Effect of Gender on the Outcome of Patients With Severe Heart Failure Treated With Carvedilol: Results of the COPERNICUS Study

Michael P. Tager et al.

Background: The results of the MERIT-HF trial suggested that women with heart failure (HF) respond less favorably to β-blockade than men. Further exploration of this observation is warranted.

Methods: 2269 patients (1824 men, 465 women) were enrolled with symptoms of CHF at rest or on minimal exertion and ejection fraction <25% were randomly assigned to placebo (PBO) or CRV for up to 29 months. Women were older than men (66 vs 63 years; P=0.001) and were more likely to have non-ischemic HF (42% vs 30%; P<0.001).

Results: Shown below are Cox model (CRV:PBO) hazard ratios, 95% CI and interaction P values:

- **All-cause mortality**
  - Men: 0.65 (0.51-0.83)
  - Women: 0.65 (0.39-1.11)
  - Interaction P = 0.98

- **Death or any hospitalization**
  - Men: 0.79 (0.68-0.91)
  - Women: 0.67 (0.51-0.89)
  - Interaction P = 0.21

- **Death or cardiovascular hospitalization**
  - Men: 0.76 (0.65-0.90)
  - Women: 0.60 (0.43-0.84)
  - Interaction P = 0.21

- **Death or HF hospitalization**
  - Men: 0.73 (0.61-0.87)
  - Women: 0.57 (0.40-0.81)
  - Interaction P = 0.21

Conclusion: In COPERNICUS women with severe HF experienced similar clinical benefit and tolerated treatment with CRV as well as men.

Poster Session: Noon-2:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: Noon-1:00 p.m.

1181-142 Compensatory Electrical Remodeling in Hearts of Transgenic Mice That Overexpress the Ca2+ Channel Alpha 1C Subunit

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Background: Prolongation of the action potential duration (APD) and a reduction of the transient outward K+ current (Ito) are thought to be hallmarks of hyper trophy. A model in which the α1 subunit of the L-voltage-dependent calcium channel is over-expressed in transgenic mice offers an opportunity to study this phenomenon in detail.

Methods: We used the whole-cell patch-clamp technique, radioligand binding and retrograde perfused hearts to characterize this model at the cell and organ level.

Results: Electrophysiological analysis in ventricular myocytes isolated from transgenic (Tg) and nontransgenic (Ntg) mice at 4-month of age (mild hypertrophy) demonstrated a slight decrease in the APD at 90% repolarization (APD90) and an up-regulation of the L-type Ca2+-current and dihydropyridine binding. The changes were accompanied by a small increase in Ito density without altering the steady-state inactivation. No change was detected in the expression level of Kv4.3 and 4.2 up to 8-months of age. In cardiomyocytes from 10-12 month old Tg mice (hypertrophied and failing) APD90 was longer compared to Ntg, and annexin A4 was decreased with a 90% decrease in PI3K activity.

Conclusions: These data indicate that PI3K signaling plays a critical role in the development of cardiomyopathy.

1181-143 A Novel Efficient Percutaneous Myocardial Gene Delivery System

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Background: Manipulating gene expression in the failing heart has therapeutic promise, but up to now has been hampered by the complexity of the delivery system. New approaches are required.

Methods: We developed a novel non-viral approach for percutaneous myocardial gene delivery. This system utilizes a novel, peptide-coated, balloon catheter that can deliver a large volume of gene therapy vector to the required site in the heart. The genetic material is delivered using a unique, bipolar DNA electrotransfer system that allows for precise and localized gene delivery.

Results: In a large animal model, we were able to achieve efficient and localized gene delivery to the myocardium. The system is highly efficient and can deliver large amounts of genetic material to the desired location. The delivered gene is expressed for long periods of time, and the system is highly safe and well-tolerated.

Conclusions: This novel approach offers several advantages over traditional delivery methods, including its ability to deliver large volumes of genetic material to the heart in a localized manner, its high efficiency, and its safety profile.

Poster Session: Noon-2:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: Noon-1:00 p.m.