer, coordinated by the EORTC. It has kicked off with a meta-analysis of clinical data and a central pathology review of tumour specimens from about 1,700 male breast cancer cases diagnosed in participating institutions over the last 20 years. Part 2 of the programme will involve building a prospective international registry of all male breast cancer cases diagnosed at participating institutions over a two-year period, to collect data on demographics, risk factors, treatment and outcomes. Funding is being sought to finance a central analysis of the biological material collected, with a virtual tumour bank being used in the meantime.

The intention is to proceed to a randomised clinical trial of endocrine therapy, which could be launched as part 3 of this programme. In view of the failure of all previous attempts to run a clinical trial in this setting, a fully committed international effort will be indispensable.

Securing funding for such a non-drug related, purely academic effort has been a daunting process, demonstrating once again the need for a central funding body in Europe. While continuing to look for additional sources of funding, work on the retrospective analysis has already begun thanks to support from the US Breast Cancer Research Foundation.

This research programme could greatly enhance our knowledge of the biology of male breast cancer—an essential first step to guide the development of future therapies. While waiting for the results, a plea is made to all those involved in the design and implementation of breast cancer trials to stop excluding male patients without a good reason. If excluding male patients from endocrine therapy trials may be understandable, excluding them from trials of cytotoxic and biological agents is not. Cancer societies and organisations also need to play their part, by increasing efforts to raise awareness and establish support groups for these patients.

Fatima Cardoso is a medical oncologist from the Jules Bordet Institute in Brussels, Belgium, and is the principal investigator of the International Male Breast Cancer Programme. e-mail: Fatima.cardoso@bordet.be
10085 - Clinical and biological characterization of Male Breast Cancer: an international EORTC, TBCRC, BIG and NABCG intergroup study

Fatima Cardoso (EU) & Sharon Giordano (US)
Study Coordinators
INTERNATIONAL PROGRAM OUTLINE

• **PART 1: RETROSPECTIVE JOINT ANALYSIS** of all Male BC patients diagnosed and treated in the participating centers within the last 20 years, with collection of tumor blocks and analysis of tumor biology

• **PART 2: PROSPECTIVE REGISTRY** of all Male BC cases in 30 ms
  - Simultaneous collection of biological material (tumor and blood) depending on funding
  - Quality of Life sub-study

• **PART 3: Potentially one or several PROSPECTIVE CLINICAL TRIALS**
RETROSPECTIVE JOINT ANALYSIS

• 24 individual sites (11 BE, 1 PL, 7 UK, 4 USA, 1 ES) + BOOG, ICORG, SABO & SAKK have participated as National groups

• Accrual of retrospective part closed on 03/09/2013

• 1822 enrolled patients & 1800 eligible patients

LARGEST SERIES EVER OF MALE BC WITH CLINICAL + BIOLOGICAL DATA

Central Pathology analysis, biomarker evaluation, deeper biological characterization ongoing
SABCS 2014 - Abstract

**Title:** Characterization of male breast cancer: First results of the EORTC10085/TBCRC/BIG/NABCG International Male BC Program

**Authors:** Fatima Cardoso1, John Bartlett2, Leen Slaets3, Carolien van Deurzen4, Elise van Leeuwen-Stok5, Peggy Porter6, Barbro Linderholm7, Ingrid Hedenfalk8, Carolien Schröder9, John Martens10, Jane Bayani11, Christi van Asperen12, Melissa Murray13, Clifford Hudis14, Lavinia Middleton15, Joanna Vermeij16, Stephanie Peeters17, Judith Fraser18, Monika Nowaczyk19, Isabel T. Rubio20, Stefan Aebi21, Catherine Kelly22, Kathryn Ruddy23, Eric Winer24, Cecilia Nisson25, Lissandra Dal Lago26, Larissa Korde27, Kim Benstead28, Danielle Van Den Weyngaert29, Oliver Bogler30, Theodora Goulioti31, Nicolas Dif32, Carlo Messina33, Konstantinos Tryfonidis34, Jan Bogaerts35 and Sharon Giordano36.
One of the main questions:
ROLE OF AR IN MALE BC

- Role of AR is different in female BC and prostate cancer
  (High AR/Low PTEN: worse prognosis in prostate cancer
  High AR/High PTEN: better DFS in female breast cancer)
- Functioning of AR if different according to hormonal environment
- TUMOR and/or HOST?
- Good “model”: MALE BC!

ORIGINAL ARTICLE
Differential regulation of PTEN expression by androgen receptor
in prostate and breast cancers

Y Wang¹, T Romigh¹, X He¹, M-H Tan¹, MS Orloff¹-², RH Silverman²-³,⁴, WD Heston²-³,⁴
and C Eng¹,²,⁴,⁵,⁶
Androgen-Receptor Splice Variant–Mediated Resistance to Therapeutics Directed at the Androgen Receptor

• Activity of abiraterone and enzalutamide is dependent on the presence of the C-terminal domain of AR.
• Instead of losing function, several AR variants (including the most predominant variant, splice variant 7) encode protein isoforms that activate the AR pathway in the absence of androgens.

PROSPECTIVE INTERNATIONAL REGISTRY

• Accrual: 30 months; expected about 200 patients
• Biological material will be collected in selected countries
• Quality of Life sub-study
• First patient enrolled 05/05/2014!
Funding

• Financial constraints → no patient nor pathology fee

• Funding obtained:
  - BCRF
  - BCWG
  - EORTC-BCG
  - Dutch Pink Ribbon (for Dutch patients)
  - Swedish Pink Ribbon
  - Susan Komen For the Cure

THANK YOU!
"As a man with breast cancer and care-giver to my wife when she had breast cancer, I have seen first hand that the identical treatment we received is effective. But as a cancer biologist I cannot help but think that more research on the differences is also needed."

Oliver Bogler, PhD
Senior Vice President Academic Affairs
Vice President Global Academic Programs
Professor Neurosurgery - Research
UT MD Anderson Cancer Center

BLOG: malebreastcancerblog.org
BACK-UP
Although ERBB2 seems to have a minor relevance in MBC, a genomic amplification mechanism seem to take place also in males since all amplicon genes are significantly correlated with ERBB2, with a comparable pattern in the two genders.

PGR associated genes selected in an independent dataset identify two clusters associated with PGR status in our FBC dataset but not in MBC.