New analysis of Novartis' Entresto® data shows long-term benefits on heart failure readmissions and total cardiovascular deaths

Nov 15, 2016

- Entresto reduced the risk of first and subsequent events of heart failure hospitalizations and cardiovascular deaths following heart failure hospitalization by 20%-24% compared to enalapril [(1)]
- These findings are consistent with the benefit Entresto showed in reducing the risk of a first event, which was the primary endpoint of the PARADIGM-HF trial [(2)]
- Additional new analyses show that compared to enalapril, Entresto was associated with more diuretic dose reductions, lowered risk of severe hyperkalemia in patients taking an MRA, and reduced risk among HFrEF patients with the most severe symptoms [(3,4,5)]

EAST HANOVER, N.J., Nov. 15, 2016 /PRNewswire/ -- Novartis announced today results of a new analysis demonstrating that Entresto® (sacubitril/valsartan) tablets reduced the risk of all events – first and repeat heart failure (HF) hospitalizations as well as cardiovascular (CV) deaths that followed HF hospitalization – compared to enalapril among heart failure patients with reduced ejection fraction (HFrEF).[1] The findings are from a post-hoc analysis of PARADIGM-HF, the largest clinical trial ever conducted in HF,[6] and are being presented at the American Heart Association (AHA) Scientific Sessions 2016 in New Orleans.

"In PARADIGM-HF, about one-third of heart failure patients with a first event experienced subsequent events – underscoring the substantial risks faced by patients with this life-threatening condition," said Professor John McMurray of the University of Glasgow, and co-principal investigator for PARADIGM-HF. "The fact that sacubitril/valsartan not only reduced the risk of a first event, but also of repeat events – which are at least as serious and costly, and all too common – is highly significant and reinforces why this medicine is now guideline-directed therapy."

Investigators conducted a comprehensive analysis of all heart failure hospitalizations and all CV deaths that took place in the PARADIGM-HF trial. A total of 3,181 primary endpoint events (including 1,251 CV deaths) were observed during the median 27-month double-blinded follow-up period of PARADIGM-HF, and about one-third of patients with a primary event also experienced a repeat event (defined as repeat HF hospitalizations or a CV death that followed HF hospitalization). Using multiple statistical analysis models, investigators found that Entresto demonstrated a risk reduction of between 20%-24% for all events (first-time and repeat events) compared to enalapril.[1] These findings are consistent with the proven benefit of Entresto for reducing the risk of a first event in PARADIGM-HF (a 20% risk reduction compared to enalapril on the primary endpoint, a composite measure of time to CV death or first HF hospitalization).[1,2]

"The better we understand the results from PARADIGM-HF, the more confident we are that Entresto can help keep many heart failure patients with reduced ejection fraction out of the hospital and alive for longer," said Fabrice Chouraqui, president of Novartis Pharmaceuticals Corporation. "These heart failure patients deserve to benefit from this breakthrough medicine, and we are pleased that Entresto is increasingly being used as a proven treatment to help reduce their risks."

Additional post-hoc analyses from PARADIGM-HF also presented at AHA Scientific Sessions further support the efficacy and safety benefits of Entresto among a range of HFrEF patients compared to enalapril.[3,4,5] These analyses found:

- Treatment with Entresto was associated with fewer diuretic dose increases and more dose reductions compared to enalapril.[3]
- Patients receiving Entresto and a mineralocorticoid receptor antagonist (MRA) had a lower risk of severe hyperkalemia (high potassium levels, >6) compared to those taking enalapril and an MRA.[4]
- In patients with severe HF symptoms (NYHA functional class IV), Entresto showed consistent benefit when compared to the overall patient population of PARADIGM-HF.[5]

About Heart Failure

Heart failure is a debilitating and life-threatening condition, which impacts nearly 6 million Americans and is the leading cause of hospitalization among Americans over the age of 65.[7,8] About half of people with heart failure have heart failure with reduced ejection fraction (HFrEF).[9] Reduced ejection fraction means the heart does not contract with enough force, so less blood is pumped out.[10] Heart failure presents a major and growing health-economic burden that currently exceeds $30 billion in the United States, which accounts for both direct and indirect costs.[11]

About Entresto

Entresto is a twice-a-day medicine that reduces the strain on the failing heart. It does this by enhancing the protective neurohormonal systems (natriuretic peptide system) while simultaneously inhibiting the harmful effects of the overactive renin-angiotensin-aldosterone system (RAAS).[12,13] Other heart failure medicines only block the harmful effects of the overactive RAAS.[14] Entresto contains the neprilysin inhibitor sacubitril and the angiotensin receptor blocker (ARB) valsartan.[12]

Entresto is indicated in the US to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction.[12] Entresto is usually administered in conjunction with other heart failure therapies, in place of an angiotensin converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB).[12] Entresto film-coated tablets are available in three dosage strengths: 24/26 mg, 49/51 mg, and 97/103 mg (sacubitril/valsartan).[12] These doses are referred to as 50 mg, 100 mg, and 200 mg in the clinical trial literature including the New England Journal of Medicine publication of the results of PARADIGM-HF. The target maintenance dose of Entresto is 97/103 mg twice daily.[12]

Novartis is committed to providing patients with affordable access and resources through Entresto Central. For more information, please call 1-888-ENTRESTO or visit www.entresto.com.

Please visit http://www.pharma.us.novartis.com/product/pi/pdf/entresto.pdf for Entresto full Prescribing Information.

IMPORTANT SAFETY INFORMATION

Entresto can harm or cause death to an unborn baby. Patients should talk to their doctor about other ways to treat heart failure if they plan to become pregnant. If a patient gets pregnant while taking Entresto, she should tell her doctor right away.

Patients are not to take Entresto if they are allergic to sacubitril or valsartan or any of the ingredients in Entresto; have had an allergic reaction including swelling of the face, lips, tongue, throat or trouble breathing

while taking a type of medicine called angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB); or take an ACE inhibitor medicine. Patients are not to take Entresto for at least 36 hours before or after they take an ACE inhibitor medicine. Patients should talk with their doctor or pharmacist before taking Entresto if they are not sure if they take an ACE inhibitor medicine. Patients are not to take Entresto if they have diabetes and take a medicine that contains aliskiren.

Before they take Entresto, patients should tell their doctor about all of their medical conditions, including if they have kidney or liver problems; are pregnant or plan to become pregnant; are breastfeeding or plan to breastfeed. Patients should either take Entresto or breastfeed. They should not do both.

Patients should tell their doctor about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. They should especially tell their doctor if they take potassium supplements or a salt substitute; nonsteroidal anti-inflammatory drugs (NSAIDs); lithium; or other medicines for high blood pressure or heart problems such as an ACE inhibitor, ARB, or aliskiren.

Entresto may cause serious side effects including serious allergic reactions causing swelling of the face, lips, tongue, and throat (angioedema) that may cause trouble breathing and death. Patients are to get emergency medical help right away if they have symptoms of angioedema or trouble breathing. Patients are not to take Entresto again if they have had angioedema while taking Entresto. People who are black or who have had angioedema may have a higher risk of having angioedema if they take Entresto. Entresto may cause low blood pressure (hypotension). Patients are to call their doctor if they become dizzy or lightheaded, or they develop extreme fatigue. Entresto may cause kidney problems or an increased amount of potassium in the blood.

The most common side effects were low blood pressure, high potassium, cough, dizziness, and kidney problems.

Please see full Prescribing Information, including Boxed WARNING available at http://www.pharma.us.novartis.com/product/pi/pdf/entresto.pdf.

Patients are encouraged to report negative side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as "confident," "can," "breakthrough," "increasingly," "growing," "committed," or similar terms, or by express or implied discussions regarding potential new indications or labeling for Entresto, or regarding potential future revenues from Entresto. 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 materialize, 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 Entresto will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that Entresto will be commercially successful in the future. In particular, management's expectations regarding Entresto 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 health care cost containment, including ongoing pricing pressures; unexpected safety, quality or 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 Pharmaceuticals Corporation offers a broad range of medicines for cancer, cardiovascular disease, endocrine disease, inflammatory disease, infectious disease, neurological disease, organ transplantation, psychiatric disease, respiratory disease and skin conditions.

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which 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 and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2015, the Group achieved net sales of USD 49.4 billion, while R&D throughout the Group amounted to approximately USD 8.9 billion (USD 8.7 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit http://www.novartis.com.

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