

**Breast cancer in elderly patients  
(70 years and older):  
The University of Tennessee Medical  
Center at Knoxville 10 year experience**

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# Introduction

- ▶ Incidence of breast carcinoma increases with age, (~30% of new breast carcinoma cases being diagnosed in patients  $\geq 70$ y/o) (1)
- ▶ There is still a paucity of data on how breast cancer biology influences outcomes in elderly patients.

# Introduction

- ▶ A few studies showed that breast carcinoma in elderly patients have a higher probability of “favorable” tumor biology:
  - ▶ Hormone receptor positive (ER and/or PR positive)
  - ▶ HER2 negative breast carcinomas
  - ▶ Node-negative carcinomas (2, 3)
- ▶ However, in spite of a higher probability of “favorable” tumor biology, almost 50% of deaths from breast carcinoma occur in the elderly patient population ( $\geq 70$  y/o) (1).

1. SEER Cancer Statistics Factsheets: Breast Cancer. National Cancer Institute. Bethesda, MD, 2014 April 2014.

2. Apro, M. and H. Wildiers, *Ann Oncol*, 2012. **23 Suppl 6**: p. vi52-5.

3. Bauer, K.R., et al. *Cancer*, 2007. **109**(9): p. 1721-8.

# Introduction

- ▶ We have shown in two previous studies on the overall survival of Caucasian women that:
  - ▶ ER/PR/HER2 status was not predictive of overall survival of Caucasian female breast carcinoma patients
  - ▶ TNM stage was predictive of overall survival (4, 5)
- ▶ Objective of this study was to assess whether **ER/PR/HER2 subtype** and **TNM stage** of invasive breast carcinoma had significant impact on overall survival in the elderly subcohort of these patients ( $\geq 70$  y/o).

4. Ferguson, N.L., et al., Breast J, 2013. **19**(1): p. 22-30.

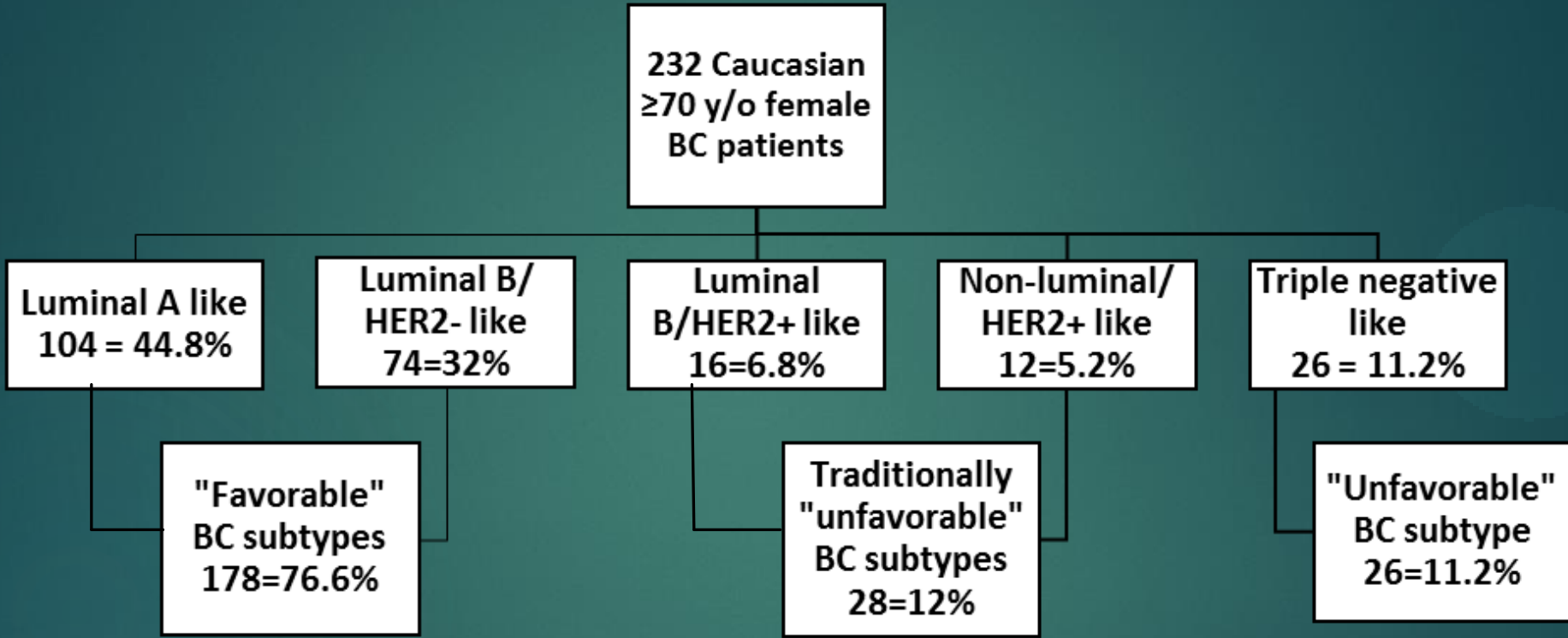
5. Orucevic, A., et al Breast J 2015. **21**(2): p. 147-154.

# Materials and methods

- ▶ Overall survival was assessed in a cohort of 232 elderly Caucasian female patients ( $\geq 70$  y/o) from our institution during a 10 year interval (01/1998-7/2008) when controlled for ER/PR/HER2 status, TNM stage and grade
  - ▶ Analyzed by Kaplan Meier curve and multivariate Cox regression analysis.
  - ▶ Last follow-up day was August 2013.

# Materials and methods

- ▶ Five ER/PR/HER2 subtypes classified per 2011 St. Gallen International Expert Consensus recommendations (6) were further subclassified into 3 subtypes:
  - ▶ - Traditionally considered “favorable” subtype-ER+/PR+/HER2-
  - ▶ - Traditionally considered “unfavorable” BC subtypes: HER2+ and triple negative





# Results: Clinicopathologic characteristics of invasive carcinomas

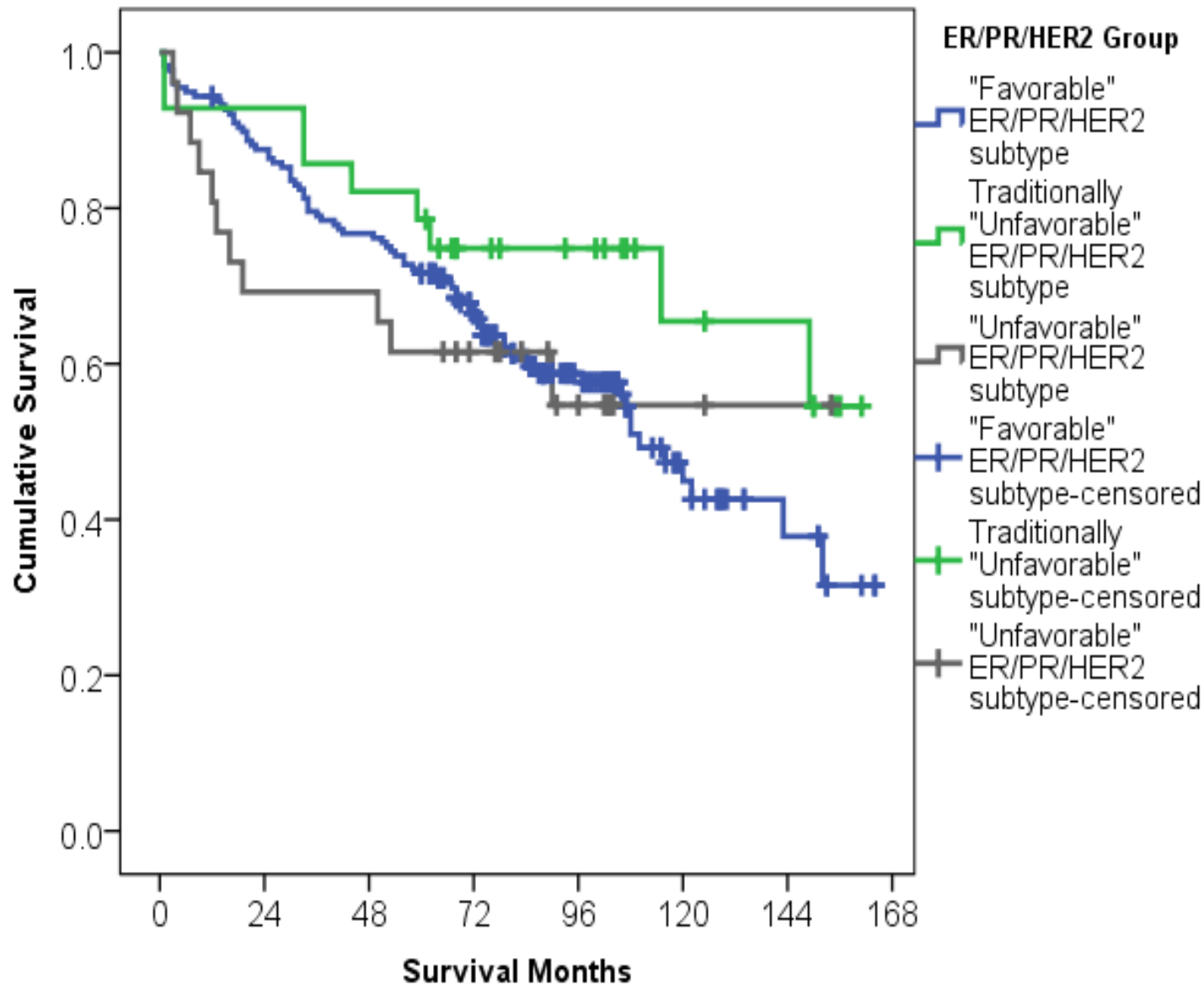
	Luminal A - like Traditionally "favorable" subtype	Luminal B /HER2- like Traditionally "favorable" subtype	Luminal B /HER2+ like Traditionally "unfavorable" subtype	Nonluminal / HER2+ like Traditionally "unfavorable" subtype	Triple negative-like Traditionally "unfavorable" subtype
<b>ER/PR/HER2 frequency</b>	104/232=44.8%	74/232=32%	16/232=6.8%	12/232=5.2%	26/232=11.2%
<b>Age (mean value)</b>	78.2	77	74.4	74.9	76.3
<b>Histologic type (most frequent)</b>	IDC	IDC	IDC	IDC	IDC
<b>Tumor grade</b>					
<b>Grade 1</b>	N=51	N=13	N=3	N=0	N=1
<b>Grade 2</b>	N=51	N=40	N=5	N=1	N=8
<b>Grade 3</b>	N=2	N=21	N=7	N=10	N=17
<b>Tumor size (mm) (mean value)</b>	19.37	23.97	17.25	24.27	23.5
<b>TNM stage</b>					
<b>Stage I</b>	N=58	N=29	N=10	N=7	N=12
<b>Stage II</b>	N=32	N=33	N=4	N=2	N=7
<b>Stage III</b>	N=8	N=10	N=2	N=3	N=5
<b>Stage IV</b>	N=6	N=2	N=0	N=0	N=2
<b>Survival months (mean value)</b>	72.2	78	101.1	72.9	64.8
<b>% of alive patients at the end of the study</b>	<b>55/104=53%</b>	<b>44/74=59%</b>	<b>11/16=69%</b>	<b>8/12=67%</b>	<b>15/26=58%</b>

Table legend: \*= mean value; \*\* = most frequent; IDC = Invasive ductal carcinoma



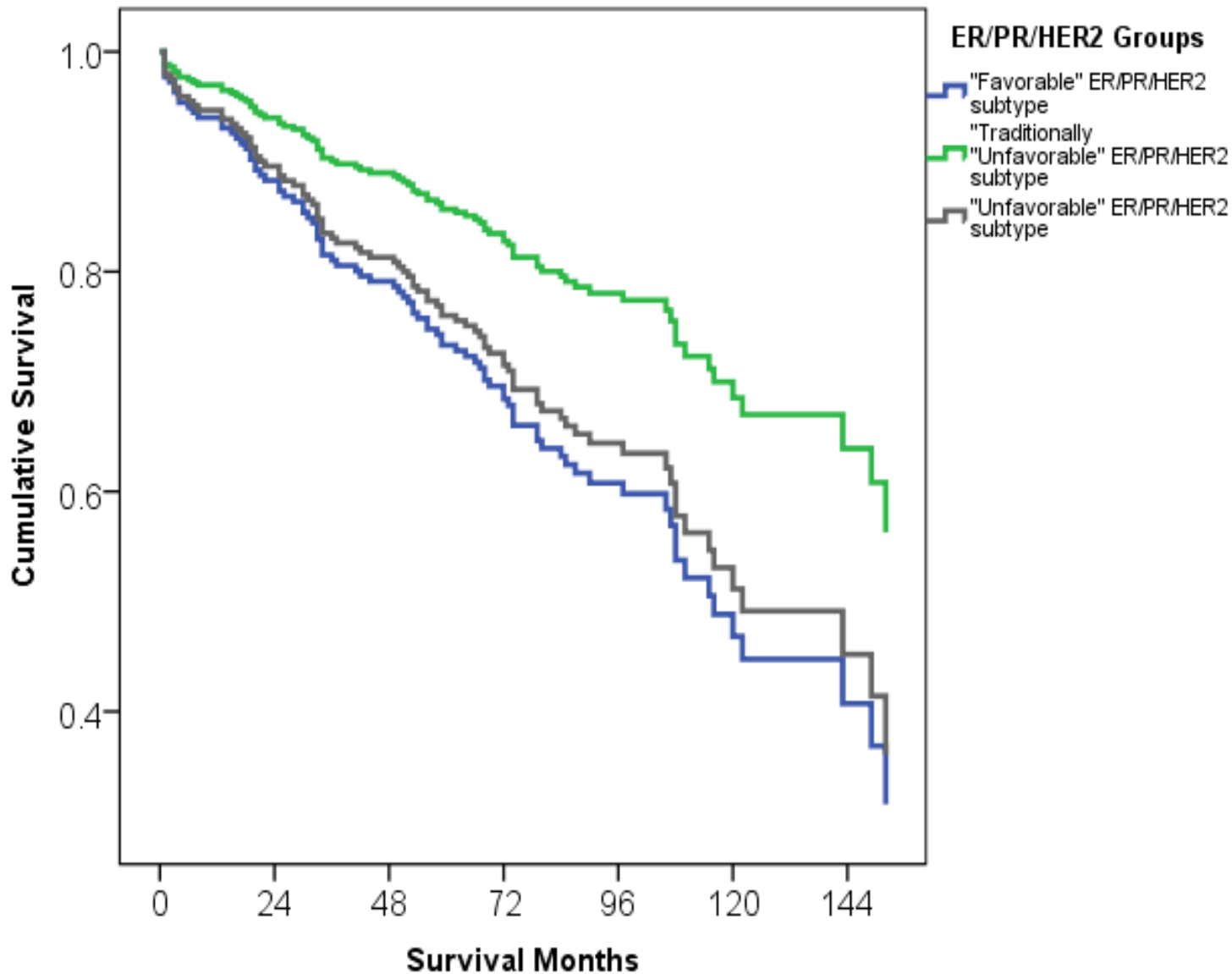
# Results

- ▶ The majority of our patients (178/232 = **76.8%**) were of the “**favorable**” breast carcinoma subtype (ER+ and/or PR+, HER2-), subdivided to the luminal A-like and luminal B/HER2 negative-like subtypes.
- ▶ **23.2%** patients were of traditionally considered “**unfavorable**” subtype:
  - ▶ 1) HER2+ subtype = 12% (28/232), subdivided to luminal B/HER2 positive-like subtype (16/232) and HER2 positive/non-luminal like subtype (12/232) and
  - ▶ 2) triple negative subtype = 11.2% (26/232)



Kaplan Meier curve:

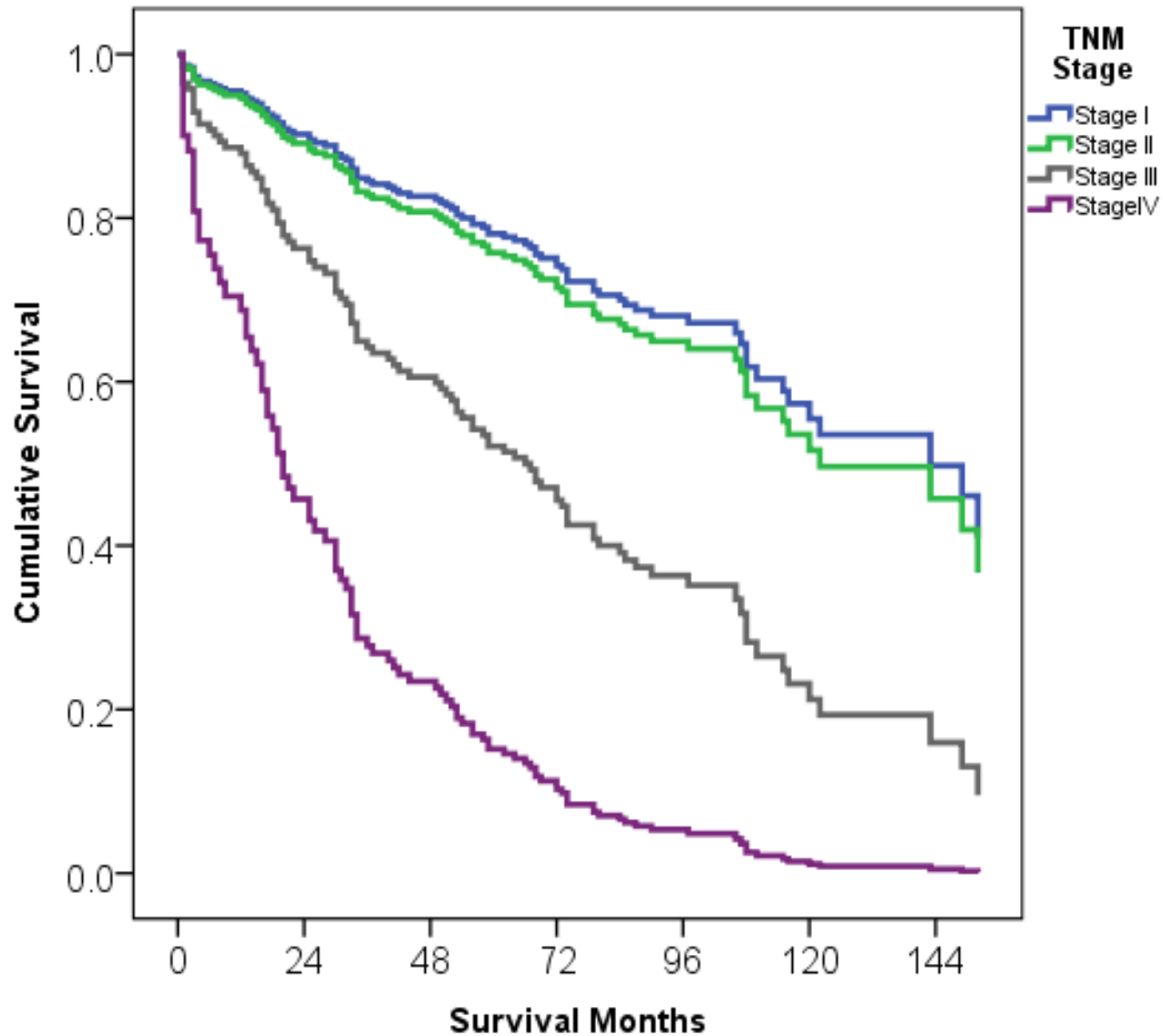
- ▶ Stratified by the ER/PR/HER2 "favorable" (luminal A-like and luminal B/HER2- like), traditionally "unfavorable" (luminal B/HER2 positive like and nonluminal/HER2+ like) and "unfavorable" triple negative subtype.
- ▶ ER/PR/HER2 subtype had no significant impact on overall survival ( $p=.285$ )



Cox regression analysis:

Overall survival curve output by ER/PR/HER2 subtype.

ER/PR/HER2 subtype was not significant predictor of overall survival ( $p=.095-.95$ )



Overall survival curve output by TNM stage:

**TNM stage was significant predictor of overall survival in stages III and IV ( $p < .001$ )**

There was no significant difference between TNM stage I and stage II in this analysis ( $p = .641$ ).

[Grade was not a significant predictor of overall survival ( $p = .47$ )]

# Treatment in the $\geq 70$ y/o age group and comparison to $\leq 40$ y/o age group

- ▶ The majority of patients underwent modified radical or total mastectomy (61.6% vs 67.9% in  $\leq 40$ y/o)
- ▶ Postsurgery treatment for  $\geq 70$  y/o in comparison to  $\leq 40$  y/o
  - ▶ 32.3% had radiation; (46.1%  $\leq 40$ y/o)
  - ▶ 21.4% received adjuvant chemotherapy (82%  $\leq 40$ y/o);
  - ▶ 57.2% ER+ patients received hormonal therapy (76.5% of  $\leq 40$ y/o).

# Summary of results

- ▶ We observed a trend for better overall survival in HER2+ breast carcinoma patients that were traditionally considered as “unfavorable” breast carcinoma subtype over patients in “favorable” breast carcinoma subtype (ER and/or PR+, HER2-);
  - ▶ Did not reach statistical significance.
- ▶ No ER/PR/HER2 subtype was significantly predictive of better overall survival.

# Summary of results

- ▶ **TNM stage** was significantly predictive of overall survival (advanced stages).
- ▶ These results were similar to our two previously published studies where ER/PR/HER2 status was not predictive of overall survival of Caucasian female breast carcinoma patients, irrespective of classification system used, while TNM stage was predictive of overall survival



# Discussion

- ▶ Possible causes for the results from our previous studies and now seen in the  $\geq 70$  y/o sub-cohort were attributed to:
  - ▶ The composition of our study population (we were only studying Caucasian female breast cancer patients)
  - ▶ Type of ER/PR/HER2 classification system used (St. Gallen breast carcinoma subtype classification or triple negative vs non-triple negative breast carcinoma subtype)
  - ▶ The time period of the study (1998-2008) when screening wherein diagnostics and treatment of breast carcinoma patients improved significantly over prior time periods.

# Discussion

- ▶ In at least two other different studies, elderly patients with “unfavorable” triple negative breast carcinoma phenotype had a better or the same outcome when compared to their corresponding younger cohort (7, 8).
- ▶ Better survival was seen in spite of significantly lower use of chemotherapy and radiotherapy in the elderly patients
  - ▶ Raises the possibility that the same “unfavorable” breast carcinoma subtype exhibit a different tumor biology in younger and older patients

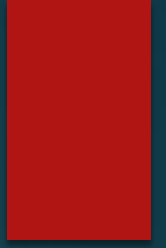
# Conclusions

- ▶ Our study on elderly Caucasian female breast carcinoma patients from our institution showed that:
  - ▶ ER/PR/HER2 status was not predictive of overall survival
  - ▶ TNM stage was predictive of overall survival
  - ▶ Results are similar to two of our previously published studies on Caucasian female breast cancer patients.

# Conclusions

- ▶ Standardized treatment recommendations for patients >70 years old are less strictly defined than for other age groups.
- ▶ Further studies (perhaps in a clinical trial setting) are warranted, may possibly reconcile and stratify given therapy with outcome.

Thank you



# References

- ▶ 1. SEER Cancer Statistics Factsheets: Breast Cancer. National Cancer Institute. Bethesda, MD, <http://seer.cancer.gov/statfacts/html/breast.html> 2014 April 2014 [cited 2015 4-8-15].
- ▶ 2. Aapro, M. and H. Wildiers, *Triple-negative breast cancer in the older population*. Ann Oncol, 2012. **23 Suppl 6**: p. vi52-5.
- ▶ 3. Bauer, K.R., et al., *Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California cancer Registry*. Cancer, 2007. **109**(9): p. 1721-8.
- ▶ 4. Ferguson, N.L., et al., *Prognostic value of breast cancer subtypes, Ki-67 proliferation index, age, and pathologic tumor characteristics on breast cancer survival in Caucasian women*. Breast J, 2013. **19**(1): p. 22-30.
- ▶ 5. Orucevic, A., Chen, J., McLoughlin, J., Heidel, R., Panella, T., Bell, J., *Is the TNM staging system for breast cancer still relevant in the era of biomarkers and emerging personalized medicine for breast cancer – an institution's 10 year experience* Breast J 2015. **21**(2): p. 147-154.
- ▶ 6. Goldhirsch, A., et al., *Strategies for subtypes--dealing with the diversity of breast cancer: highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011*. Annals of Oncology : Official Journal of the European Society for Medical Oncology / ESMO, 2011. **22**(8): p. 1736-1747.
- ▶ 7. Dreyer, G., et al., *Triple negative breast cancer: clinical characteristics in the different histological subtypes*. Breast, 2013. **22**(5): p. 761-6.
- ▶ 8. Thike, A.A., et al., *Triple negative breast cancer: outcome correlation with immunohistochemical detection of basal markers*. Am J Surg Pathol, 2010. **34**(7): p. 956-64.