

A Toolbox for Navigating Young Women's Metastatic Breast Cancer

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**Young Women's Breast Cancer
Translational Program**

Objectives

- Young Women's Breast Cancer –what is it and who gets it?
- Understand the magnitude of impact a metastatic diagnosis imparts to YWBC
- Specific Strategies to Taking Care of your metastatic YWBC patient
- Survivorship Priorities in metastatic YWBC
- Surviving the Care of metastatic YWBC

Disclosures

- *Dr. Borges has no conflict of interest to disclose for this presentation.*
- *Dr Borges conducts clinical trials at U of Colorado funded to the institution from Merck, Seattle Genetics, Genentech, Abbvie, Medivation, Biothera and Pfizer*

YOUNG WOMEN'S BREAST CANCER

Why is this a
problem?

US YWBC Stats

27,000 cases under age 45 in 2011

11-13% of all cases/year are <45

~54% arise in AA women

Enriched for poor prognostic subtypes

Leading cause of cancer death US and worldwide for women age 15-54

Higher than the next 4 cancers combined in this age range

1/228 women age 30

1/69 women age 40

will get breast cancer
in the next 10 years



ACS BCFF 2011 and 2013

Typical Clinic Day

- 30 year old woman with a palpable lump for 3 months. Mammogram with vague density underlying the marker. Ultrasound with 4cm mass, suspicious LN in Axilla
- Core Biopsy - Invasive ductal carcinoma, grade 3, positive LVI, Node +, ER+, PR+, Her 2 amplified
- Married, G1P1, 6 month old son, nursed for 4 months, was thinking of child #2 this summer, works as a CPA, no FH of cancer, exercises, BMI of 22
- Husband and Mother in the exam room with her.

Where to start?

Issue #1: Why is this woman in my office?

WHO GETS YWBC?

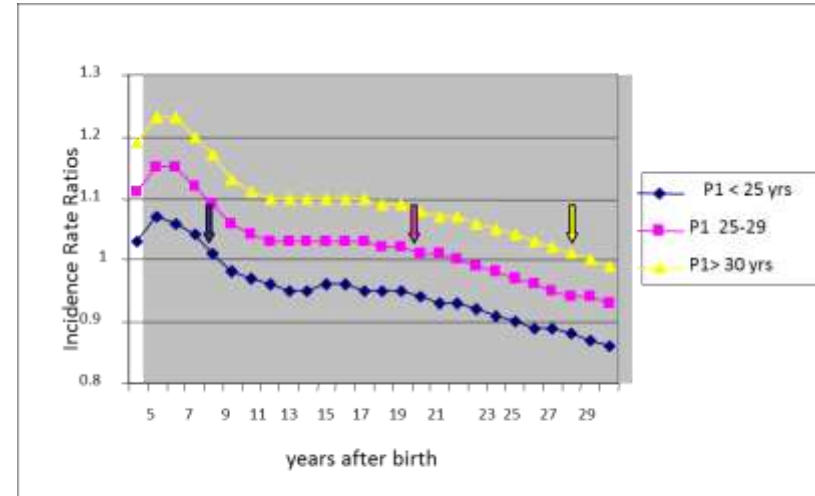
Risk factors are not fully understood...
and that is Problem #1...

Risk Factors for Breast Cancer

- **Woman**
- **Age**
- **Hormones**
 - **OCPs**, HRT, DES
- **Reproductive factors**
 - Menarche
 - Menopause
 - **Full-term pregnancy**
 - Late age 1st pregnancy
 - Nulliparity
 - **No lactation**
 - Post-menopausal obesity
- **Lifestyle/environment**
 - **Ionizing XRT**
 - ETOH
 - Extremes of exercise
 - Environmental Exposures
- **Inherited Disposition**
 - **FH**
 - **Genetic mutation**
- **Prior Breast Disease**
 - ADH
 - LCIS
 - **AGE UNDER 40 for Prior BCA**

Known YWBC Risks

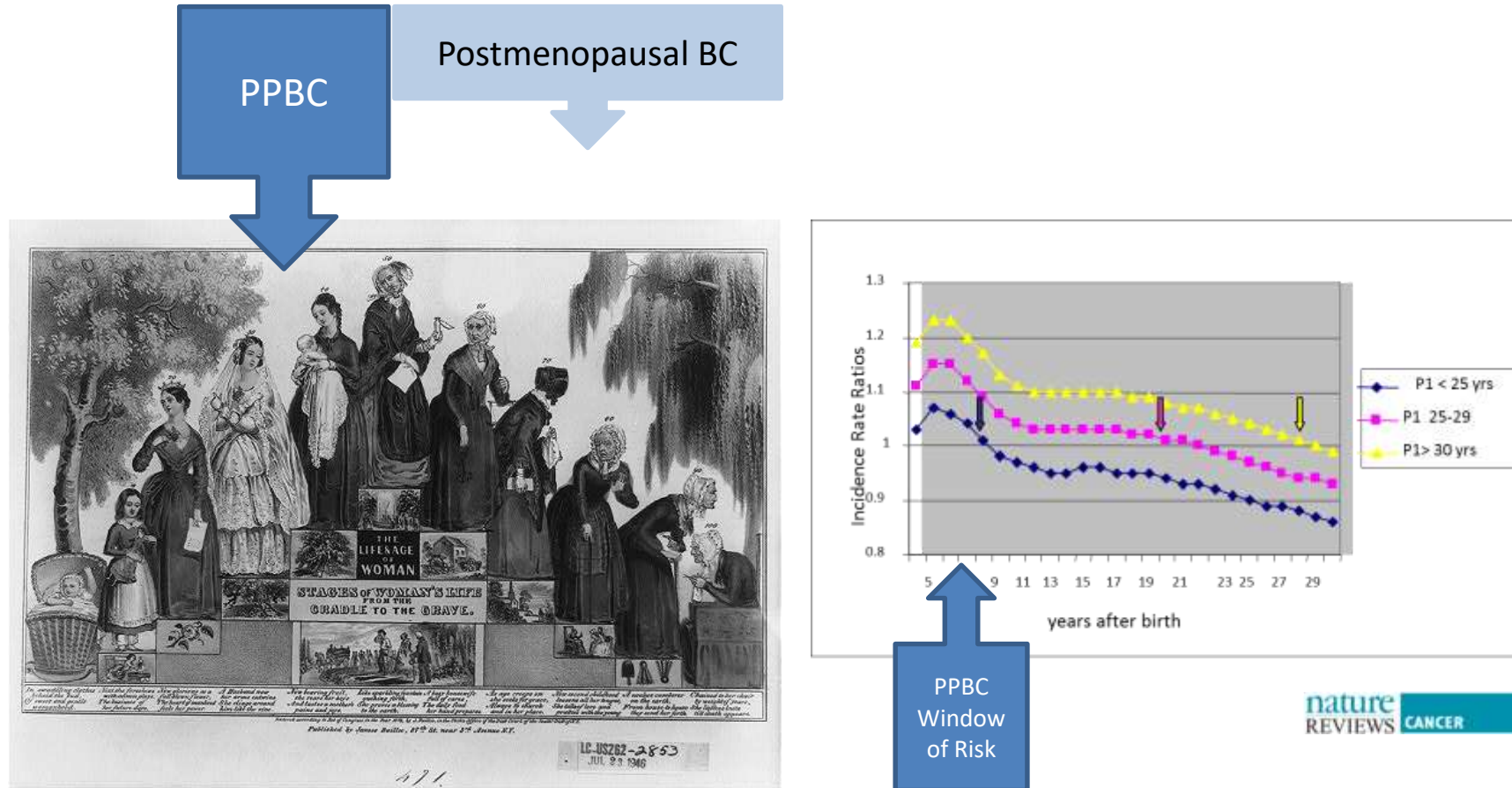
Life windows of BCA Risk



nature
REVIEWS CANCER

Schedin, *Nature Reviews Cancer* 6, 281–291, 2006

Life Windows of BC Risk



Pregnancy is a Risk Factor for Young Women's Breast Cancer

Women are delaying childbearing

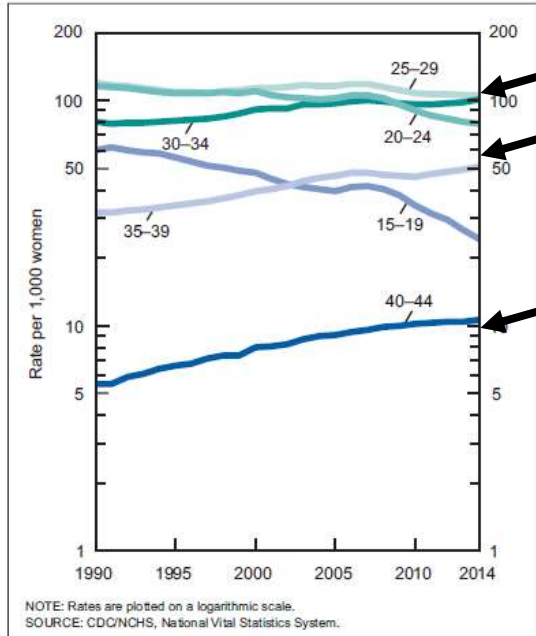


Figure 4. Birth rates, by age of mother: United States, 1990–2014

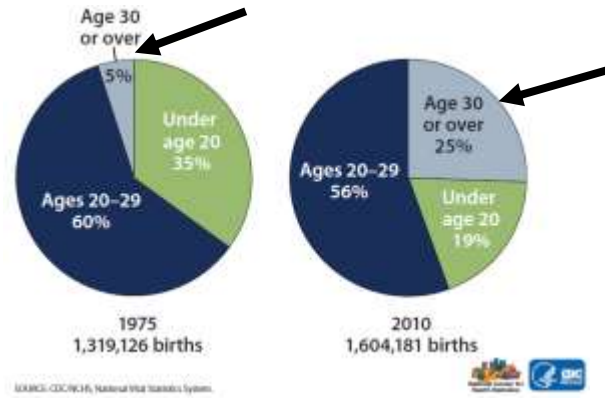
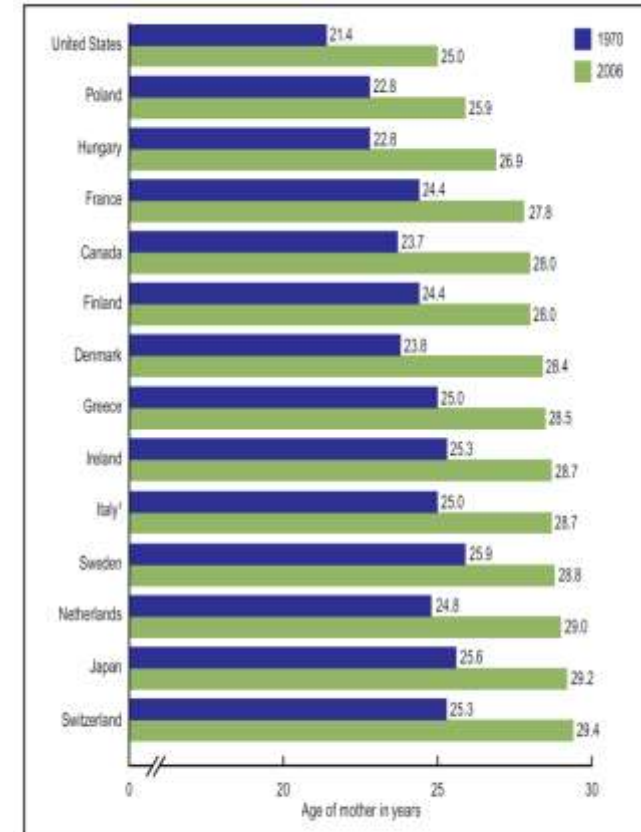


Figure 5. Average age of mother at first birth: Selected countries, 1970 and 2006



¹ Latest data are for 2006.
SOURCES: CDC/NCHS, National Vital Statistics System; Council of Europe, Vienna Institute of Demography; Statistics Canada; and Japanese Ministry of Health, Labour and Welfare.

- ❖ Global statistics are similar but with even older age at first birth for most developed nations
- ❖ As expected, postpartum breast cancer rates are increasing

Issue #2:

Her unique needs and concerns

- 30 year old woman
- Married, G1P1, 6 month old son, nursed for 4 months, was thinking of child #2 this summer, works as a CPA, no FH of cancer, exercises, BMI of 22
- Husband and Mother in the exam room with her.

Fertility Issues

- If a woman has never been pregnant, her fertility status is unknown
- Fertility rapidly declines after age 35, normally
- Modern chemotherapy regimens less frequently alter fertility than older ones
 - ? Delay of therapy for egg harvesting
 - Oocytes/ovarian tissue if NO Acceptable Sperm on hand.
- Post treatment pregnancy does NOT increase breast cancer recurrence risk [POSITIVE trial]
- Right now is a REALLY BAD TIME for pregnancy, so fertility must be controlled in a definitive manner.

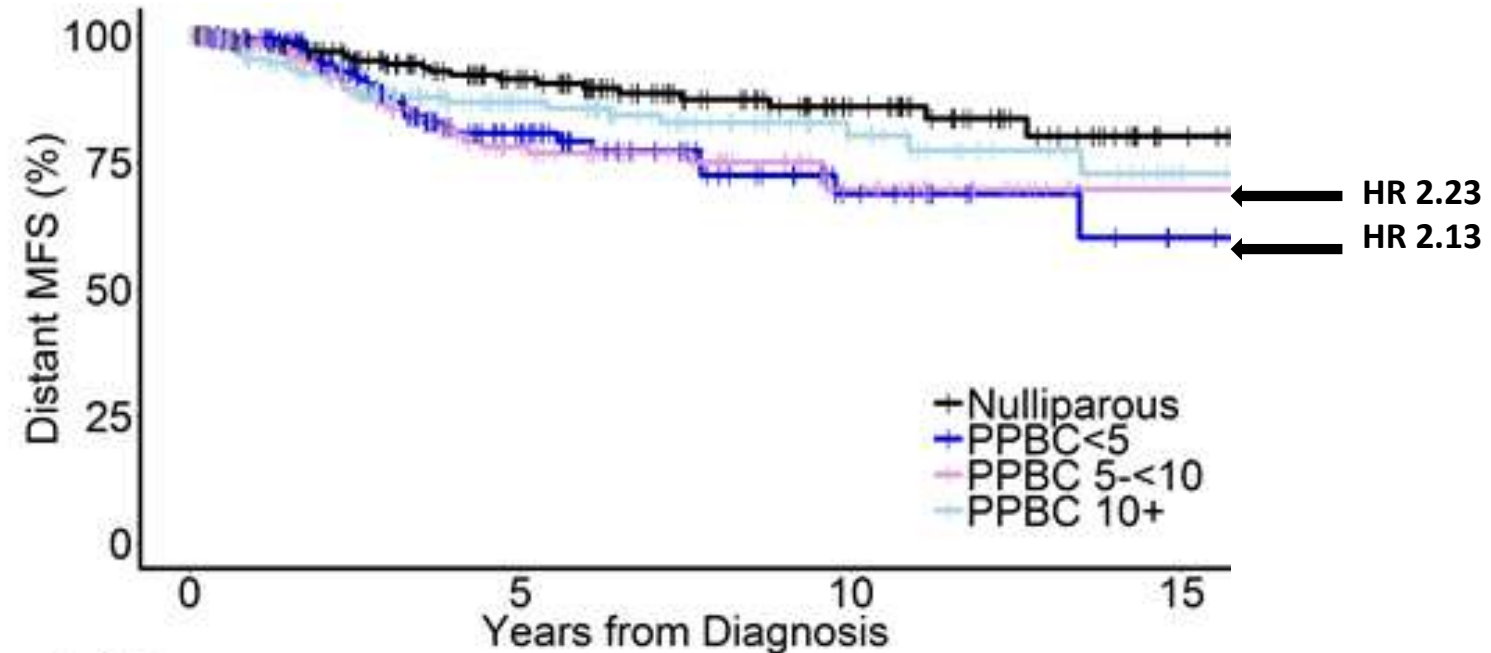


The risk factors for YWBC need better refinement

The prognosis can be worse too based on the simple factors of life too.

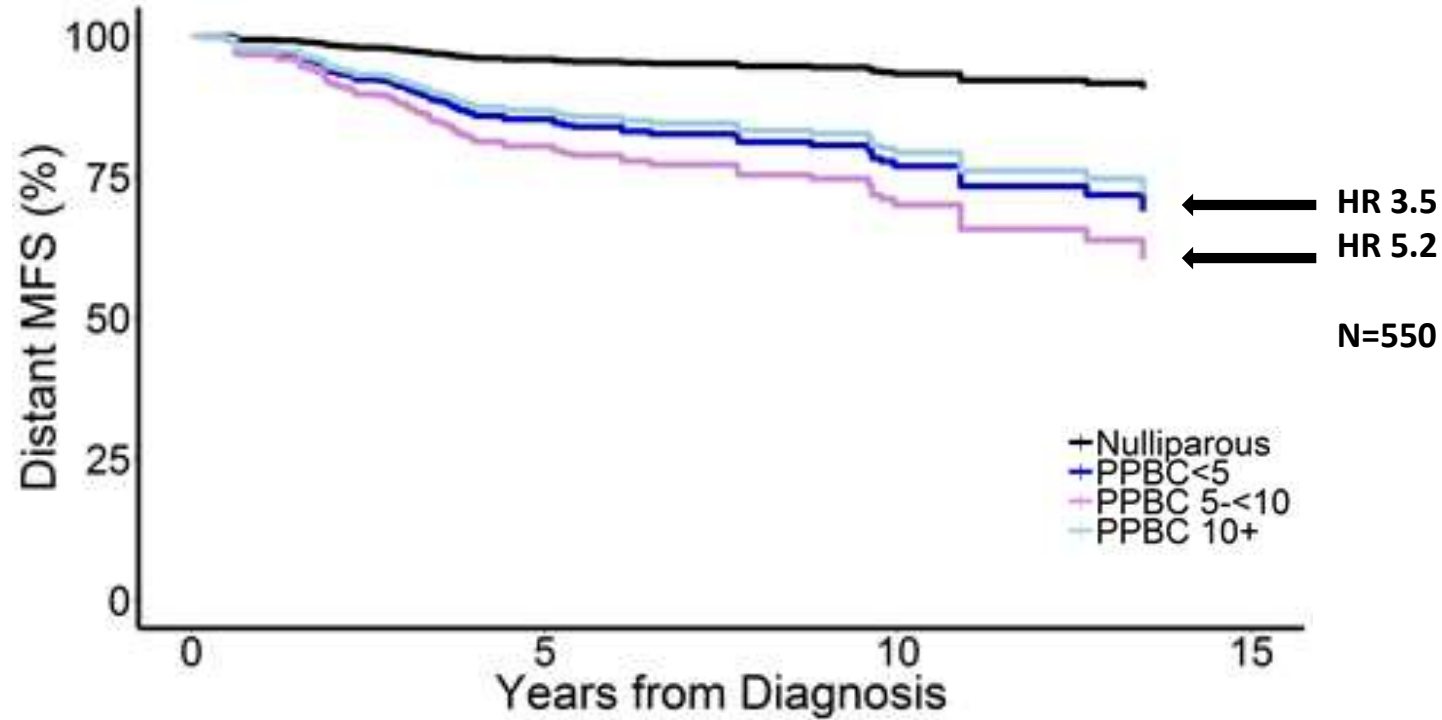
JAMA Network Open Original Investigation Oncology January 11, 2019
Association Between Postpartum Breast Cancer Diagnosis and Metastasis and the Clinical Features Underlying Risk

Erica T. Goddard, PhD; Solange Bassale, MS; Troy Schedin, BS; Sonali Jindal, MD; Jeremy Johnston, BS; Ethan Cabral, BS; Emile Latour, MS; Traci R. Lyons, PhD; Motomi Mori, PhD; Pepper J. Schedin, PhD; Virginia F. Borges, MD, MMSc



Number at risk				
	0	5	10	15
Nulliparous	217	110	45	6
PPBC <5	175	58	17	4
PPBC 5-<10	153	64	23	1
PPBC 10+	156	75	31	9

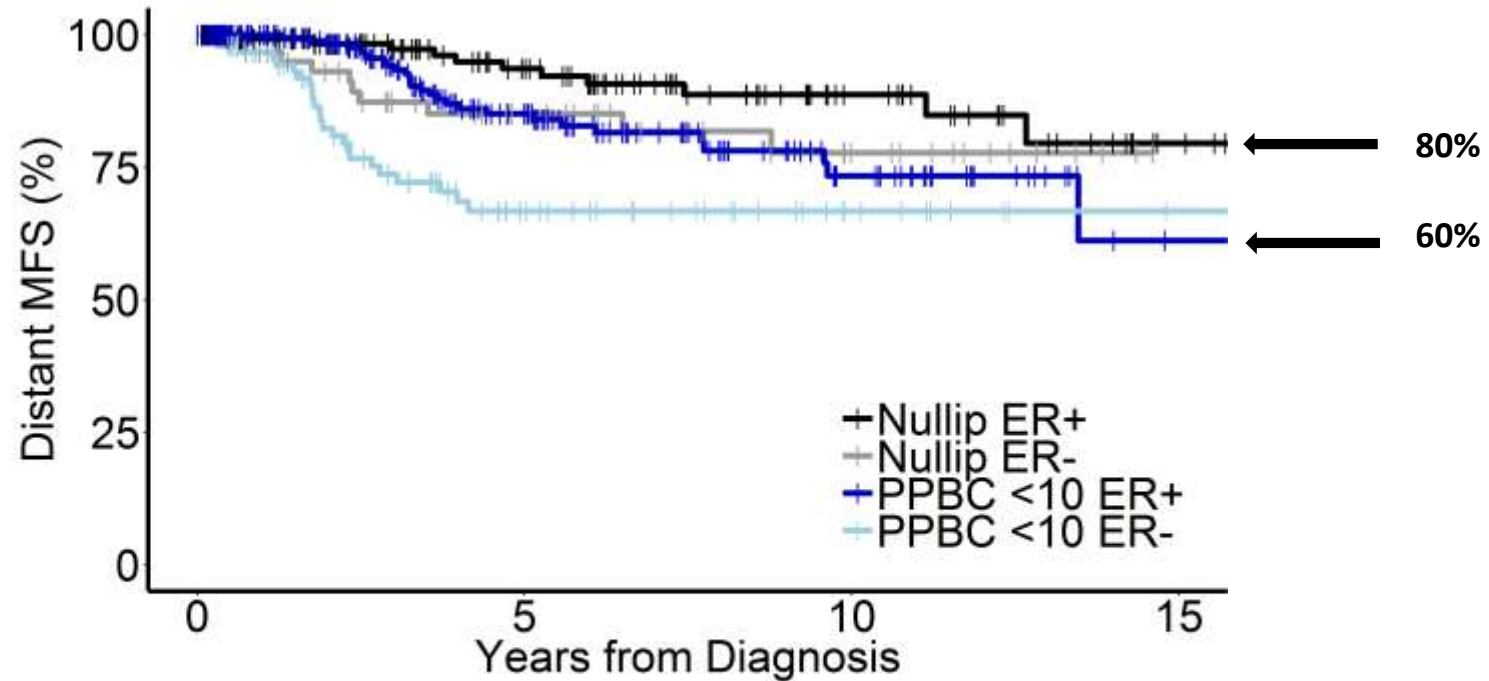
METASTATIC RISK MAGNIFIED FOR STAGE I-II CASES



Results adjusted for biologic subtype, age and year of diagnosis

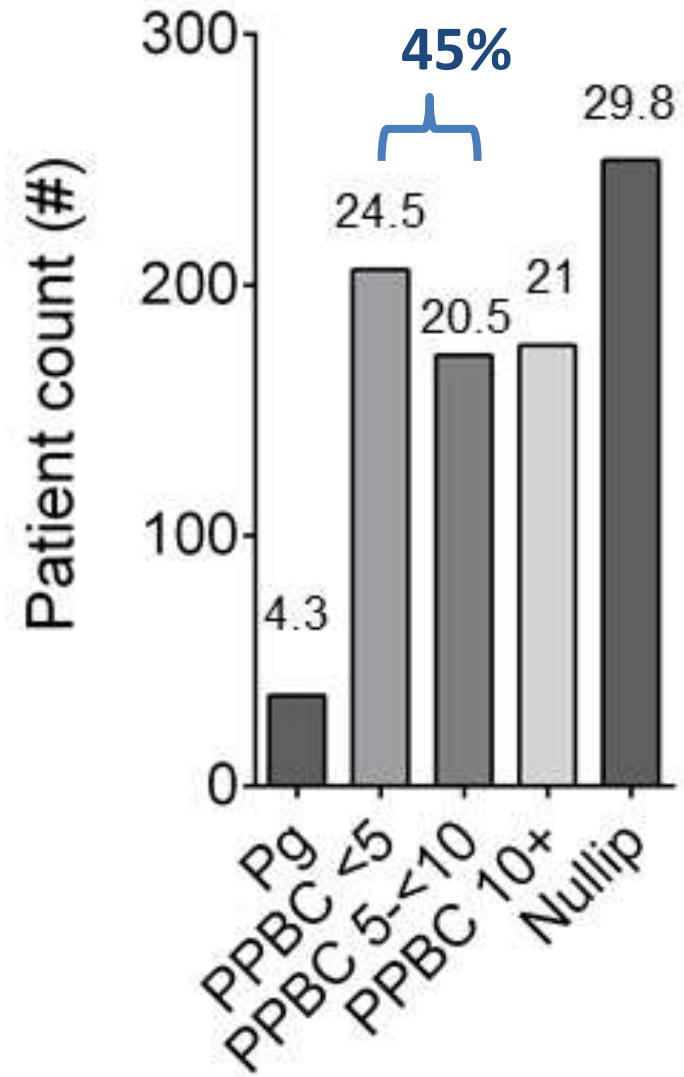
-The increased risk of a postpartum diagnosis has not been overcome by advances in treatment of the past 30 years

Association Between Postpartum Breast Cancer Diagnosis and Metastasis and the Clinical Features Underlying Risk

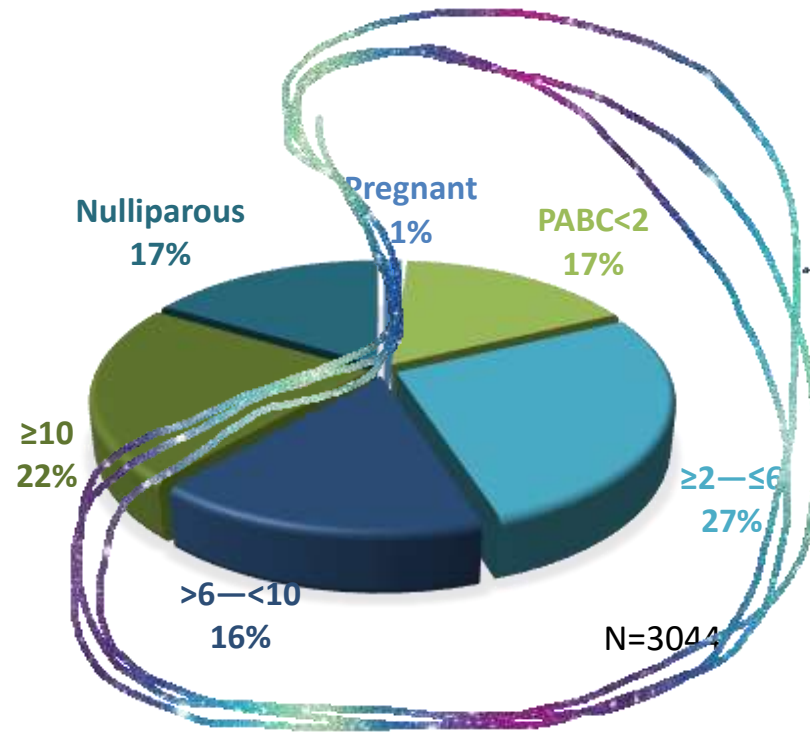


Number at risk

	0	5	10	15
Nullip ER+	142	70	28	5
Nullip ER-	62	33	12	0
PPBC <10 ER+	218	82	28	3
PPBC <10 ER-	93	29	9	1



Combinations of Pregnancy and Breast Cancer in Women



Virginia Borges, Eryn Callihan, & Grethe Albrektsen

Postpartum Breast Cancer

The Facts of PPBC

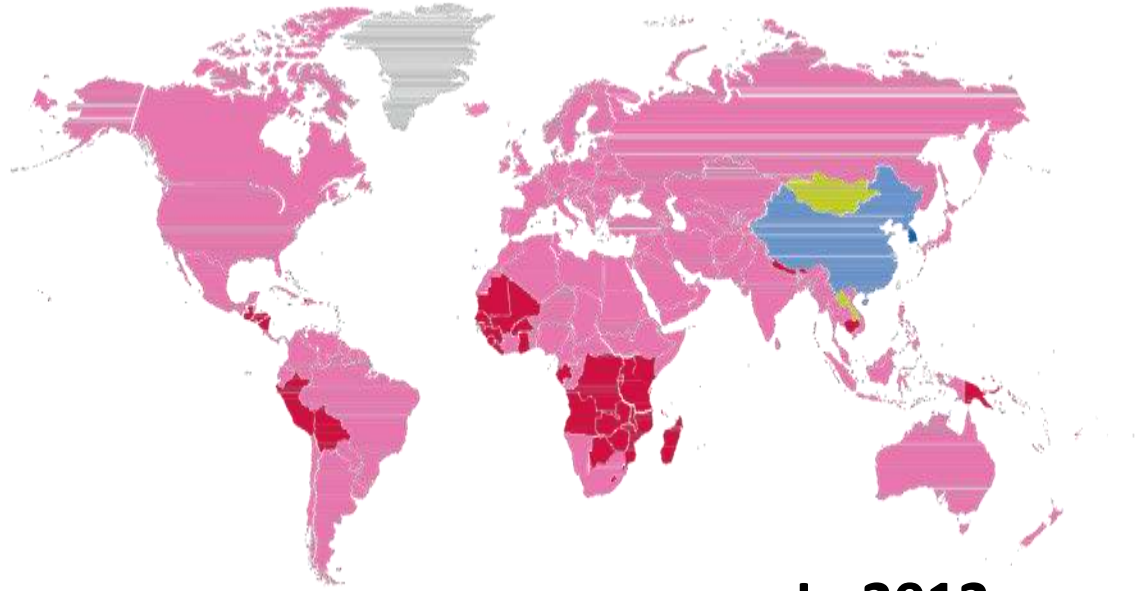
*Common [60% <10years]

50,000 PPBC deaths/decade/US

*POOR Prognosis

*Not enriched for, but interacting with ER status

Breast Cancer is a Global Problem with Disparity of Outcomes



In 2012

1,676,000 BCA cases worldwide

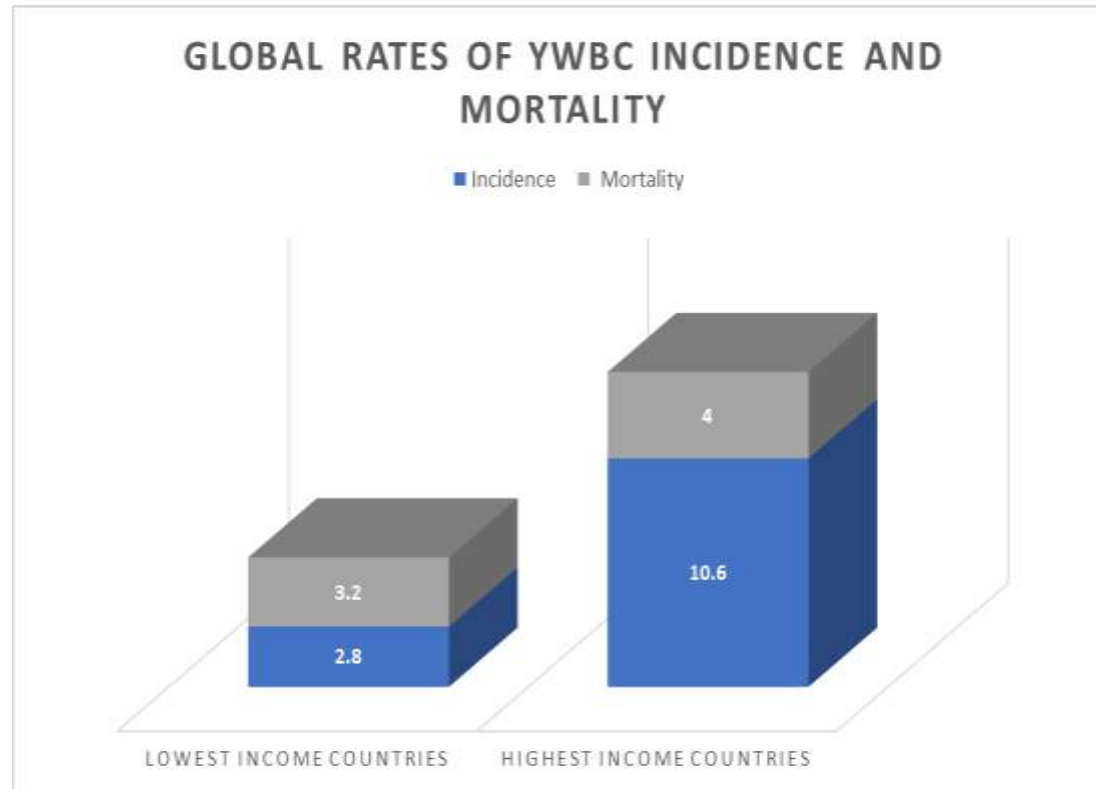
521,900 deaths worldwide

197,600 developed world

324,300 developing world

www.cancer.org ~ 2017

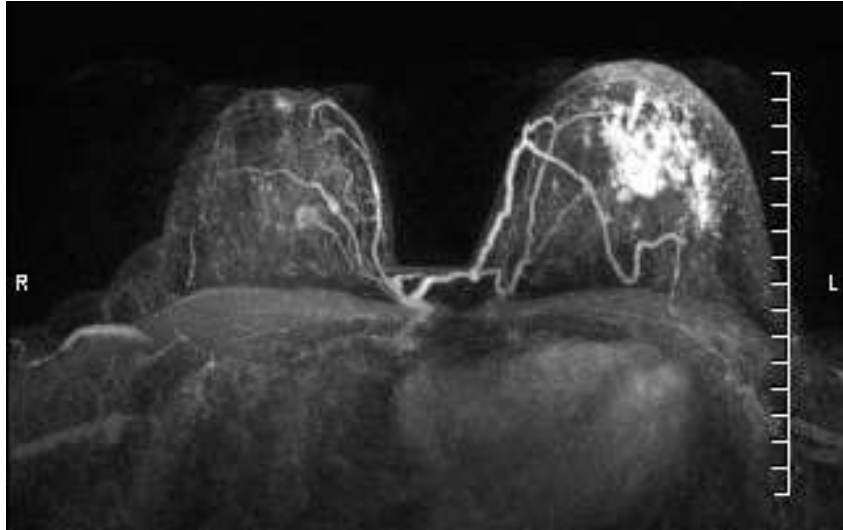
YWBC MORTALITY DISPROPORTIONALLY HIGHER IN COUNTRIES WITH LOWER ECONOMIES



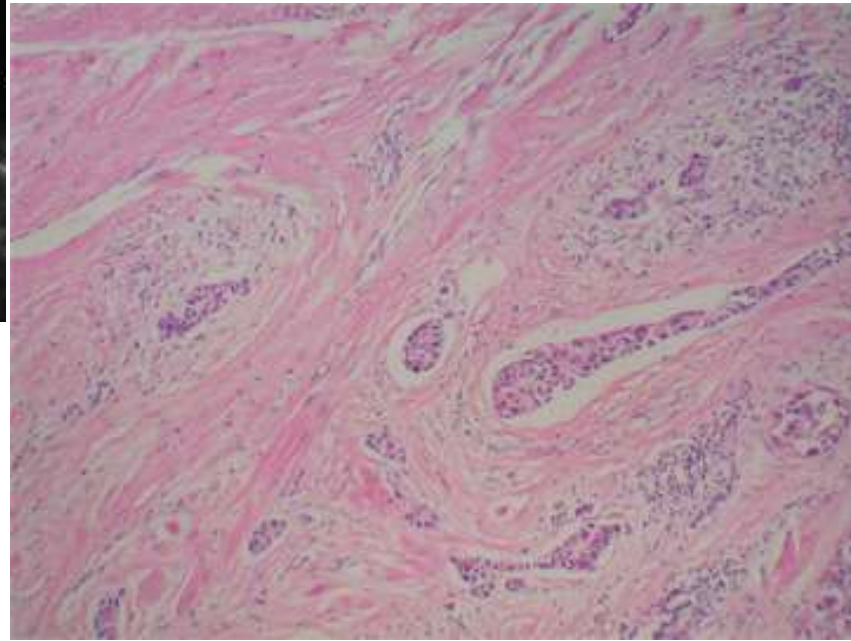
Bellanger M, et al. DOI: 10.1200/JGO.17.00207 J Global Oncology 2018

Younger women in the lowest income countries bear a relatively higher global burden of disease and years of life lost as a result of breast cancer mortality, which is disproportionately increasing with time.

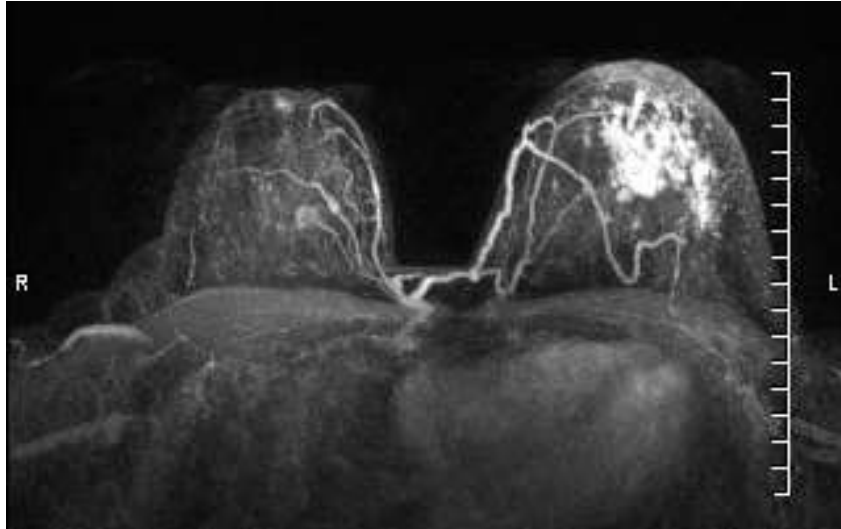
Issue #3: The Cancer



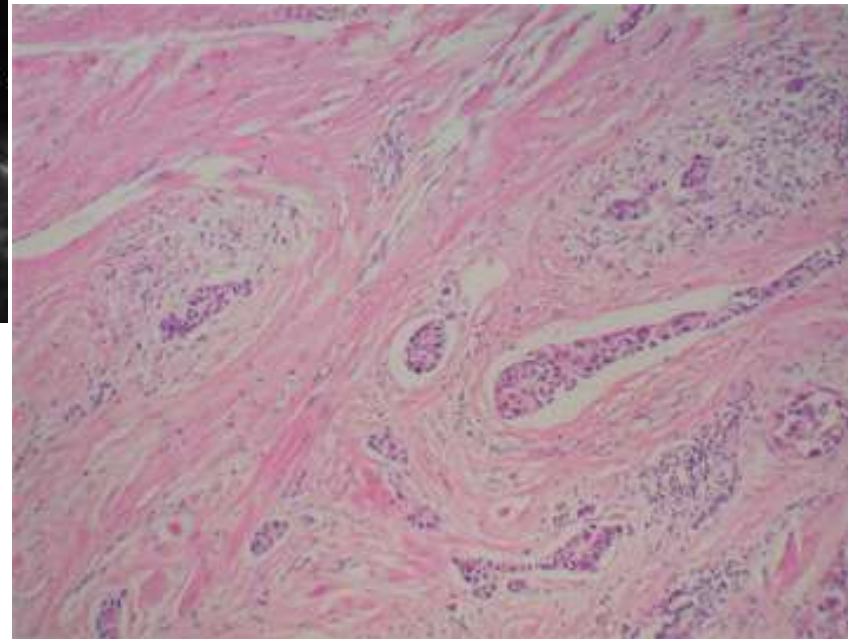
Staging so far:
(cT2, N1, MX) Luminal B, triple
positive IDC



Issue #3: The Cancer



Staging so far:
(cT2, N1, MX) Luminal B, triple
positive IDC



Neoadjuvant chemo + Her 2 targeted tx
Mastectomy v. Bilateral Mastectomy
PMCWRT
Hormonal Therapy –ovarian
suppression and AI or tamoxifen
Completion of Trastuzumab-based
therapy
**NOT A WHOLE LOT REALLY DIFFERENT
BASED ON AGE YET**

What is influencing this woman's risk for recurrence and death?

**ALL ELSE BEING EQUAL IN THE TUMOR - YOUNG
AGE PREDICTS FOR WORSE BCA OUTCOMES**

Future Clinic Follow up

Sometimes this moment is one week later after the staging scans are resulted

Sometimes this moment is 3 years later after she calls with a new symptom or the blood work is off

Either way, this moment is miserable for all involved, but especially her and her family

Now is the moment that can set the stage for the duration of her medical treatment and viewpoint on MBC

Now is the moment we have to remember that medicine is an art we practice.

Science is the paint and brushes we have to have to be competent in our art, but science is not what makes us good practitioners in our delivery.



Metastatic Breast Cancer

- Where to start and what matters most to ask first
- Fertility control! Preservation?
- Supports and resources
- The tumor is #4 on the list
- Differences in treatments and outcomes
- Unique things about YWBC and treatment for metastatic disease
- How to manage Dr. Google, your silent omnipresent partner
- Practice “leave no trace” oncology when possible

Survivorship Priorities in metastatic YWBC

Dos

- Surveillance and listening
- “Sharing the remote”
- The long game - reassurance that no matter what the team will be there to help.
- Be as clear and specific as you can

Dont's

- Let anxiety override listening
- Demand control
- Get flustered by them being flustered
- Hesitate to say you do not know

Surviving the Care of metastatic YWBC



Self-care



Connection and boundaries



Hope through seeing the
progress

The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer

R.K. Murthy, S. Loi, A. Okines, E. Paplomata, E. Hamilton, S.A. Hurvitz, N.U. Lin,
V. Borges, V. Abramson, C. Anders, P.L. Bedard, M. Oliveira, E. Jakobsen,
T. Bachelot, S.S. Shachar, V. Müller, S. Braga, F.P. Duhoux, R. Greil, D. Cameron,
L.A. Carey, G. Curigliano, K. Gelmon, G. Hortobagyi, I. Krop, S. Loibl, M. Pegram,
D. Slamon, M.C. Palanca-Wessels, L. Walker, W. Feng, and E.P. Winer

HER2CLIMB Trial Design

Key Eligibility Criteria

- HER2+ metastatic breast cancer
- Prior treatment with trastuzumab, pertuzumab, and T-DM1
- ECOG performance status 0 or 1
- Brain MRI at baseline
 - Previously treated stable brain metastases
 - Untreated brain metastases not needing immediate local therapy
 - Previously treated progressing brain metastases not needing immediate local therapy
- No evidence of brain metastases

N=410

R*
(2:1)

N=202

Tucatinib + Trastuzumab + Capecitabine (21-day cycle)

Tucatinib 300 mg PO BID
+
Trastuzumab 6 mg/kg Q3W (loading dose 8 mg/kg C1D1)
+
Capecitabine 1000 mg/m² PO BID (Days 1-14)

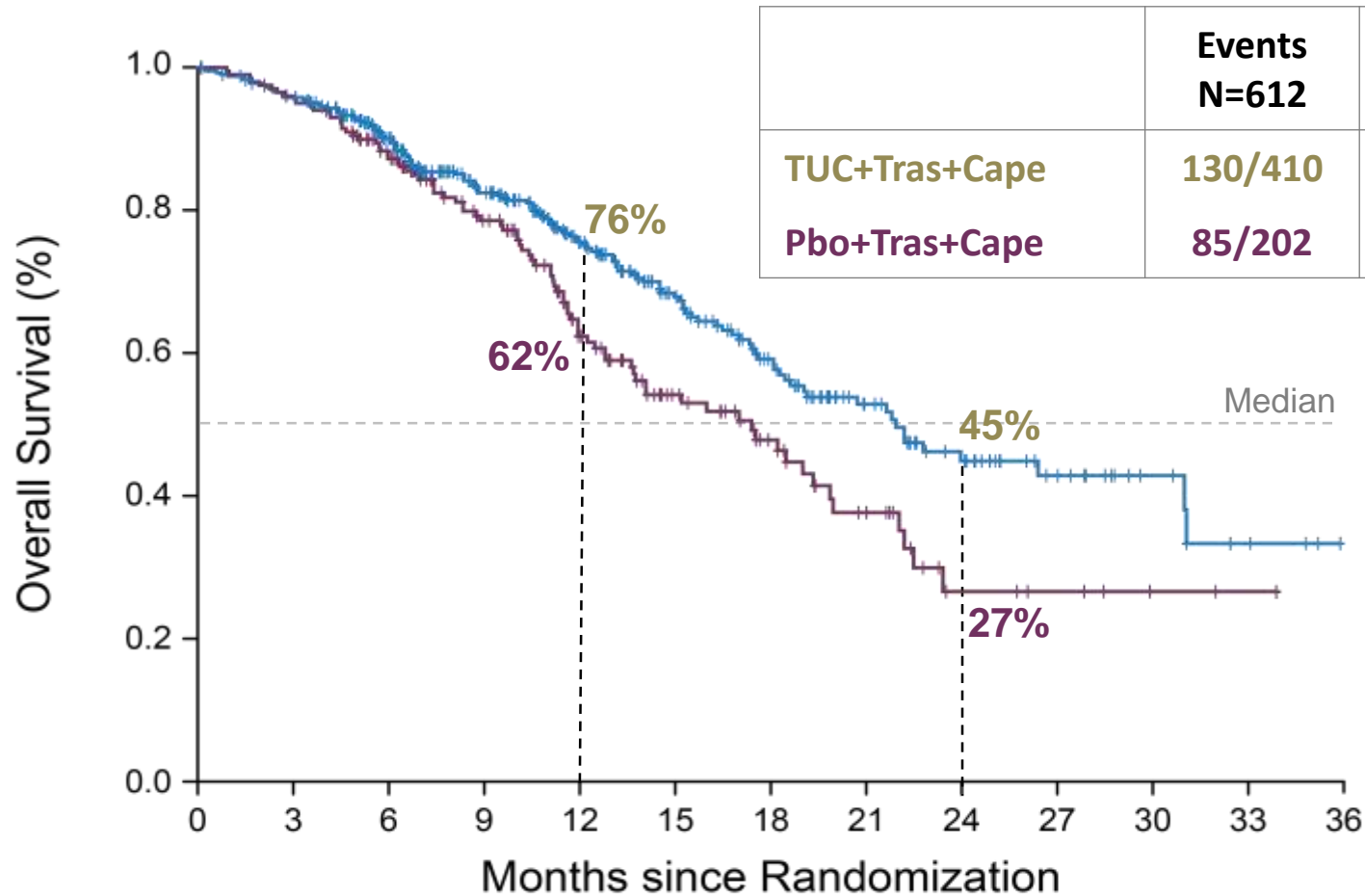
Placebo + Trastuzumab + Capecitabine (21-day cycle)

Placebo
+
Trastuzumab 6 mg/kg Q3W (loading dose 8 mg/kg C1D1)
+
Capecitabine 1000 mg/m² PO BID (Days 1-14)

*Stratification factors: presence of brain metastases (yes/no), ECOG status (0 or 1), and region (US or Canada or rest of world)

<https://clinicaltrials.gov/ct2/show/NCT02614794>

Overall Survival in the Total Study Population



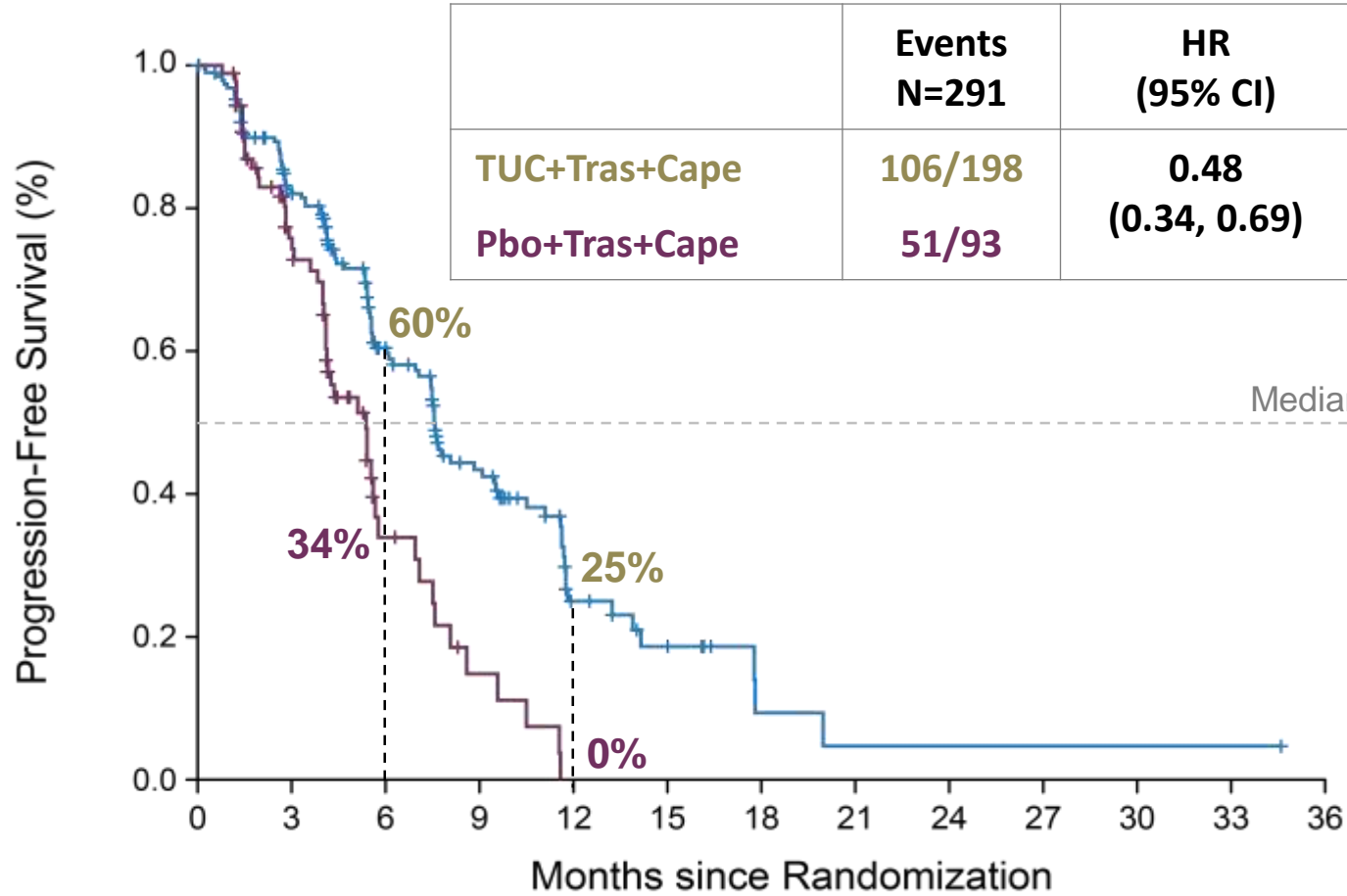
No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36
TUC+Tras+Cape 410	410	388	322	245	178	123	80	51	34	20	10	4	0
Pbo+Tras+Cape 202	202	191	160	119	77	48	32	19	7	5	2	1	0

Risk of death was reduced by 34% in the total population	
Two-year OS (95% CI):	
TUC+Tras+Cape	Pbo+Tras+Cape
45%	27%
(37, 53)	(16, 39)
Median OS (95% CI):	
21.9 months	17.4 months
(18.3, 31.0)	(13.6, 19.9)

Prespecified efficacy boundary for OS (P=0.0074) was met at the first interim analysis.

Data cut off: Sep 4, 2019

Progression-Free Survival for Patients with Brain Metastases



	Events N=291	HR (95% CI)	P Value
TUC+Tras+Cape	106/198	0.48 (0.34, 0.69)	<0.00001
Pbo+Tras+Cape	51/93		

No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36
TUC+Tras+Cape	198	144	78	45	14	8	2	1	1	1	1	1	0
Pbo+Tras+Cape	93	49	12	4	0	0	0	0	0	0	0	0	0

Risk of progression or death in patients with brain metastases was reduced by 52% in the total population

One-year PFS (95% CI):

TUC+Tras+Cape
25%
(17, 34)

Pbo+Tras+Cape
0%

Median PFS (95% CI):

7.6 months
(6.2, 9.5)

5.4 months
(4.1, 5.7)

Prespecified efficacy boundary for PFS_{BrainMets} (P=0.0080) was met at the first interim analysis.

Data cut off: Sep 4, 2019