**Echocardiographic Detection of Increases in Ejection Fraction in Patients with Heart Failure Receiving the Selective Cardiac Myosin Activator, CK-1827452**

JH. Goldman, JR. Teerlink, KG. Saikali, F. Malik, AA. Wolff

1 ICON Medical Imaging, Warrington, United States of America; 2 University of California, San Francisco, San Francisco, United States of America; 3 Cytokinetics, Inc., South San Francisco, United States of America

**ABSTRACT**

Purpose: Ejection fraction (EF) remains a standard measure of left ventricular function in heart failure. Stroke volume by Doppler interrogation of the left ventricular outflow tract (LVOT SV) is more accurately measured than EF by the standard 2D image-derived Method of Discs (MoD), but it is not as familiar as EF. CK-1827452 (CK-452) increases LVOT SV in heart failure patients by prolonging systolic ejection time (SET). We compared EF changes calculated by "hybrid" methods (employing both Doppler and 2D data) to EF changes calculated by MoD for patients receiving CK-452.

**METHODS**

Methods: Using echos obtained before, during and after infusion of the selective cardiac myosin activator, CK-452, EF was assessed by MoD and by Doppler derived LVOT SV as a percentage of ventricular volumes assessed by MoD.

Results: EF by MoD did not increase significantly; hybrid EFs increased significantly at [CK-452] >300 ng/mL. Correlation (r-square) of change from baseline in SET was 0.73 (p=0.02) for EF by MoD and by each of two “hybrid” methods that employed both Doppler-derived LVOT SV and ventricular volumes assessed by MoD:

- EF_HYBD_ESV = (LVOT SV/[LVESV + LVOT SV]) x 100
- EF_HYBY_ESV = (LVOT SV/LVESV + LVOT SV) x 100

**CONCLUSIONS**

- CK-452 increases systolic ejection time, stroke volume, cardiac output, and ejection fraction in a concentration-dependent manner.
- While ejection fraction by all three methods increased with the plasma concentration of CK-452, increases of greater magnitude were observed with the hybrid methods.
- As expected, ejection fraction assessed by hybrid methods that employ a measurement of stroke volume based on Doppler interrogation of the left ventricular outflow tract correlates much better with systolic ejection time (a measure also based on Doppler interrogation of the left ventricular outflow tract) than does ejection fraction assessed by the Method of Discs.

**REFERENCES**

1 Malik FI, Saikali KG, Clark CP, Teerlink JR, Wolff AA. Systolic Ejection Time is a Sensitive Indicator of Left Ventricular Systolic Function During Treatment with the Selective Cardiac Myosin Activator, CK-1827452. 2007 Annual Heart Failure Society of America Meeting, Washington, DC. September, 2007.

**RESULTS**

- **DEMOGRAPHICS AND BASELINE CHARACTERISTICS**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (min-max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>58 (30–77)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72 (52–115)</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>136 (98–183)</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>75 (57–117)</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>69 (48–96)</td>
</tr>
<tr>
<td>Ejection Fraction (%)</td>
<td>33 (20–55)</td>
</tr>
</tbody>
</table>

- **COHORTS 1-5**

<table>
<thead>
<tr>
<th>Cohorts 1-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>39 Men</td>
</tr>
<tr>
<td>29 HD</td>
</tr>
</tbody>
</table>

- **ECHO PK/PD RELATIONSHIP: POOLED ANALYSIS**

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