**PHASE II SAFETY STUDY EVALUATING THE NOVEL CARDIAC MYOSIN ACTIVATOR, CK-1827452, IN PATIENTS WITH ISCHEMIC CARDIOMYOPATHY AND ANGINA**

BH Greenberg, W Chou, KG Saikali, R Escandon, JH Lee, MM Chen, F Malik, AA Wolff, T Shaburishvili, and the CY 1221 Investigators

University of California, San Diego, United States; Cytokinetics, Inc., South San Francisco, United States; Diagnostic Services Clinic, Tbilisi, Georgia

**INTRODUCTION AND STUDY RATIONALE**

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**METHODS**

**STUDY DESIGN**

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**STUDY ENDOPOINTS**

- **Primary Safety Endpoint**
  - Proportion who stop ET3 due to angina at a stage earlier than baseline (defined as shorter of the 2 screening ET3s)

- **Secondary Safety Endpoints**
  - Proportion who stop ET3 for any reason at a stage earlier than baseline
  - Exercise duration during ET3
  - Proportion who stop ET3 for angina
  - Time to angina during ET3
  - Proportion with 1 mm ST depression during ET3
  - Time to 1 mm ST depression during ET3

- **Other Safety Assessments**
  - Vital signs, ECGs
  - Cardiac enzymes
  - AEs and SAEs

**BASELINE CHARACTERISTICS**

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Placebo (N=31)</th>
<th>CK-452 Cohort 1 (N=34)</th>
<th>CK-452 Cohort 2 (N=34)</th>
<th>Total (N=98)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>63 (18)</td>
<td>69 (10)</td>
<td>63 (18)</td>
<td>63 (18)</td>
</tr>
<tr>
<td>LVEF, mean (SD), %</td>
<td>32 (10)</td>
<td>25 (10)</td>
<td>26 (10)</td>
<td>27 (10)</td>
</tr>
<tr>
<td>LVFV, mean (SD), cm</td>
<td>1.7 (0.9)</td>
<td>1.7 (0.9)</td>
<td>1.7 (0.9)</td>
<td>1.7 (0.9)</td>
</tr>
<tr>
<td>ETT duration (minutes)</td>
<td>15 (4)</td>
<td>15 (4)</td>
<td>15 (4)</td>
<td>15 (4)</td>
</tr>
<tr>
<td>Target Cmax, ng/mL</td>
<td>12.5</td>
<td>25</td>
<td>30</td>
<td>23.5 (9)</td>
</tr>
</tbody>
</table>

**RESULTS**

- **No clinically important changes in summary vital signs (BP/HR, RR, O₂ saturation) for any of the treatment groups were observed**
- **No clinically important changes in summary ECG parameters (QT & QRS intervals, RR interval, QR interval, PR interval) for any of the treatment groups were observed**
- **No clinically important changes in cardiac enzymes (troponin I, CK-MB, total CK) for any of the treatment groups were observed**

**ADVERSE EVENTS**

- **19 patients experienced at least one treatment-emergent AE**
- **29 distinct AEs, including 2 distinct SAs**
  - 23 out of 29 AEs were reported as mild in severity, 4 out of 29 as moderate in severity, and 2 out of 29 as serious in severity
  - 14 out of 29 AEs were not related to treatment, 8 out of 29 as possibly related to treatment, and 7 out of 20 as probably related to treatment

**SERIOUS ADVERSE EVENTS**

- **Both SAs were from the same patient who experienced angina and ST depression during ET3 which was also observed during baseline ETTs**
  - First SAE reported as Acute Coronary Syndrome during ET3
  - Second SAE reported as Acute Coronary Syndrome during ET3

**CONCLUSIONS**

1. In heart failure patients with ischemic cardiomyopathy and angina, who theoretically should be most vulnerable to the adverse effects of SET prolongation, treatment with CK-452 at concentrations that increase cardiac function did not deleteriously affect a broad range of safety assessments in the setting of exercise

2. Results of this study, together with previous studies evaluating the pharmacodynamic effects of CK-452 in healthy volunteers and stable heart failure patients, support further clinical assessment of CK-452 in patients with acute and chronic heart failure

**REFERENCES**

[Text from the original document]

**STUDY INVESTIGATORS**

[Text from the original document]