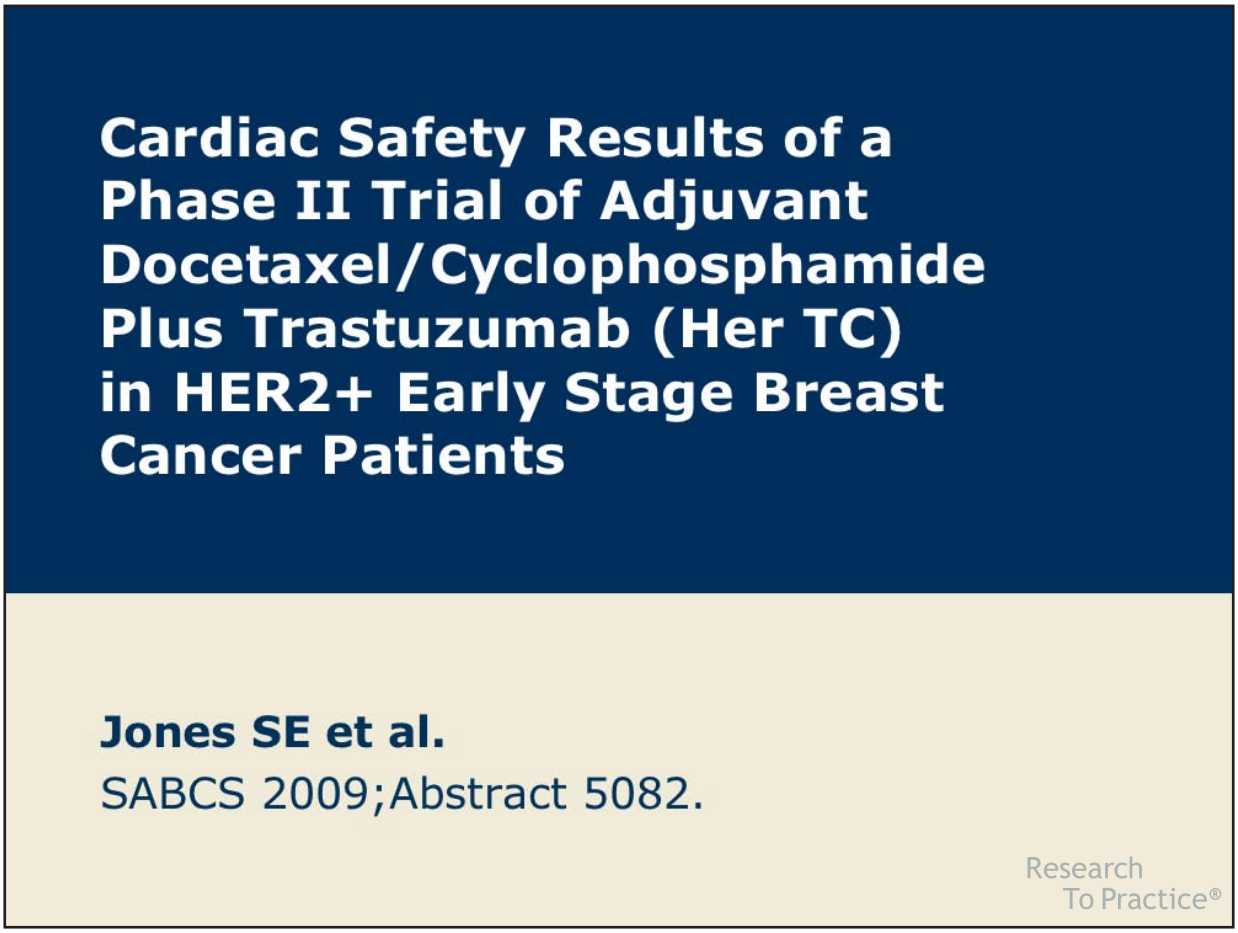
Cardiac Safety Results of a Docetaxel/Cyclophosphamide/ Trastuzumab Combination in Patients with HER2-Positive Early-Stage Breast Cancer

Presentation discussed in this issue:

Jones SE et al. **Cardiac safety results of a Phase II trial of adjuvant docetaxel, cyclophosphamide plus trastuzumab in Her2+ early stage breast cancer patients.** San Antonio Breast Cancer Symposium 2009;**Abstract 5082**.

Slides from a presentation at SABCS 2009



Introduction

- Phase III US Oncology Research trial 9735 demonstrated that docetaxel/cyclophosphamide (TC) was significantly superior to doxorubicin/cyclophosphamide in patients with early breast cancer (BC) in the adjuvant setting (*JCO* 2009;27:1177).
  - Disease-free survival (median 7 yrs): 81% vs 75%, p=0.033
  - Overall survival: 87% vs 82%, p=0.032
- Addition of anthracycline therapy to trastuzumab treatment is associated with an increase in the risk of cardiotoxicity.
- Phase II trial demonstrated that trastuzumab combined with TC (Her TC) is a nonanthracycline-containing regimen that was well tolerated as an adjuvant therapy in patients with HER2+ early BC (SABCS 2008;Abstract 2111).
- **Current study objective:**
  - Determine the cardiac safety of Her TC in patients with HER2+ early breast cancer.

Jones SE et al. SABCS 2009;Abstract 5082.

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Phase II Trial of Her TC in Patients with HER2+ Early BC

Accrual: 263
(260 patients comprised cardiac safety population)

Eligibility
Invasive BC
T1 or T2 Tumor size
N0 or N1 Lymph node status
Her2+ (IHC 3+ or FISH+)
LVEF ≥ 50% by MUGA or ECHO

→ **Docetaxel (T)**
Cyclophosphamide (C)
Trastuzumab (H)

T = 75mg/m² IV q 3 weeks x 4
C = 600mg/m² IV q 3 weeks x 4
H = 4mg/Kg Wk 1 →
2mg/Kg/week Wk 2-12 →
6mg/Kg q 3 weeks Wk 13-52

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Methods

- LVEF assessed at baseline and then q3 months.
- Trastuzumab held for any of the following reasons:
  - ≥15% decline in absolute LVEF from baseline
  - ≥10% decline in absolute LVEF from baseline and current LVEF ≥1% lower than lower limit of normal.
- Repeat MUGA (or ECHO) in 4 weeks for any of the following reasons:
  - Trastuzumab held for the above reason
  - LVEF >5% below lower limit of normal
- If criteria for continuation are met at repeat MUGA then trastuzumab is resumed.
- If trastuzumab held for 2 consecutive periods or for a total of 3 holds, then trastuzumab may be discontinued.

Jones SE et al. SABCS 2009;Abstract 5082.

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Treatment Outcomes (1-year follow-up)

Outcome	n (%)
Normal completion	206 (78.3)
Remains on treatment	11 (4.2)
Study discontinuations	46 (17.5)
Reason for discontinuation	
Patient request	12 (4.5)
Disease progression on study	1 (0.4)
Other	5 (1.9)
Lost to follow-up	1 (0.4)
Toxicity	27 (10.3)

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Cardiac Events and Parameters (n = 260)

- Number of patients with cardiac toxicity leading to discontinuation: 11 (4.2%)
  - LVEF dysfunction: 9 (3.4%)
  - Brachycardia/syncope: 1 (0.4%)
  - Chest pain: 1 (0.4%)
- Number of patients with absolute ↓LVEF ≤ 50% any time during treatment: 16 (6.1%)
- Median LVEF at baseline: 64%
- Median LVEF at ≥ 10 months: 63%
- No cases of CHF were observed.

Jones SE et al. SABCS 2009;Abstract 5082.

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Conclusions

- Cardiac events are uncommon with Her TC regimen administered to patients with HER2+ early BC.
  - Sixteen patients (6.1%) experienced LVEF decline to ≤ 50% any time during treatment.
  - Nine patients (3.4%) discontinued trastuzumab due to decrease in LVEF.
  - No cases of CHF were observed.

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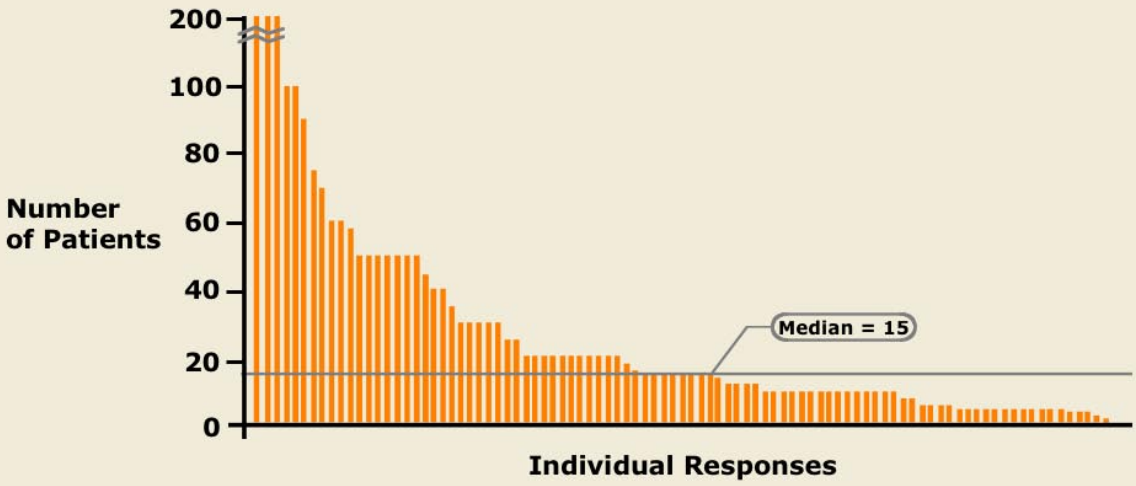
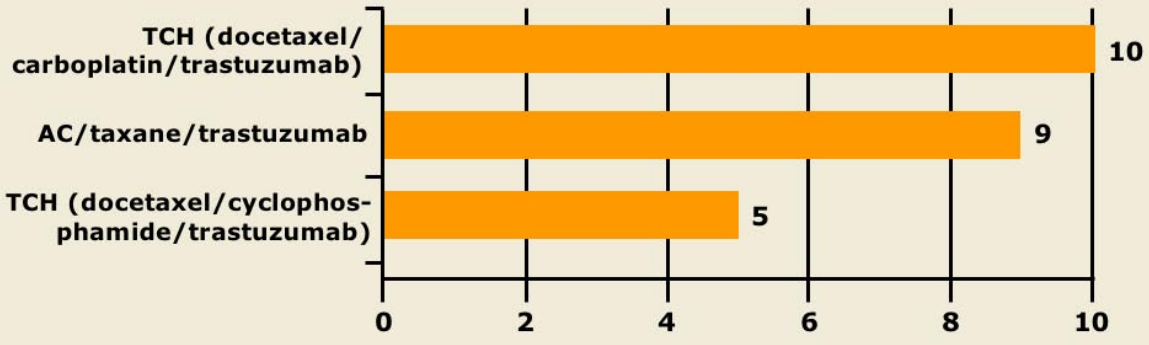
In the past year, how many patients have you treated with adjuvant trastuzumab?



Responses from 94 of 100 physicians who have treated patients with adjuvant trastuzumab in the past year.

Patterns of Care in Breast Cancer — Survey of 100 US-based Medical Oncologists.

How many patients have you treated with each of the following trastuzumab regimens in the adjuvant setting? (median)



Patterns of Care in Breast Cancer — Survey of 100 US-based Medical Oncologists.