

PRESS RELEASE

With the BEAUTIFUL results, Procoralan* (ivabradine) is the first antianginal treatment shown to reduce myocardial infarction (heart attack) and revascularisation in stable coronary patients

Munich, Germany, 31 August, 2008. The results of the much awaited BEAUTIFUL (*morBidity-mortality EvAIUaTion of the If inhibitor ivabradine in patients with CAD and left ventricULar dysfunction*) trial have shown that **coronary artery disease (CAD) patients with left ventricular dysfunction (LVD) and a heart rate more than 70 bpm have a significantly higher risk of cardiovascular death and other cardiovascular events and in these patients (heart rate above 70 bpm) treatment with ivabradine further reduces the risk of the most important coronary events** such as fatal and non-fatal myocardial infarction and coronary revascularisation by one third, even when these patients are already receiving optimal therapy. Commenting after the results presentation, the Chairman of the BEAUTIFUL Executive Committee, Prof Kim Fox said *'Ivabradine was always known to relieve ischemia. With the BEAUTIFUL results, ivabradine is the first antianginal treatment shown to reduce myocardial infarction and revascularisation and to have a good tolerability profile even when used with other drugs. This is the gold standard for any antianginal, anti-ischemic drug'*.

The BEAUTIFUL trial was initiated in December 2004, under the guidance of an independent Executive Committee with the first patient being enrolled in early 2005. 10917 CAD patients with LVD, were recruited in 781 centres in 33 countries across 4 continents. The mean heart rate in these patients was 71 bpm and half of the patients had a heart rate more than 70 bpm. The results of the BEAUTIFUL study have shown that these patients with heart rate ≥ 70 bpm are more likely to die or suffer from another cardiovascular event. The increase in risk is 34% for cardiovascular death, 46% for myocardial infarction, 56% for heart failure and 38% for coronary revascularisation.

In the overall study population treatment with ivabradine did not result in a significant reduction of the primary composite end point (Cardiovascular death, admission to hospital for acute MI and admission to hospital for heart failure). However in patients with baseline heart rate more than 70 bpm, ivabradine significantly reduced the risk of hospitalisation for fatal and non-fatal myocardial infarction by 36% ($p=0.001$) and the risk of coronary revascularisation by 30% ($p=0.016$). What is important to note is that most of these patients were already receiving the guidelines-recommended cardiovascular therapy: antiplatelet agents (94%), angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (91%), β -blockers (87%), as well as lipid-lowering agents (76%).

Hence the **results of BEAUTIFUL constitute a step further in the management of these coronary patients with heart rate above 70 bpm because, for the first time it has been shown that pure heart rate reduction with ivabradine further reduces coronary events even in patients receiving the current optimal cardiovascular therapy.** This study also confirms that ivabradine is safe and well tolerated and can be used with all routinely prescribed cardiovascular drugs. Commenting on the results the Chairman of the Steering Committee, Prof Roberto Ferrari said *'Often a lot of investigations are performed in coronary patients but a simple heart rate measurement is not done. BEAUTIFUL has reinforced the need to measure heart rate in all CAD patients and if the heart rate is more than 70 bpm to reduce it by using ivabradine on top of background therapy.'*

BEAUTIFUL results with ivabradine can be explained by its well documented ability to relieve myocardial ischemia in patients with chronic stable angina.¹ New research has demonstrated that ivabradine improves endothelial dysfunction² and prevents the progression of atherosclerosis.

Despite all the advances, the World Health Organisation reports that till 2030 coronary artery disease will remain the leading healthcare problem worldwide³. Ivabradine would help to reduce this burden because as shown by the BEAUTIFUL study, ivabradine reduce the risk of myocardial infarction and revascularisation. *'Half of the CAD patients have a resting heart rate more than 70 bpm. These patients can now benefit from a treatment that will greatly reduce their chances of having another heart attack or needing further surgery'*. Concluded Professor Kim Fox, the Chairman of the BEAUTIFUL Executive Committee.

References:

1. Tardif J-C, Ford I, Tendera M, et al. *Eur Heart J.* 2005;26:2529-2536.
2. Florian Custodis, MD*; Magnus Baumhäkel, et al *Circulation* 2008;117:2377-2387.
3. Projections of Global Mortality and Burden of Disease from 2002 to 2030 *PLoS Med* 3(11): e442. doi:10.1371/journal.pmed.0030442.

**Depending on the country, ivabradine is available as Procoralan[®], Coralan[®], Coraxan[®], or Corlentor[®]*