PRADA Commentary
The Role of Cardioprotection in Breast Cancer Therapy
Cardiac Dysfunction

Study Rationale and Methodology
Results and Interpretation
Questions and Implications

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Disclosures

• Investigator-initiated award from Pfizer, Inc.

• Consultant for Bristol Myers Squibb

• Research funding from National Institutes of Health
Study Rationale

• Highly important clinical problem
  – Growing burden of CV disease in breast cancer

HF and Cardiomyopathy Cumulative Incidence

Percent Mortality

Study Methodology

• Study Population
  – Single-center
  – Low burden of CV risk factors (1.5% diabetes, 6.3% HTN)
  – All received epirubicin, 22% received trastuzumab

• Study Design
  – Double-blind, placebo-controlled
  – Stratification according to anthracycline dose & trastuzumab

• Primary Outcome Measure – LVEF
  – Derived via Cardiac Magnetic Resonance imaging
  – Highly reproducible and precise
  – LVEF is essentially a surrogate measure
Results and Interpretation

• Changes in LVEF at 10 to 64 weeks
  – Statistically significant, but very modest attenuation of LVEF changes with candesartan, on the order of 2-3%
  – No attenuation of LVEF changes with metoprolol
  – No patients developed heart failure or substantial LVEF declines
Questions

• What are the distinct biologic and physiologic effects of each therapy? Why was there no effect of metoprolol? Would carvedilol have a different result?

• What study population should we target? Higher CV risk?

• What is the optimal primary outcome measure? What is valid and clinically meaningful in cardio-oncology?

• Are there effects on secondary outcome measures? How can we better understand potential benefit?

• What is the effect of longer follow-up time? Will we see more events?
Implications

• Although a positive effect of candesartan may exist, additional research is of necessity prior to clinical practice implementation
  – Larger sample size
  – Extended follow-up time

• This study highlights the critical need to develop a robust consensus definition of cardiotoxicity and a methodology to identify high CV risk patients in cardio-oncology
EXTRA SLIDES
# Cardiotoxicity Reported in Clinical Trials

- More profound changes reported in prior trials

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<th>Trial</th>
<th>N</th>
<th>Median Followup (yrs)</th>
<th>EF Decline (%)</th>
<th>NYHA III/IV HF or Death (%)</th>
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