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**New data from PARADIGM-HF show Novartis’ heart failure drug LCZ696 keeps patients alive longer and in better health than current gold standard ACE inhibitor (enalapril)**[[1]](#footnote-1)**[[2]](#endnote-1),****[[3]](#endnote-2)**

* *New analyses presented at the American Heart Association (AHA) Scientific Sessions show LCZ696 cuts incidence of sudden deaths, accident and emergency (A&E) visits, hospitalisations, worsening symptoms and the need for more intense treatment in heart failure patients with reduced ejection fraction (HFrEF) versus a gold standard ACE inhibitor, enalapril1*
* *Data presented earlier this year at the European Society of Cardiology meeting announced LCZ696 demonstrated a 20% reduction in cardiovascular death and a 21% reduction in heart failure hospitalisations on top of current best standard of care%**[[4]](#endnote-3)*
* *Heart failure has a poor prognosis with around 60% of patients dying within five years of diagnosis[[5]](#endnote-4),[[6]](#endnote-5)*

**Frimley, 17 November 2014** – New data from PARADIGM-HF, the largest-ever heart failure study showed that LCZ696 has the potential to change the course of the disease for patients with HFrEF.1,2 LCZ696 is an ARNI (Angiotensin Receptor Neprilysin Inhibitor) and has a unique mode of action, which is thought to reduce stress and damage on the failing heart and has been shown to cut deaths and hospitalisations by 20% compared to gold standard ACE inhibitor, enalapril.3

The new data being presented for the first time at the AHA Scientific Sessions 2014 in Chicago, with a paper being simultaneously published in *Circulation*, show that versus enalapril, LCZ696 significantly:

* Cut the risk of sudden death by 20% (p=0.008)2
* Cut first heart failure hospitalisation by 21% (537 vs 658; p<0.001) and all heart failure hospitalisations by 23% (851 vs 1079; P<0.001) respectively1,2
* Cut hospitalisations for any reason and for any CV reason by 16% (any reason 3564 vs. 4053; P<0.0001, CV reason 2216 vs. 2537; P<0.001)1
* Cut the need for intensification of heart failure treatment by 16% (520 vs 604; P=0.003)1
* Cut A&E visits for heart failure by 30% (151 vs. 208; P=0.017)1

Patients reporting how well they felt and doctors’ assessments of the disease severity were significantly better with LCZ696 than enalapril.1 Additionally, LCZ696 patients had 18% (771 vs 880; P=0.017) fewer stays in intensive care and were 31% (161 vs 229; P<0.001) less likely to need intravenous drugs to help their heart pump compared to those taking enalapril.1

“The impact of heart failure is often underestimated and it accounts for a significant number of A&E visits and hospital admissions,” says Angela Graves, Consultant Nurse in Heart Failure, Clinical Lead for the Pumping Marvellous Foundation. “The effects of the condition can be truly debilitating so it is encouraging to see new developments that could really improve the quality of life for these people.”

“LCZ696 works in a new way to the treatments that have been the mainstay of heart failure management for over two decades. LCZ696 acts to enhance the protective neurohormonal systems of the heart (Natriuretic peptide [NP] system), while also reducing the detrimental effects of the harmful Renin-Angiotensin-Aldosterone System (RAAS). This appears to slow progression of the disease, meaning fewer deaths and hospitalisations and also a better quality of life for patients” says Professor Iain Squire, lead UK trialist for the PARADIGM-HF study.

Analysis of cardiac biomarkers (NTpro-BNP and troponin), substances that indicate the progression of cardiac disease and risk, showed levels were consistently lower with LCZ696 than enalapril, reflecting reduced heart stress and subsequent damage.1,2

LCZ696, a twice-daily oral medicine, acts to enhance the protective neurohormonal systems of the heart (NP system) while simultaneously suppressing the Renin- Angiotensin-Aldosterone System (RAAS). Currently available medicines for HFrEF only block the harmful effectsand mortality remains very high, with up to 60% of patients dying within five years of a diagnosis of heart failure.[[7]](#endnote-6),[[8]](#endnote-7)

Novartis plans to complete the file for marketing authorisation with the US FDA by the end of 2014 and in the European Union in early 2015.

Analysis of the safety data from PARADIGM-HF showed that fewer patients on LCZ696 discontinued study medication for any adverse event compared to those on enalapril (10.7% vs 12.3%, respectively, p=0.03). The LCZ696 group had more hypotension although this did not lead to greater discontinuation of therapy. The LCZ696 group had less renal impairment, hyperkalaemia and cough than the enalapril group. There was no statistically significant difference in angioedema between the two groups.3

**About the PARADIGM-HF study**

PARADIGM-HF is a randomised, double-blind, Phase III study that evaluated the efficacy and safety profile of LCZ696 versus enalapril (a widely studied ACE inhibitor) in 8,442 patients with HFrEF.3 The baseline characteristics showed the patients enrolled were typical HFrEF patients with NYHA Class II-IV heart failure.[[9]](#endnote-8) PARADIGM-HF was specifically designed to see if LCZ696 could decrease CV mortality by at least 15% vs. enalapril.6 Patients received LCZ696 or enalapril in addition to a current best treatment regimen. The primary endpoint was a composite of time to first occurrence of either CV death or heart failure hospitalisation, and it is the largest heart failure study ever done.6,8

Secondary endpoints were a change in the clinical summary score for heart failure symptoms and physical limitations (as assessed by Kansas City Cardiomyopathy Questionnaire) at eight months; time to all-cause mortality; time to new onset atrial fibrillation; and time to occurrence of renal dysfunction.6 PARADIGM-HF was initiated in December 2009, and in March 2014, the Data Monitoring Committee (DMC) confirmed that patients given LCZ696 were significantly less likely to die from CV causes, leading to the trial being stopped early.[[10]](#endnote-9) The DMC also confirmed the primary endpoint had been met.

**About LCZ696 in heart failure**

LCZ696 is an ARNI (Angiotensin Receptor Neprilysin Inhibitor) and has a unique mode of action, which is thought to reduce the strain on the failing heart.6,[[11]](#endnote-10) It harnesses the body's natural defences against heart failure, simultaneously acting to enhance the levels of natriuretic and other endogenous vasoactive peptides, while also inhibiting the Renin- Angiotensin-Aldosterone System (RAAS).

Heart failure is a debilitating and life-threatening disease in which the heart cannot pump enough blood around the body. Symptoms such as breathlessness, fatigue and fluid retention can appear slowly and worsen over time, significantly impacting quality of life.[[12]](#endnote-11)

Heart failure presents a growing health-economic burden globally, and consumes almost 2% of the National Health Service (NHS) budget in the UK, which equates to approximately £1.9 billion.[[13]](#endnote-12)-,[[14]](#endnote-13),[[15]](#endnote-14),[[16]](#endnote-15)

**Disclaimer**

The foregoing release contains forward-looking statements that can be identified by words such as “being investigated” “thought” “plans” “growing” or similar terms, or by express or implied discussions regarding potential marketing approvals for LCZ696, or regarding potential future revenues from LCZ696. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialise, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that LCZ696 will be approved for sale in any market, or submitted for approval in any additional markets, or at any particular time. Neither can there be any guarantee that LCZ696 will be submitted or approved for any additional indications or labelling in any market, or at any particular time. Nor can there be any guarantee that LCZ696 will be commercially successful in the future. In particular, management’s expectations regarding LCZ696 could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays, or government regulation generally; the company’s ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward healthcare cost containment, including ongoing pricing pressures; unexpected manufacturing issues, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

**About Novartis**

Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, preventive vaccines, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2013, the Group achieved net sales of USD 57.9 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortisation charges). Novartis Group companies employ approximately 133,000 full-time-equivalent associates and sell products in more than 150 countries around the world. For more information, please visit <http://www.novartis.com>.

**Novartis Media Relations**

**Media contacts**

Novartis Communications UK Ltd.

Tel: +44 7920 467679 (Press Office)

Email: press.office@novartis.com

**Aurora Healthcare Communications**

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| --- | --- |
| **Sarah Nixon**Director+44 20 7148 4178 (direct)+44 78 091 27499 (mobile)sarah.nixon@auroracomms.com | **Kristen Barrett**Account Manager+44 20 7148 4177(direct)+44 7864 284 881 (mobile)kristen.barrett@auroracomms.com  |

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