Outcomes in Peripartum Cardiomyopathy: Lessons from IPAC

Dennis M. McNamara, MD, MS
Professor of Medicine
Director, Center for Heart Failure Research

University of Pittsburgh Medical Center
Investigations of Pregnancy Associated Cardiomyopathy (IPAC)

- Evaluate Clinical and Biologic predictors of Recovery in PPCM
- 100 women enrolled at 30 sites of the Peripartum Cardiomyopathy Network (PCN)
- Followed for one year
- Completed follow up in fall 2013
## IPAC Cohort (n=100)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>$30 \pm 6$ (18-43)</td>
</tr>
<tr>
<td>Gravida</td>
<td>$2.8 \pm 1.9$ (1-10)</td>
</tr>
<tr>
<td>Para</td>
<td>$2.2 \pm 1.4$ (1-6)</td>
</tr>
<tr>
<td>Race (W / B / Other)</td>
<td>65 / 30 / 5</td>
</tr>
<tr>
<td>NYHA Class (1-4)</td>
<td>12 / 47 / 24 / 17</td>
</tr>
<tr>
<td>BP (sys)</td>
<td>$112 \pm 17$</td>
</tr>
<tr>
<td>BP (dia)</td>
<td>$70 \pm 13$</td>
</tr>
<tr>
<td>Days post partum</td>
<td>$31 \pm 24$ (0-91, median 24)</td>
</tr>
<tr>
<td>beta blockers (entry)</td>
<td>88%</td>
</tr>
<tr>
<td>ACEI/ARB (entry)</td>
<td>81%</td>
</tr>
</tbody>
</table>

*Only 1 of 100 treated with bromocriptine*
Myocardial Recovery in IPAC

- final LVEF $\geq 0.50$ in 72%
- final LVEF $\geq 0.55$ in 52%
- Events in 7% by one year (LVAD/Death)
Outcomes stratified by Initial LVEF

- **LVEF ≤ 0.30 (n=27)**
  - Event or LVEF < 0.35: 37%
  - LVEF 0.35 to 0.49: 26%

- **LVEF ≥ 0.30 (n=65)**
  - Event or LVEF < 0.35: 3%
  - LVEF 0.35 to 0.49: 11%
  - LVEF ≥ 0.50: 86%
Myocardial Recovery by race in IPAC: JACC, 2015
GNB3 C825T Polymorphism and Myocardial Recovery in Peripartum Cardiomyopathy
Results of the Multicenter Investigations of Pregnancy-Associated Cardiomyopathy Study

Richard Sheppard, MD; Eileen Hsich, MD; Julie Damp, MD; Uri Elkayam, MD; Angela Kealey, MD; Gautam Ramani, MD; Mark Zucker, MD; Jeffrey D. Alexis, MD; Benjamin D. Horne, MD; Karen Hanley-Yanez, BS; Jessica Pisarcik, RN, BSN; Indrani Halder, PhD; James D. Fett, MD; Dennis M. McNamara, MD; for the IPAC Investigators
LVEF by GNB3 genotype:
IPAC (n=97) TT versus CC+TC

LVEF (%)

- **baseline**
  - GNB3 TT: 31 ± 9
  - GNB3 TC+CC: 35 ± 9
  - N=22
  - N=75
  - p=0.054

- **6 month**
  - GNB3 TT: 45 ± 15
  - GNB3 TC+CC: 53 ± 8
  - N=19
  - N=58
  - P=0.002

- **12 month**
  - GNB3 TT: 45 ± 15
  - GNB3 TC+CC: 56 ± 7
  - N=17
  - N=57
  - P=0.0001

Sheppard et al., Circ HF 2016
LVEF by GNB3: IPAC (black subset, n=29)

TT versus CC+TC

Sheppard et al, Circ HF 2016

<table>
<thead>
<tr>
<th>Time</th>
<th>GNB3 TT</th>
<th>GNB3 TC+CC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>28 ± 9</td>
<td>35 ± 8</td>
</tr>
<tr>
<td>6 month</td>
<td>41 ± 16</td>
<td>52 ± 10</td>
</tr>
<tr>
<td>12 month</td>
<td>37 ± 16</td>
<td>53 ± 9</td>
</tr>
</tbody>
</table>

N=29

p=0.04

N=29

p=0.08

N=29

p=0.02

N=29
Delivery method in IPAC: No recovery advantage to C-section over Vaginal delivery (Marino, Koczo, ACC 2017)
Multi-fetal pregnancy in 19% of the cohort in IPAC: Higher LVEF at entry and Follow up
Impact of Breastfeeding in IPAC

• Pathogenic role of Prolactin has been hypothesized

• Bromocriptine inhibits prolactin release and has been proposed as therapy for PPCM

• Significant Implications
<table>
<thead>
<tr>
<th></th>
<th>Breastfeeding (n=15)</th>
<th>No Breastfeed (n=85)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age (median)</td>
<td>32±6</td>
<td>30±6</td>
<td>0.27</td>
</tr>
<tr>
<td>Black (%, n)</td>
<td>27</td>
<td>31</td>
<td>0.51</td>
</tr>
<tr>
<td>Days post partum</td>
<td>20±15</td>
<td>33±25</td>
<td>0.06</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>67</td>
<td>95</td>
<td>0.15</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>80</td>
<td>89</td>
<td>0.26</td>
</tr>
<tr>
<td>LVEF at entry</td>
<td>39±6</td>
<td>34±10</td>
<td>0.06</td>
</tr>
<tr>
<td>NYHA class I or II</td>
<td>80%</td>
<td>54%</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Marino, Koczo, ACC, 2017
Breastfeeding in IPAC: LVEF at entry, 6 and 12 month Follow up

LVEF Recovery: Breastfeeding vs No Breastfeeding

- Baseline: No Breastfeeding: 0.34 ± 0.10, Breastfeeding: 0.39 ± 0.06, p=0.06
- 6 Months: No Breastfeeding: 0.50 ± 0.11, Breastfeeding: 0.56 ± 0.05, p=0.048
- 12 Months: No Breastfeeding: 0.52 ± 0.11, Breastfeeding: 0.57 ± 0.04, p=0.004

ACC, 2017
“Optimal breastfeeding of infants under two years of age has the greatest potential impact on child survival of all preventive interventions, with the potential to prevent over 800,000 deaths (13 per cent of all deaths) in children under five in the developing world” (Lancet 2013).
Corrected Comparison with IPAC and clinical trial of bromocriptine using LVEF $\leq 35\%$ by either core or clinical echo

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Bromocrip Trial ($\leq35%$) (n=63)</th>
<th>Bromocrip registry ($\leq45%$) (n=96)</th>
<th>IPAC ($&lt;30%$) core (n=30)</th>
<th>IPAC ($\leq35%$) core (n=45)</th>
<th>IPAC ($&lt;45%$) clinical (n=92)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full recovery</td>
<td>62%</td>
<td>47%</td>
<td>37%</td>
<td>60%</td>
<td>72%</td>
</tr>
<tr>
<td>Severe heart failure (LVEF$&lt;0.35$)</td>
<td>3%</td>
<td>5%</td>
<td>18.5%</td>
<td>11%</td>
<td>7%</td>
</tr>
<tr>
<td>Death/Tx/LVAD</td>
<td>0%</td>
<td>10%</td>
<td>18.5%</td>
<td>11%</td>
<td>7%</td>
</tr>
</tbody>
</table>
Corrected Comparison with IPAC and clinical trial of bromocriptine using LVEF $< 35\%$ by either core or clinical echo

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Bromocrip trial (&lt;35%) (n=63)</th>
<th>Bromocrip registry (&lt;45%) (n=96)</th>
<th>IPAC (&lt;30%) core (n=30)</th>
<th>IPAC (&lt;35%) core (n=45)</th>
<th>IPAC (&lt;45%) clinical (n=87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full recovery</td>
<td>62%</td>
<td>47% (LVEF 55%)</td>
<td>37%</td>
<td>60%</td>
<td>52% (LVEF 55%)</td>
</tr>
<tr>
<td>Severe heart failure (LVEF$&lt;0.35$)</td>
<td>3%</td>
<td>5%</td>
<td>18.5%</td>
<td>11%</td>
<td>9%</td>
</tr>
<tr>
<td>Death/Tx/LVAD</td>
<td>0%</td>
<td>10%</td>
<td>18.5%</td>
<td>11%</td>
<td>9%</td>
</tr>
</tbody>
</table>
IPAC and clinical Outcomes in PPCM

• Most women recover on therapy, however, the event rate remains unacceptably high

• LVEF and LVEDD at presentation remain the best clinical predictors of recovery

• Black women at greater risk and demonstrate less recovery

• No apparent adverse impact of breastfeeding evident in IPAC
The recent trial of bromocriptine shows no difference between low dose and high dose bromocriptine therapy, but suggested a difference between this randomized trial and the high risk IPAC registry subset.

Advocating bromocriptine therapy as “standard” for PPCM has significant implications particularly in developing countries where PPCM is more prevalent.

There remains a need for a true randomized trial of bromocriptine vs placebo in high risk PPCM subjects.
Peripartum Cardiomyopathy Network (PCN)
Peripartum Cardiomyopathy Network (PCN)

• http://www.peripartumcmnetwork.pitt.edu

• mcnamaradm@upmc.edu