MADRID 2014 ESMO congress

Management of BC in specific populations

MANAGEMENT OF BREAST CANCER IN MALES

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EORTC European Organisation for Research and Treatment of Cancer

ESO European School of Oncology learning to care

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JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

Multidisciplinary Meeting on Male Breast Cancer: Summary and Research Recommendations

Larissa A. Korde, Jo Anne Zujewski, Leah Kamin, Sharon Giordano, Susan Domchek, William F. Anderson, John M.S. Bartlett, Karen Gelmon, Zeina Nahleh, Jonas Bergh, Bruno Cutuli, Giancarlo Pruneri, Worta McCaskill-Stevens, Julie Gralow, Gabriel Hortobagyi, and Fatima Cardoso

From the University of Washington; Seattle Cancer Care Alliance, Seattle, WA; Clinical Investigations Branch, Division of Cancer Diagnosis and Treatment; Biosta-

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*<.001)
(26% increase)

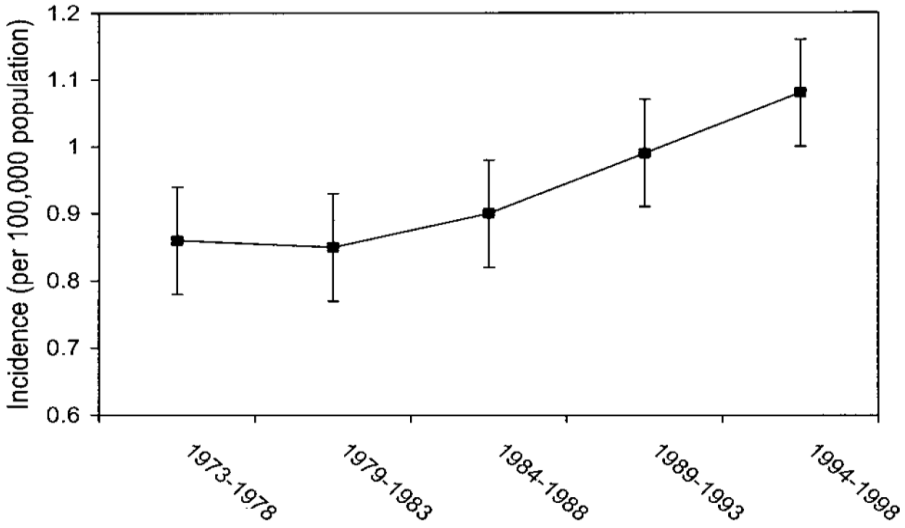
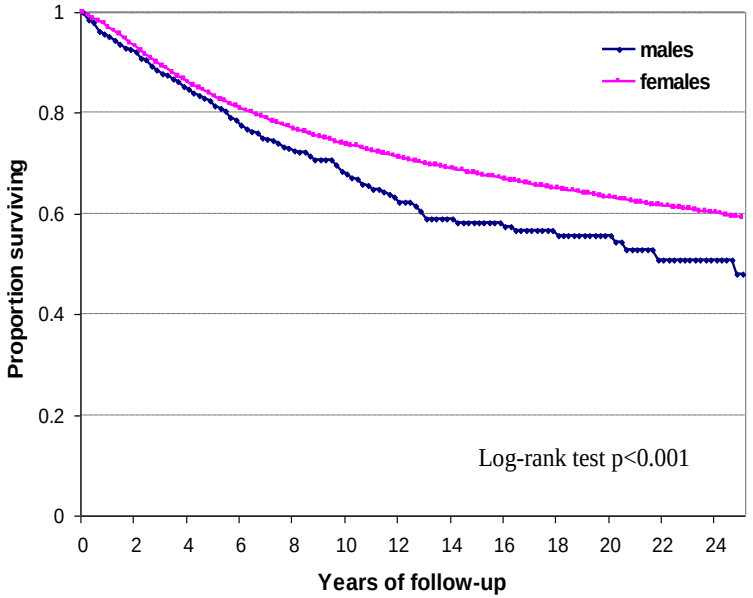


FIGURE 2. Male breast carcinoma incidence (with 95% confidence interval) by year of diagnosis.

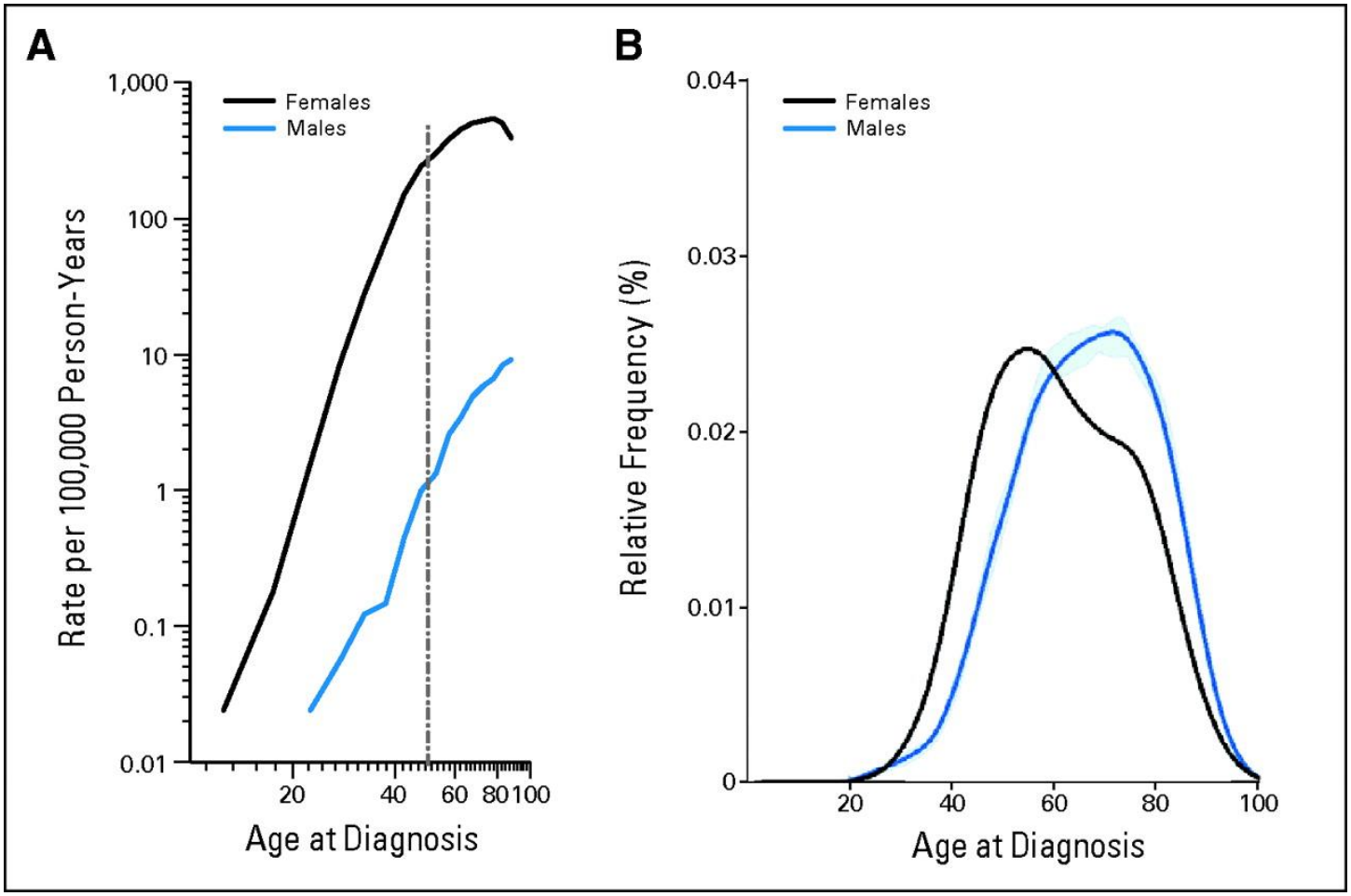
BC-specific survival



Kamila C, et al. *Breast*. 2007;16(2s):147-154.
Giordano SH, et al. *Cancer.* 2004;101(1):51-57
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.

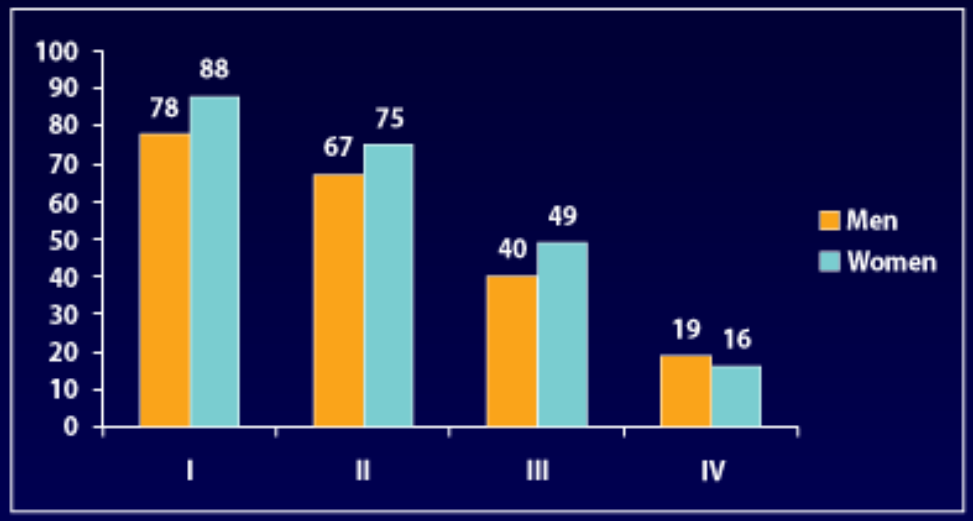


Bimodal distribution for FBC
One peak (+/- 75 y for MaleBC

Korde L A et al. JCO 2010;28:2114-2122

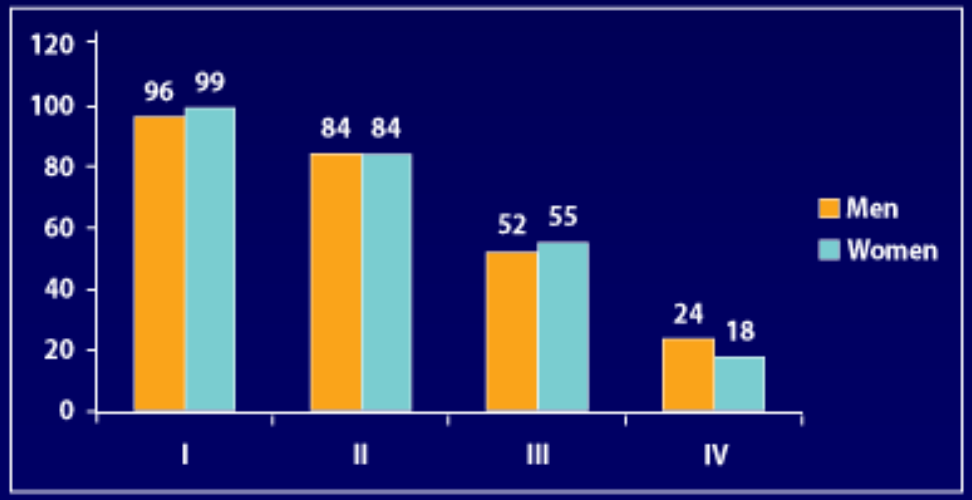
JOURNAL OF CLINICAL ONCOLOGY

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

Giordano SH, et al. *Cancer.* 2004;101(1):51-57.

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)

Korde LA, et al. *J Clin Oncol*. 2010;28(12):2114-2122.

MALE BC: GENETICS

- ***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

Tai YC, et al. *J Natl Cancer Inst.* 2007;99(23):1811-1814.
Giordano SH. *Oncologist*. 2005;10(7):471-479.
Thompson D, et al. *Am J Hum Genet*. 2001;68(2):410-419.

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**

(Easton et al., Am J Hum Genet 1997, 61, 120-8; Thompson et al., Am J Hum Genet 2001, 68, 410-9)

Courtesy K. Ruddy

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!

Cutilu B. *Expert Opion Pharmacother. 2007;*8(2)193-202.
Fentiman IS, et al. *Lancet.* 2006;367(9525):595-604.
Korde LA, et al. *J Clin Oncol*. 2010;28(12):2114-2122.

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

1. **Oncotype Dx in series of Male BC patients. S. Shak et al. ASCO 2009, Genomic Health, US**

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

3. **Shaaban et al. A comparative biomarker study of 514 matched cases of male and female BC. Breast Cancer Res Treat DOI 10.1007/s10549-011-1856-9**

GENE PROFILING: ONCOTYPE Dx

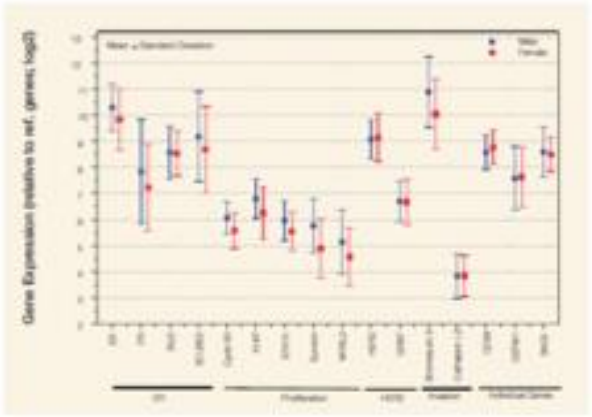
Molecular characterization of male breast cancer by standardized quantitative RT-PCR analysis: First large genomic study of 347 male breast cancers compared to 82,434 female breast cancers.

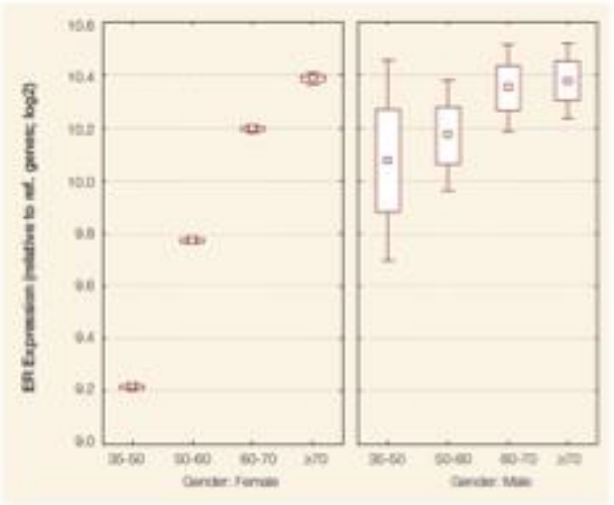
S Shak et al, ASCO 2009, poster

- **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%)**

	Male	Female
n	347	82,434
RS < 18	53.6%	53.4%
RS 18–30	35.2%	36.3%
RS ≥ 31	11.2%	10.3%

S Shak et al, ASCO 2009





- **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.

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BUT

NO OUTCOME DATA.

SO NO DATA ON THE PROGNOSTIC VALUE OF ONCOTYPE DX IN MALE BC PTS

• 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

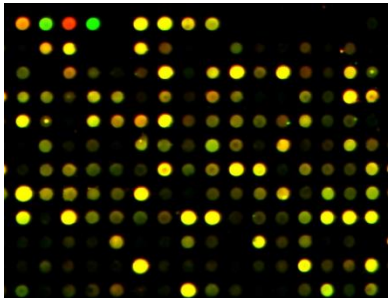
Gene expression profile study comparing breast cancer samples from male and female patients

- **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)**

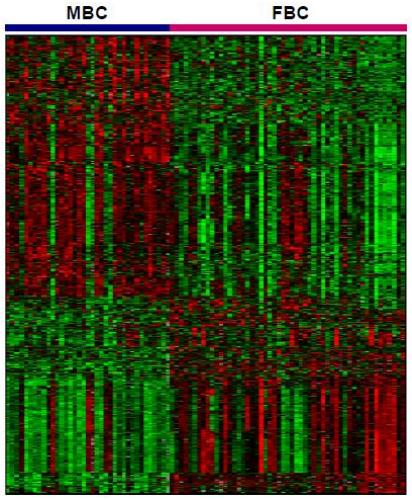
	MBC	FBC
Age		
Range (years)	32–87	45–81
Median (years)	66	66
≤50 years	4 (11%)	5 (9%)
>50 years	33 (89%)	48 (91%)
Size		
Range (cm)	1–5	1–7
Median (cm)	2	2.2
≤2 cm	12 (32%)	17 (32%)
>2 cm	25 (68%)	36 (68%)
ER		
Pos	37 (100%)	53 (100%)
Neg	0 (0%)	0 (0%)
PgR		
Pos	29 (78%)	41 (77%)
Neg	8 (22%)	12 (23%)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

Callari , Daidone et al. 2010

Gender specific signature



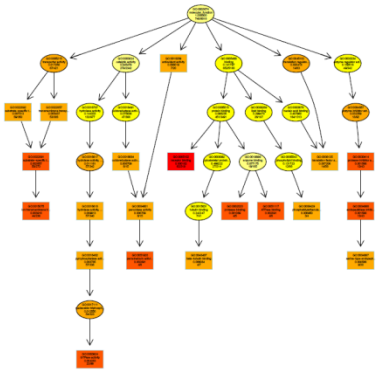
Pre-processing & class comparison



- 920 differentially expressed genes (FDR<1%)

Functional annotation

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



Callari , Daidone et al. 2010

Differentially expressed biological functions

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

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

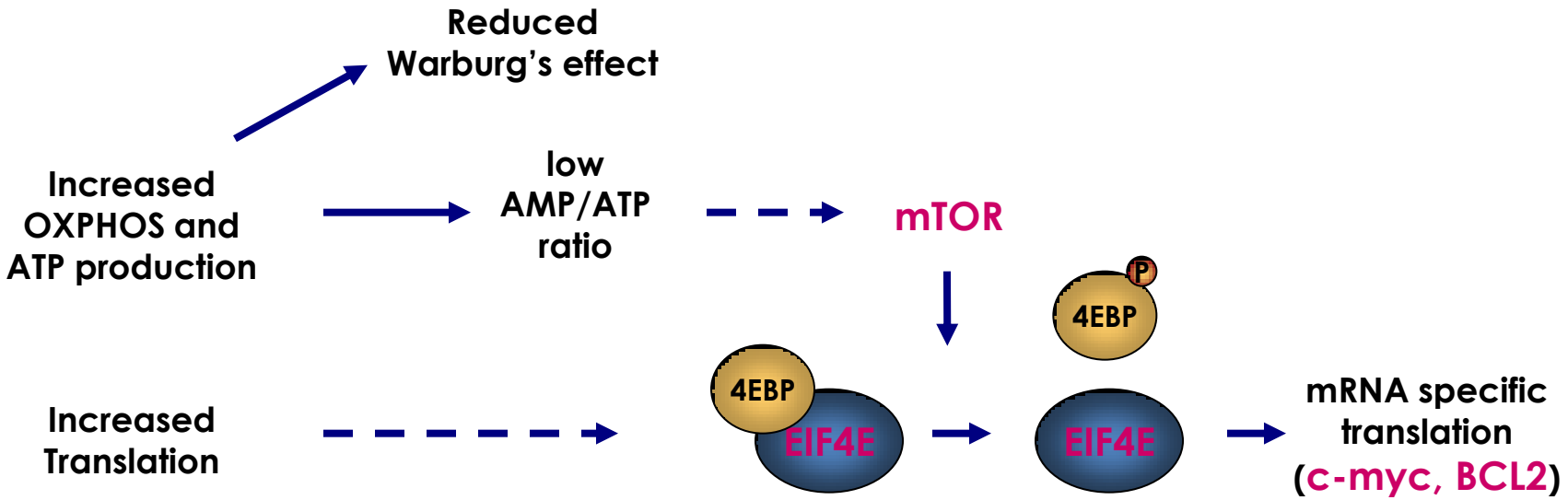
Energy metabolism

Tubulin/microtubule system → **target therapy**

Tumor microenvironment → **association with prognosis**

Callari , Daidone et al. 2010

Differentially expressed biological functions



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

Correlated clones			
Gene	MBC	FBC	Common
ERBB2	243	2288	45
PGR	159	582	26
AR	441	86	7

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**

Breast Cancer Res Treat (2007) 103:177–183
DOI 10.1007/s10549-006-9363-0

CLINICAL TRAIL

A prospective study of adjuvant CMF in males with node positive breast cancer: 20-year follow-up

Janice M. Walshe · Arlene W. Berman · Ujala Vatas · Seth M. Steinberg · William F. Anderson · Marc E. Lippman · Sandra M. Swain

Korde LA, et al. *J Clin Oncol*. 2010;28(12):2114-2122.

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**

Mauras N, et al. *J Clin Endocrin Metab.* 2000;85(7): 2370-2377.
Trunet PF, et al. *J Clin Endocrin Metab*. 1993;77(2):319-323.

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)

Anelli TF, et al. *Cancer.* 1994;74(1);74-77. Visram H, et al. *Current Oncology.* 2010;17(5):17-21.

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

TREATMENT OF METASTATIC MALE MBC

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).

TREATMENT OF METASTATIC MALE MBC

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

Doyen J, et al. *Ann Oncol.* 2010;21(6):1243-1245.

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 1st-line therapy; 1 PR & 1 SD**

1. Masci G, et al. *Ann Oncol*. 2011;22(4):985-993.
2. de la Haba Rodríguez JR, et al. *Ann Oncol.* 2009;20(11):1896–1897.
3. Agrawal A, et al. *Breast Cancer Res Treat.* 2007;101(1):123.

Metastatic Male Breast Cancer - Chemotherapy

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

Genetic Testing	
Referred for genetic counseling	74%
Had genetic testing	60%
Found to carry BRCA mutation	12%

Fertility Concerns Results

Fertility Issues	
Have no biological children	24%
Desire future biological children	5%
Told that treatment could impact fertility	7%
Stored sperm prior to treatment	2%

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

Courtesy K. Ruddy

Male BC QUALITY OF LIFE Pilot Study:
ANXIETY & DEPRESSION

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

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

Courtesy K. Ruddy

Stop excluding male patients

Fatima Cardoso ■ GUEST EDITOR

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 expected that around 1910 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 their 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 done by extrapolation from its female counterpart.

The Breast International Group and the North American Breast Cancer Groups 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 1700 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

EDITORIAL
CANCER WORLD
March/April 2010

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**

EORTC tbcrc Translational Breast Cancer Research Consortium BIG Breast International Group TBCI The Breast Cancer Intergroup of North America *The future of cancer therapy*

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**

EORTC tbcrc Translational Breast Cancer Research Consortium BIG Breast International Group TBCI The Breast Cancer Intergroup of North America *The future of cancer therapy*

Oral presentation!

SABCS 2014- Abstract

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

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The future of cancer therapy

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!**

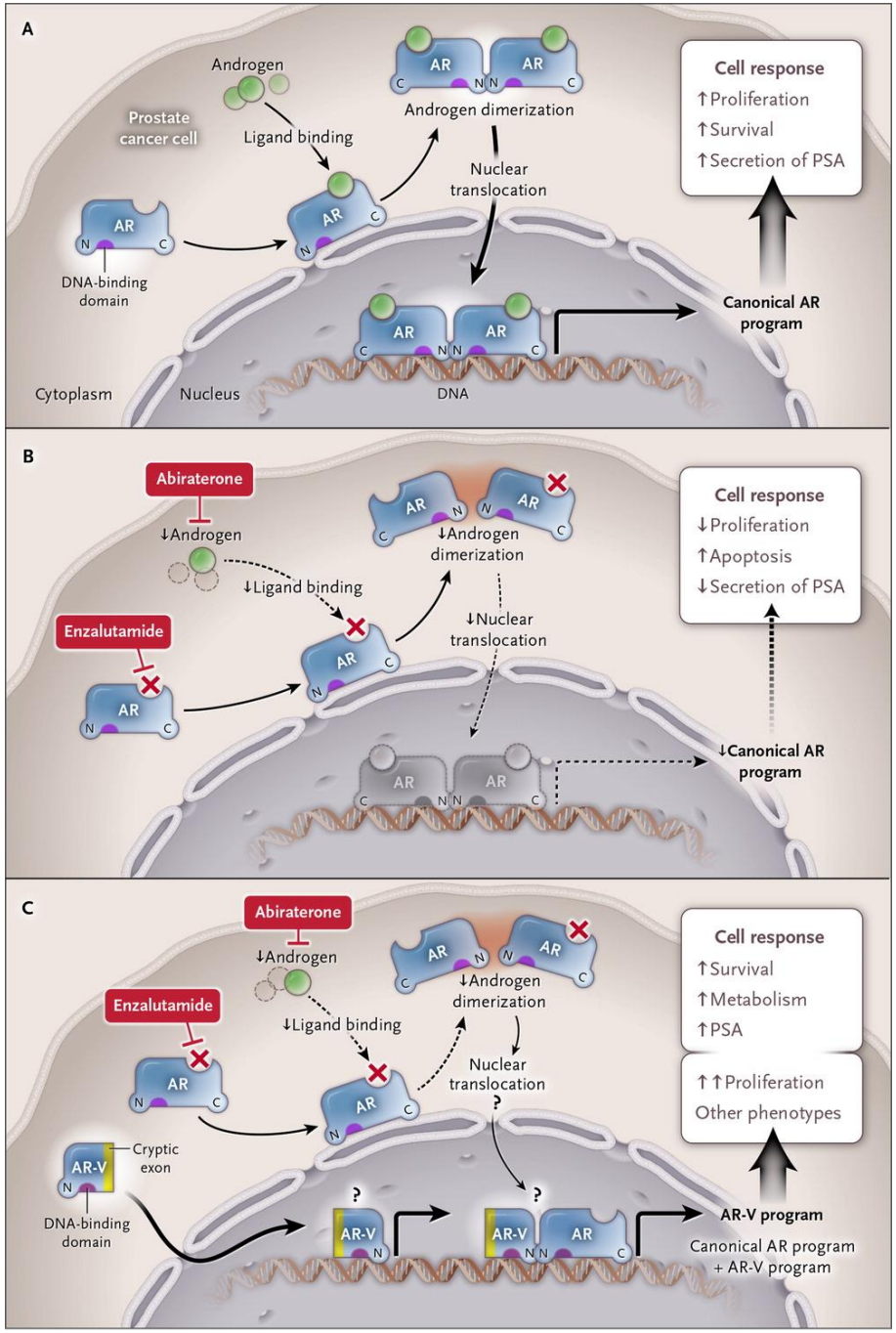
Oncogene (2011) 30, 4327–4338

www.nature.com/onc

ORIGINAL ARTICLE

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

Y Wang[1], T Romigh[1], X He[1], M-H Tan[1], MS Orloff[1,2], RH Silverman[2,3,4], WD Heston[2,3,4] and C Eng[1,2,4,5,6]



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.**

Nelson PS. N Engl J Med 2014;371:1067-1069

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!**

EORTC tbcrc Translational Breast Cancer Research Consortium BIG Breast International Group TBCI The Breast Cancer Intergroup of North America *The future of cancer therapy*

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!

EORTC TBCI The Breast Cancer Intergroup of North America The BIG Breast International Group tbcrc Translational Breast Cancer Research Consortium

"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."

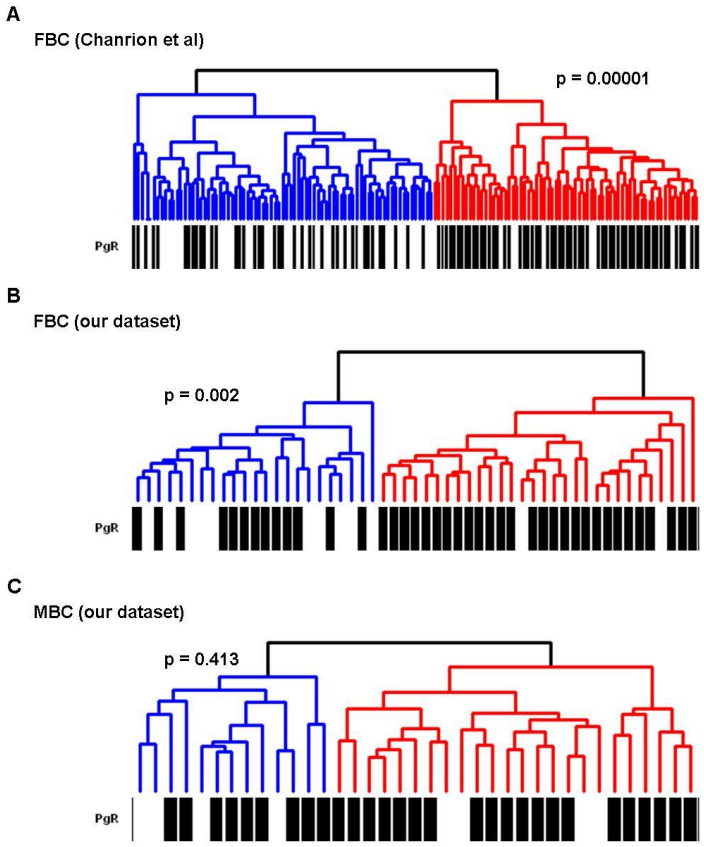
Oliver Bogler, PhD
Senior Vice President Academic Affairs
Vice President Global Academic Programs
Professor Neurosurgery - Research
UT MD Anderson Cancer Center

BLOG: malebreastcancerblog.org

EORTC tbcrc Translational Breast Cancer Research Consortium BIG Breast International Group TBCI The Breast Cancer Intergroup of North America *The future of cancer therapy*

BACK-UP

ERBB2, PGR and AR in MBC



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

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