HER2 POSITIVE BREAST CARCINOMA IN THE PRE AND POST ADJUVANT ANTI-HER-2 THERAPY ERA: A SINGLE ACADEMIC INSTITUTION EXPERIENCE IN THE SETTING OUTSIDE OF CLINICAL TRIALS

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INTRODUCTION

- HER2+ breast carcinoma (BC)
  - Considered "unfavorable" due to its aggressive nature and high mortality rate[1]
    - High tumor grade, high cell proliferation rate, high frequency of visceral metastasis
    - Often negative estrogen and progesterone receptors
- Adjuvant anti-HER2 therapy
  - FDA approved in 1998 for HER2+ metastatic disease
  - Used since 2005 for adjuvant treatment of operable HER2+ BC
  - In large randomized clinical trials (NCCTG N9831 and NSABP B-31)[2-6]
    - Reduces the risk of recurrence
    - Improves survival in patients

1. Ross, J.S., et al., 2009, The oncologist, 14(4): p. 320-368.
2. Slamon, D., et al.,, 2011, NEJM, 365(14): p. 1273-1283.
3. Seal, M.D., et al., 2012., Current oncology, 19(4): p. 197-201.
4. Rodrigues, M.J., et al., 2012, Annals of Oncology
5. Gianni, L., et al., 2011, The lancet oncology. 12(3): p. 236-244.
6. Perez, E.A., et al., 2011, Journal of clinical oncology29(25): p. 3366-3373.

OBJECTIVES

- Evaluate whether adjuvant anti-HER2 therapy has similar beneficial effect on survival outside of trials
  - Existing data from clinical trials
    - Highly controlled population of patients studied
    - Want to see if therapy is similarly beneficial in community-based practice
- HER2+BC in Caucasian females at our academic institution
  - Clinicopathologic characteristics
  - Measured their overall survival
    - Comparing the treatments that they received before or after 11/2005
      - Implementation date of treatment with adjuvant anti-HER2 therapy as standard practice[7]

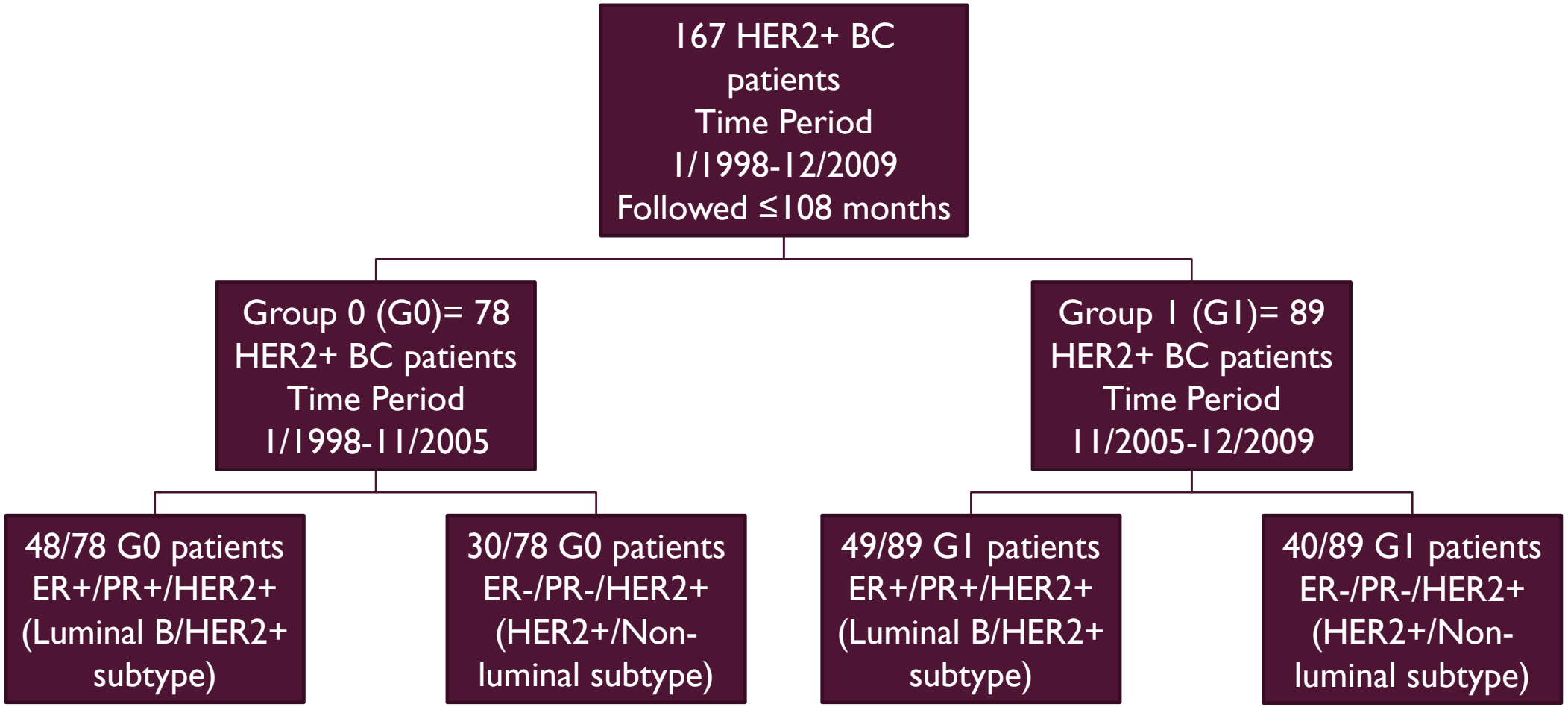
7. Romond, E.H., et al, 2005, N Eng J Med, 353(16): p. 1673-1684.

METHODS

- Stage I-III HER2+BC patients from 1998-2009
  - 167 patients
  - Divided into 2 groups
    - Group 0: patients diagnosed before 11/2005
      - 78/167 patients
    - Group 1: patients diagnosed after 11/2005
      - 89/167 patients
  - Further divided into HER2+ subtypes[8]

8. Goldhirsch A, et al. 2011. Ann Onc. 22(8): 1736-1746

METHODS


167 HER2+ BC patients
Time Period 1/1998-12/2009
Followed ≤108 months
Group 0 (G0)= 78 HER2+ BC patients
Time Period 1/1998-11/2005
Group 1 (G1)= 89 HER2+ BC patients
Time Period 11/2005-12/2009
48/78 G0 patients ER+/PR+/HER2+ (Luminal B/HER2+ subtype)
30/78 G0 patients ER-/PR-/HER2+ (HER2+/Non-luminal subtype)
49/89 G1 patients ER+/PR+/HER2+ (Luminal B/HER2+ subtype)
40/89 G1 patients ER-/PR-/HER2+ (HER2+/Non-luminal subtype)

RESULTS

HER2+ patient's grouping	Group 0 Luminal B /HER2+ subtype	Group 0 HER2+/Non-luminal subtype	Group 1 Luminal B /HER2+ subtype	Group 1 HER2+/Non-luminal subtype
HER2+ subtype frequency	48/78 = 61.5%	30/78 = 38.5%	49/89 = 55.1%	40/89 = 44.9%
Age*	57.1	59.4	54.6	57.5
Type of BC**	IDC	IDC	IDC	IDC
Grade**	3	3	3	3
Size in mm*	25.6	22.5	22.9	33.1
TNM Anatomic stage	Stage III	Stage I	Stage I	Stage II
Survival months*	78.75	69.63	80	78.73
Alive patients - frequency	21/48 = 43.8%	15/30 = 50.0%	43/49 = 87.8%	34/40 = 85.0%

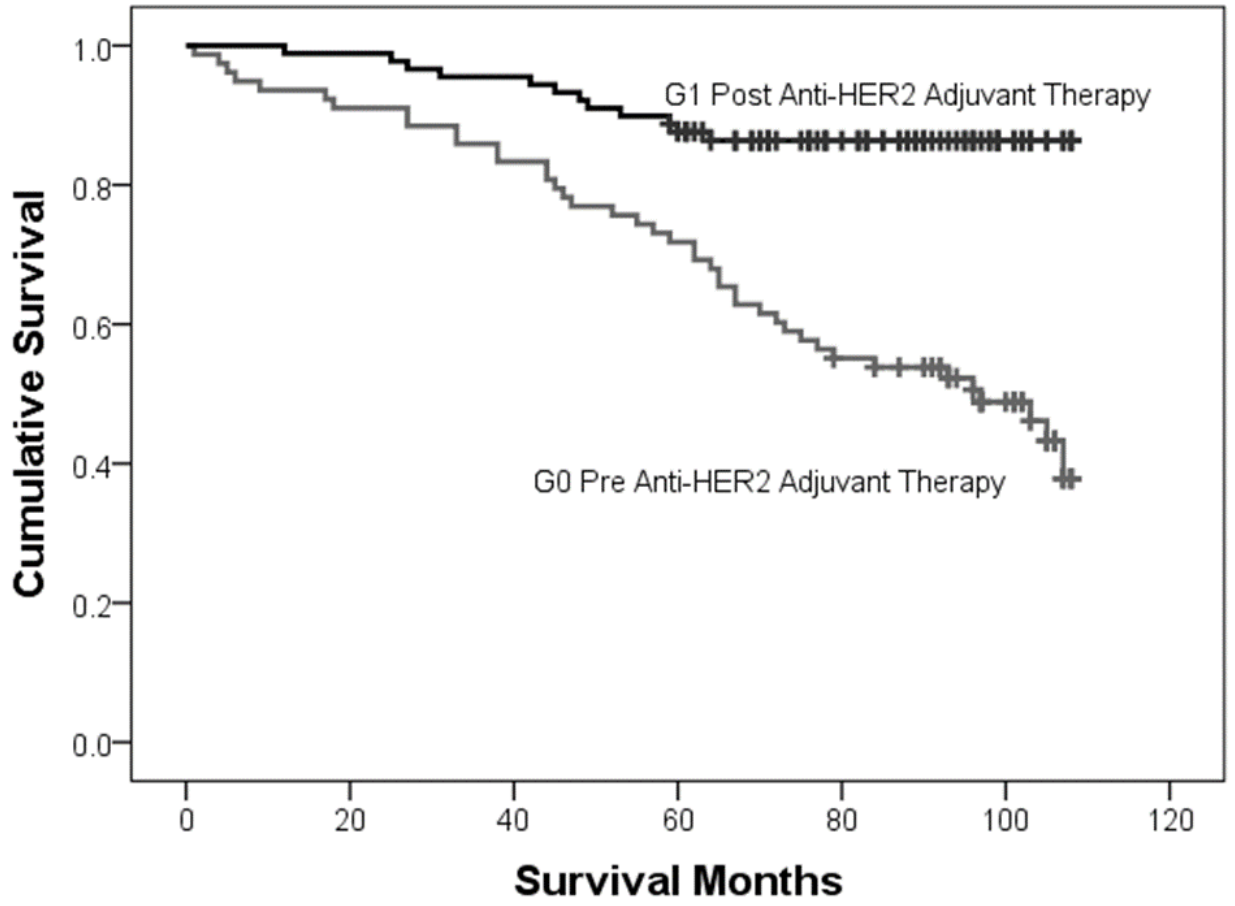
RESULTS: TREATMENTS

HER2+ patient's grouping	Group 0 Luminal B /HER2+ subtype	Group 0 HER2+/Non-luminal subtype	Group 1 Luminal B /HER2+ subtype	Group 1 HER2+/Non-luminal subtype
Most frequent surgery type	MRM 25/48 = 52.1%	MRM 20/30 = 66.6%	MRM 20/49 = 40.8%	MRM 20/40 = 50.0%
Radiation therapy received	27/46 = 58.6%	10/29 = 34.4 %	26/47 = 55.3%	21/40 = 52.5%
Hormonal therapy received	39/48 = 81.3%	0/30 = 0%	43/49 = 87.8%	0/40 = 0%
Chemotherapy received	31/48 = 64.6%	21/30 = 70.0%	31/47 = 66.0%	38/40 = 95.0%
Anti-HER2 therapy received	5/48 = 10.4%	7/30 = 23.3%	30/49 = 61.2%	35/40 = 87.5%

RESULTS

- Clinicopathologic characteristics
  - Mostly high grade
  - >20 mm in size
- G0: 53.8 % mortality at 108 months
- G1
  - 73% received adjuvant anti-HER2 therapy
  - 13.5% mortality at 108 months ($p<0.001$)
- ER/PR phenotype: No significant impact on OS ($p=0.672$)

RESULTS



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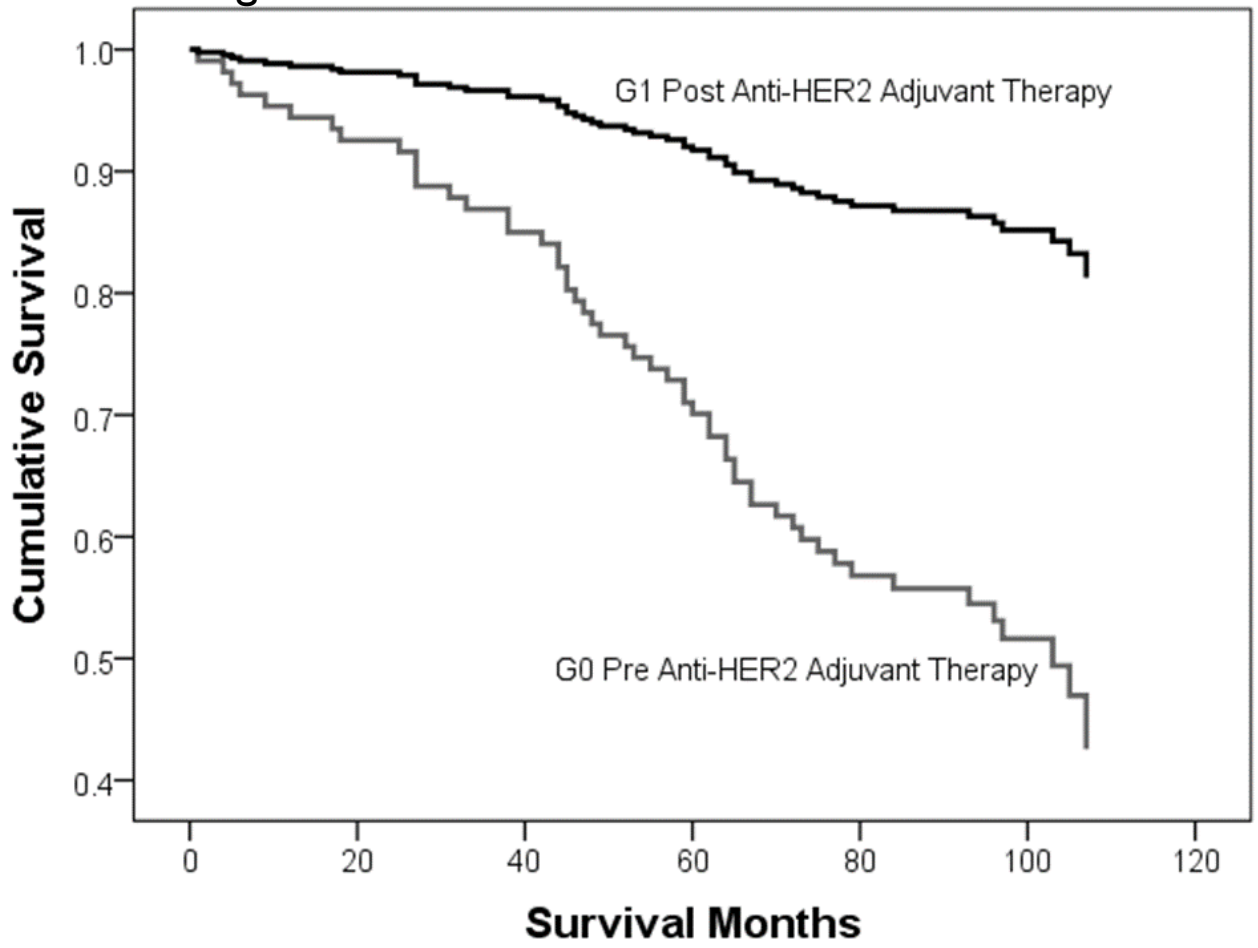
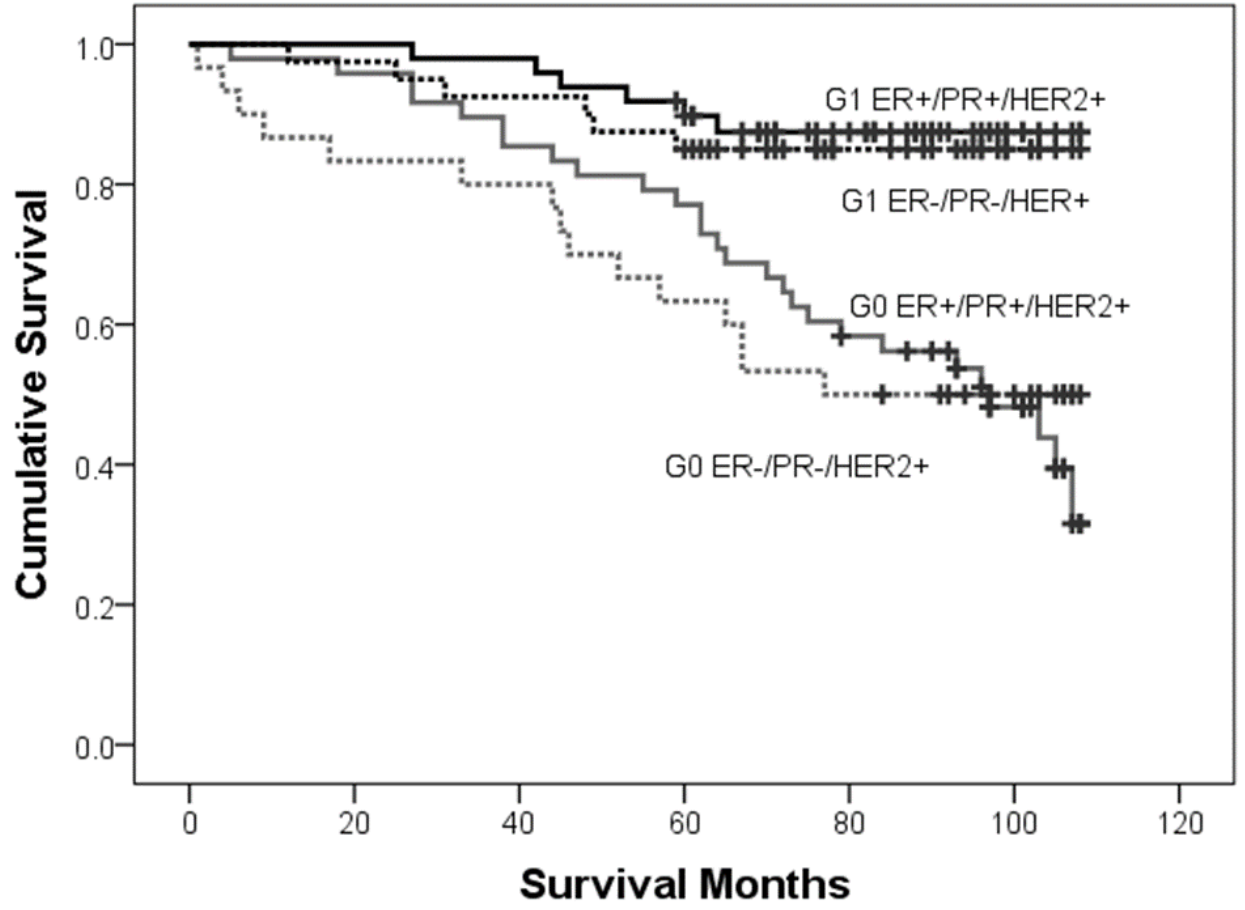
RESULTS

Controlled for age, grade, and TNM stage



RESULTS



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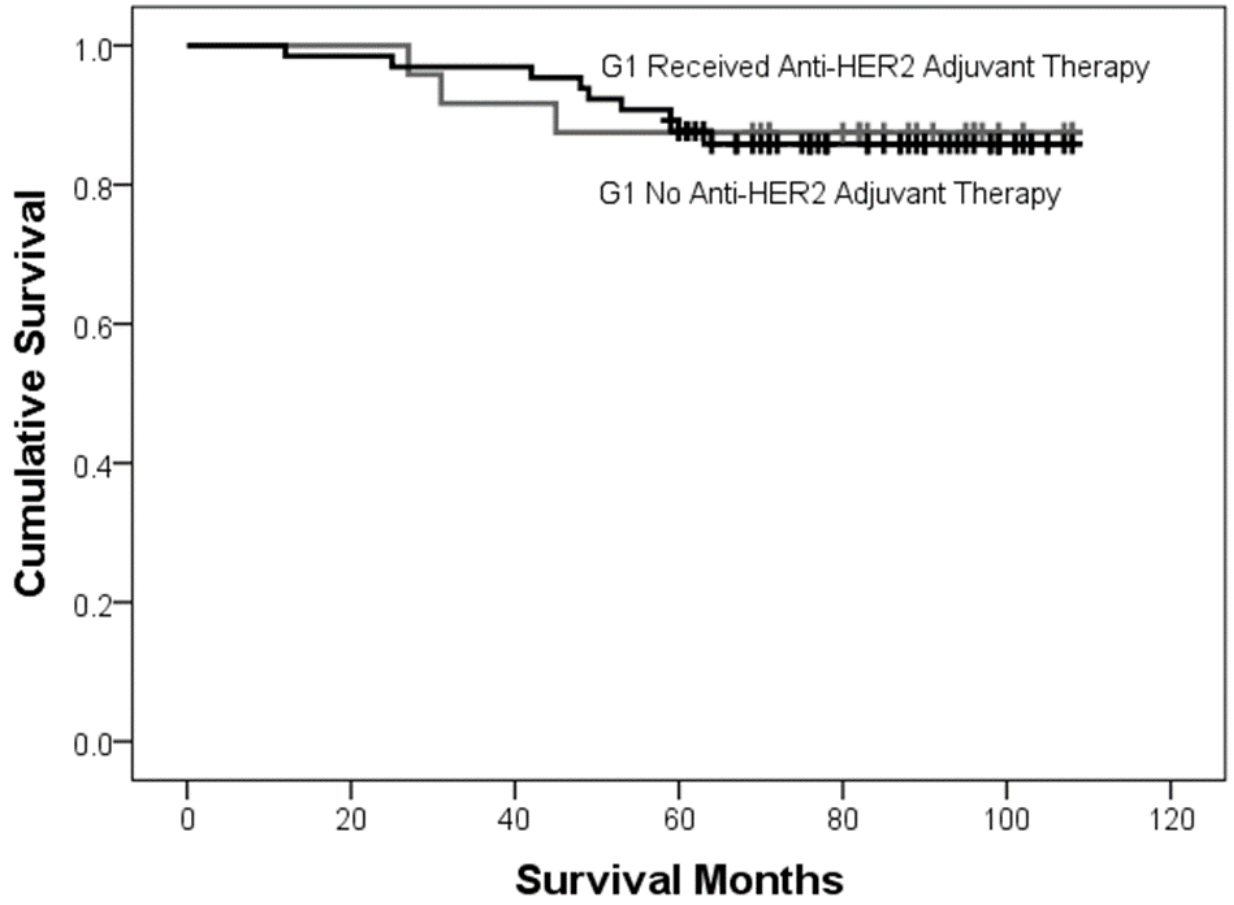
RESULTS



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CONCLUSIONS

- Overall survival
  - Significantly improved in G1 versus G0
- Supports adjuvant anti-HER2 therapy as a valuable treatment for significantly improving outcomes in HER2+ breast carcinoma in the settings outside of clinical trials
- Community-based data on overall survival emerging now

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- 2. Slamon, D., et al., Adjuvant trastuzumab in HER2-positive breast cancer. The New England journal of medicine, 2011. 365(14): p. 1273-1283.
- 3. Seal, M.D., et al., Outcomes of women with early-stage breast cancer receiving adjuvant trastuzumab. Current oncology (Toronto, Ont.), 2012. 19(4): p. 197-201.
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- 6. Perez, E.A., et al., Four-year follow-up of trastuzumab plus adjuvant chemotherapy for operable human epidermal growth factor receptor 2-positive breast cancer: joint analysis of data from NCCTG N9831 and NSABP B-31. Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 2011. 29(25): p. 3366-3373.
- 7. Romond, E.H., et al., Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. The New England journal of medicine, 2005. 353(16): p. 1673-1684.
- 8. 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, 2011. 22(8): 1736-1747