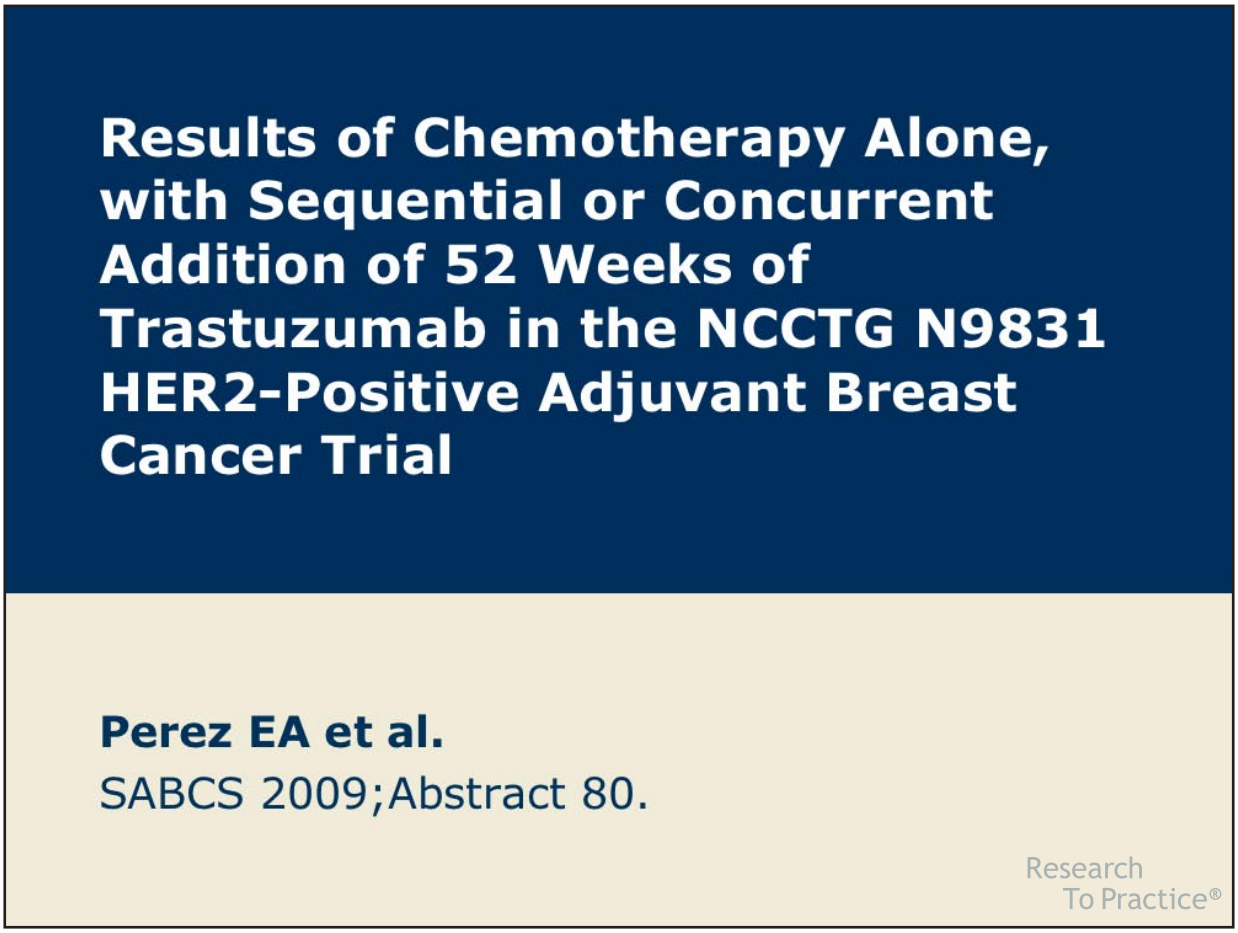
NCCTG-N9831: Adjuvant Chemotherapy Alone or with Sequential or Concurrent Addition of 52 Weeks of Trastuzumab in HER2-Positive Breast Cancer

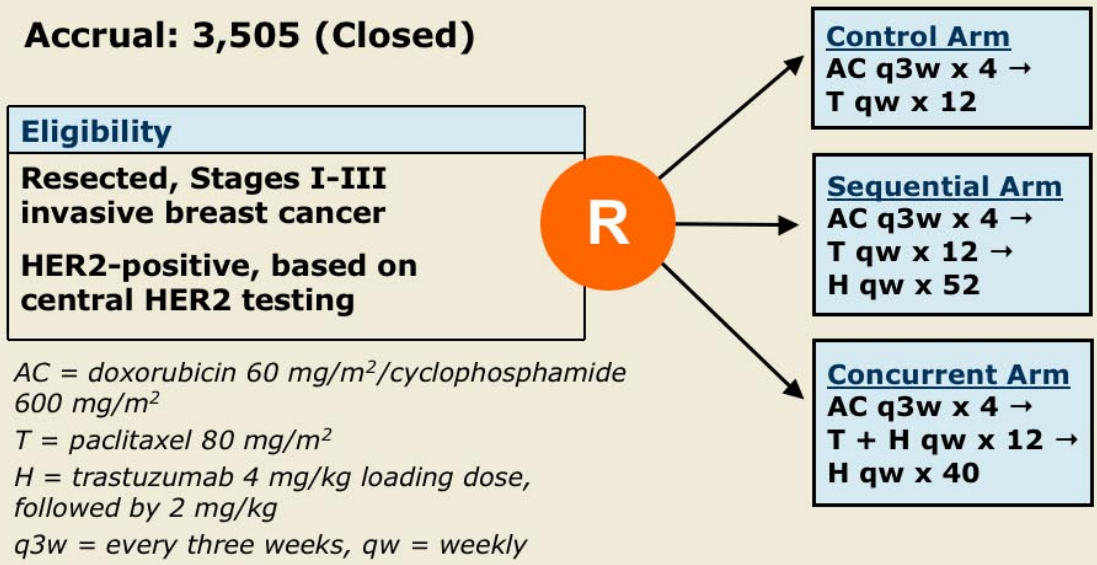
Presentation discussed in this issue:

Perez EA et al. **Results of chemotherapy alone, with sequential or concurrent addition of 52 weeks of trastuzumab in the NCCTG N9831 HER2-positive adjuvant breast cancer trial.** SABCS 2009;**Abstract 80**.

Slides from a presentation at SABCS 2009



NCCTG N9831: Trial Schema



AC = doxorubicin 60 mg/m^2/cyclophosphamide 600 mg/m^2

T = paclitaxel 80 mg/m^2

H = trastuzumab 4 mg/kg loading dose, followed by 2 mg/kg

q3w = every three weeks, qw = weekly

Source: Perez EA et al. SABCS 2009;Abstract 80.

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Introduction

- 2000 → NCCTG N9831 study is activated.
  - Objective is to assess the efficacy and cardiotoxicity of chemotherapy administered concurrently or sequentially with trastuzumab (H) in patients with HER2+ breast cancer (BC).
- 2005 → N9831 and NSABP-B-31 joint data published establishing H as standard treatment for patients with HER2+ early stage BC (*NEJM* 2005;353:1673).
- 2008 → Three-year cumulative incidence of NYHA class III or IV congestive heart failure or sudden cardiac death is published (*JCO* 2008;26:1231):
  - 0.3% control arm, 2.8% sequential arm, 3.3% concurrent arm
- 2009 → Efficacy comparisons between the sequential and concurrent study arms are reported.

Source: Perez EA et al. SABCS 2009;Abstract 80.

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Disease-Free Survival (median follow-up > 5 years)

	AC → T	AC → T → H	*p*-value
Disease free survival rate[1]	71.9%	80.1%	0.0005
Pairwise Comparison	**Number of events**	**Adjusted hazard ratio**	***p*-value**
AC → T (n=1,087) AC → T → H (n=1,097)	222 164	0.67	<0.0001

[1]Second interim analysis.

	AC → T → H	AC → T+H → H	*p*-value
Disease free survival rate[2]	79.8%	84.2%	0.0190[3]
Pairwise Comparison	**Number of events**	**Adjusted hazard ratio**	***p*-value**
AC → T → H (n=954) AC → T+H → H (n=949)	174 138	0.75	0.0134[3]

[2]First interim analysis, sequential arm censored during concurrent arm closure;
[3]Statistical significance preset at 0.00116.

Source: Perez EA et al. SABCS 2009;Abstract 701.

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Overall Survival (median follow-up > 5 years)

Pairwise Comparison	Number of events	Unadjusted hazard ratio	*p*-value
AC → T vs AC → T → H (n=2,184)	220	0.86	0.281
AC → T → H vs AC → T+H → H (n=1,903)*	168	0.79	0.135

*Patients on the sequential arm were excluded when the concurrent arm was closed.

Source: Perez EA et al. SABCS 2009;Abstract 701.

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Conclusions

- DFS is significantly improved with the addition of 52 weeks of trastuzumab to AC → T.
  - 5-year DFS: 72% (control) vs 80% (sequential) vs 84% (concurrent)
- The risk of an event is significantly reduced by 33 percent by sequential addition of trastuzumab to chemotherapy.
  - Number of events: 222 (control) vs 164 (sequential)
- A strong trend exists for a 25 percent reduction in the risk of an event when trastuzumab is administered concurrently with taxane chemotherapy relative to sequentially.
- Adjuvant trastuzumab should be incorporated in a concurrent fashion with the taxane portion of chemotherapy (AC → T + H → H).

Source: Perez EA et al. SABCS 2009;Abstract 80.

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