Collaboration with Cardiology
The Oncologists’ Perspective and Needs

Moderator: Durand
Panelists: Susan Dent, MD, FRCPC and Weiss

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MD Anderson Cancer Center
Cancer and Heart Disease – Common Risk Factors

Case Study: Mrs. B.R

- 75 y.o post-menopausal women seen by the oncologist with a recent diagnosis of stage I breast cancer: ER +/PR -/ HER2 +
- Oncologist recommends adjuvant systemic therapy with weekly paclitaxel x 12 and trastuzumab q 3 weeks x one year; radiation and the endocrine therapy (aromatase inhibitor) x 5 years
- Baseline echo: LVEF= 50 % (borderline)
- PMH
  - atrial fibrillation x 10 years – on coumadin with stable INR (2.2)
  - Borderline hypertension (160/95) (at home 140/90)
  - hypercholesterolemia
  - Meds: coumadin, metoprolol (rate control), lipitor
Oncologists Perspective

- Should I be concerned about her cardiac risk factors?
- Is it safe to treat her with chemotherapy/trastuzumab/aromatase inhibitors?
- Are there any preventative strategies we could use?
- What about coumadin? Would you switch her to a NOAC?
Cardiologist Perspective

- What is her risk of breast cancer recurrence?
- Is trastuzumab a necessary component of her cancer treatment?
- Given her cardiac risk factors would tamoxifen be a reasonable choice for endocrine therapy vs an aromatase inhibitor?
- Are there any differences in Selective vs Non-Selective Beta Blockers?
Optimize Cardiac Health

Best Cancer Care
What we don’t know....

- Long term sequelae of modern cancer agents in non–clinical trial patients (registry data)
- Cardiotoxicity in patients exposed to multiple cancer drugs
- Cardiac monitoring long term (survivors)
- Monitoring of patients on long term cancer therapy (e.g. pertuzumab/trastuzumab in metastatic breast cancer)
- If cardiac medication (primary prevention) is started when do you stop?
Save the Date

Global Cardio-Oncology Summit 2017
September 20-21, 2017
London, UK

Additional details to follow.

British Cardio-Oncology Society
BC-OS.org

Topics include:
• How to deliver a Cardio-Oncology service
• Training in Cardio-Oncology
• eHealth and Cardio-Oncology
• How do I measure the quality of my service?
• Role of primary care in cancer survivors
• Immunotherapy and emerging cardiotoxicity
• Personalised medicine & genetics
• EP session – who should have ablation, ICDs, CRT?
• Anticoagulation and antithrombotic (AF, ACS)
Binding to specific adrenergic receptors, β-blockers inhibit cancer cell migration and metastasis, suggesting a novel targeted therapeutic application in protecting against breast cancer disease progression.

Powe, D. G. & Entschladen, F. Nature Reviews Clinical Oncology 8, 511-512 (2011)
Triple Negative and Estrogen Receptor Positive outcomes

Fig 1. (A) Relapse-free survival (RFS) and (B) overall survival (OS) in patients with triple-negative breast cancer. (C) RFS and (D) OS in patients with estrogen receptor-positive breast cancer.
Baseline Hypertensive BC Patients Treated with Beta Blockers Live Longer

Figure 1a: Hypertensive BC patients therapeutically treated with beta-blockers showed significantly (p=0.022) longer times before acquiring metastases compared to non-treated patients.

Figure 1b: Hypertensive BC patients receiving beta-blocker therapy showed significantly (p=0.011) improved 10 year survival rates compared to non-treated patients.
Open-label randomized study of IDC patients with EF <40% on long-term metoprolol (>1 year).
Patients receiving ACE inhibitors; follow-up 12 months.

Effects of Carvedilol in Patients With Persistent LVD Despite Continuous Metoprolol

- At 12 months, carvedilol patients had mean EF increase of 7 units vs -0.8 units in metoprolol patients

Switched to carvedilol (n=14); mean dose, 74 mg
Continued on metoprolol (n=16); mean dose, 142 mg
### Major Trials of β-Blockade in Heart Failure

<table>
<thead>
<tr>
<th></th>
<th>Patients (n)</th>
<th>Follow-up (yrs.)</th>
<th>Target dose (total/day)</th>
<th>Mean dose achieved (total/day)</th>
<th>Effects on outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIBIS</td>
<td>641</td>
<td>1.9</td>
<td>5 mg (total/day)</td>
<td>3.8 mg (total/day)</td>
<td>All-cause mortality: NS</td>
</tr>
<tr>
<td>CIBIS-II</td>
<td>2647</td>
<td>1.3</td>
<td>10 mg (total/day)</td>
<td>7.5 mg (total/day)</td>
<td>All-cause mortality: ↓34% (P &lt; .0001)</td>
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<tr>
<td>MDC</td>
<td>383</td>
<td>1</td>
<td>100 to 150 mg (total/day)</td>
<td>108 mg (total/day)</td>
<td>Death or need for transplant (primary endpoint): NS</td>
</tr>
<tr>
<td>MERIT-HF</td>
<td>3991</td>
<td>1</td>
<td>200 mg (total/day)</td>
<td>159 mg (total/day)</td>
<td>All-cause mortality: ↓34% (P = .0062)</td>
</tr>
<tr>
<td>US Carv trials†</td>
<td>1094</td>
<td>7.5 mo.</td>
<td>50 to 100 mg (total/day)</td>
<td>45 mg (total/day)</td>
<td>All-cause mortality*: ↓65% (P = .0001)</td>
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<tr>
<td>ANZ Trial</td>
<td>415</td>
<td>1.5</td>
<td>50 mg (total/day)</td>
<td>41 mg (total/day)</td>
<td>Death or all-cause hospitalization: ↓26% (P = .02)</td>
</tr>
</tbody>
</table>

*Not a planned endpoint.
†Carvedilol is the only agent approved by the FDA for the treatment of mild to moderate heart failure.
Patients receiving diuretics, ACE inhibitors, ± digoxin; follow-up 6 months; placebo (n=84), carvedilol (n=261). *Multicenter Oral Carvedilol Heart Failure Assessment.

### Carvedilol Dose-Response Trial (MOCHA*):
**Effect on Ejection Fraction and Mortality**

![Changes in LVEF](chart)

- Placebo
- 6.25 mg bid
- 12.5 mg bid
- 25 mg bid

Δ LVEF (EF units)

$P<.001$

‡$P<.05$ vs placebo.
Carvedilol Dose-Response Trial (MOCHA*): Effect on Mortality and Morbidity

**Mortality†**

- Placebo
- Carvedilol: 6.25 mg bid, 12.5 mg bid, 25 mg bid

Mean number/subject

- Cardiovascular Hospitalizations

- Placebo
- Carvedilol: 6.25 mg bid, 12.5 mg bid, 25 mg bid

Mortality (%)

Patients receiving diuretics, ACE inhibitors, ± digoxin; follow-up 6 months; placebo (n=84), carvedilol (n=261).

*MOCHA, Multicenter Oral Carvedilol Heart Failure Assessment.

†Mortality was not a planned endpoint in this study.


‡ P<.05 vs placebo.

§ P=.07 vs placebo.
Effect of Bucindolol on Mortality by Race

Hazard ratio = 1.31

Probability of Survival

$P = .014$

Nonblacks

Blacks

US Carvedilol HF Trials: Effect of Race on Death or Hospitalization for Any Cause

**Black Patients**

- **Carvedilol**
- **Placebo**

**Nonblack Patients**

- **Carvedilol**
- **Placebo**

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Placebo</th>
<th>Carvedilol</th>
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<tbody>
<tr>
<td>Days</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>300</td>
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<tr>
<td></td>
<td>400</td>
<td>500</td>
</tr>
</tbody>
</table>

\[ P = .01 \]

Effects of Beta Blocker Trials on Mortality and Ejection Fraction

% Decrease in Mortality

Increase in Ejection Fraction

Placebo

Bucindolol

Metoprolol

Carvedilol