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### The BEAUTIFUL trial: Heart Rate

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Resting heart rate has repeatedly been shown to be a strong predictor of overall and cardiovascular mortality in a wide range of patients, including the ones with CAD and post myocardial infarction (MI).<sup>1-3</sup> In addition, recent data have shown that heart rate reduction in post-MI patients is essential for improvement of prognosis; with each 10 beats per minute (bpm) decrease in heart rate, the odds of cardiac death is estimated to be reduced by approximately 30%.<sup>4</sup>

It is well known that heart rate is a key determinant of ischemia. Elevated resting heart rate and increase in heart rate due to any triggering factor like stress in patients with diminished blood flow to the heart, as a result of arteriosclerosis, deprives the heart muscle of oxygen. Depending on the severity of atherosclerosis it can manifest clinically as angina or heart attack (myocardial infarction). This could lead to insufficient heart muscle function, or even total death of heart muscle, resulting in congestive heart failure. Slowing the heart rate reduces the heart's need for oxygen. Consistent with this understanding, the American College of Cardiology/American Heart Association (ACC/AHA), recommends a target heart rate < 60 bpm for patients with stable angina.<sup>5</sup>

Beta-blockers are among the current treatment options to lower heart rate, improve cardiac function and significantly reduce mortality and sudden cardiac death in patients that are post-MI and in patients with heart failure.<sup>6-9</sup> Heart rate reduction seems to be the principal mechanism of action of beta-blockers.<sup>9,10</sup> However despite the availability of beta-blockers and all advances in the field of cardiovascular medicine, coronary artery disease remains the leading cause of death.<sup>11</sup> The presence of left ventricular dysfunction (LVD) has a further dramatic negative influence on the mortality.<sup>12</sup> Furthermore not all patients can take beta-blockers due to their side effects,<sup>13-15</sup> and resting heart rate may not be sufficiently controlled in all CAD patients on beta-blockers.<sup>16</sup>

Based on this understanding of the importance of heart rate, it was reasoned that patients with CAD and LVD could derive particular benefit from pure heart rate lowering. Therefore it was decided to investigate the effect of a new drug ivabradine (Procoralan®)\*, the first I<sub>f</sub> inhibitor that leads to unique pure heart rate reduction. Ivabradine reduces the heart rate by a direct effect on the sinoatrial node without any effect on other cardiac ionic currents.<sup>17-19</sup>

The BEAUTIFUL trial was thus designed to assess the morbid-mortality benefits of pure heart rate reduction above and beyond conventional treatment in CAD patients with LVD. The results of the BEAUTIFUL trial will be presented at a leading international congress in the forthcoming months.

\*Depending on the country ivabradine is available as Procoralan®, Coralan®, Coraxan®, Corlentor®

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