

Eplerenone Cut Events in Heart Failure Patients

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PARIS – The aldosterone antagonist eplerenone cut cardiovascular events and the need for hospitalization significantly across all risk levels in patients with mild heart failure, according to a subanalysis of the EMPHASIS-HF trial.

Eplerenone (Inspra) was also shown to trim troublesome and costly repeat heart failure hospitalizations in a subset of patients followed for up to 10 additional months after the pivotal, phase III trial

head data show that the aldosterone antagonist spironolactone (Aldactone) raises hemoglobin A_{1c} and cortisol levels and reduces adiponectin in patients with diabetes, whereas eplerenone does not.

When Dr. Pitt and colleagues looked at patients with diabetes in the subanalysis, the benefit was stronger than that observed in the overall EMPHASIS-HF cohort, with a 46% reduction in the primary end point (HR, 0.54).

Dr. Pitt noted that the current American Heart Association, American College of Cardiology and European Society of Cardiology guidelines for aldosterone blockade do not specify a particular agent, but look at the agents as a class.

“We believe with [these] data, that in the next guidelines there should at least be some consideration for the specific use of eplerenone, at least in the subset

of patients with diabetes,” he said.

Among patients with an estimated glomerular filtration rate less than 60 mL per minute per 1.73 m², the improvement in the primary outcome reached 38% with eplerenone over placebo.

The study excluded patients with a baseline serum potassium level above 5.0 mmol/L and estimated GFR below 30 mL per minute per 1.73 m² in an attempt to minimize the risk of hyper-

VITALS **Major Finding:** Among patients with diabetes who took eplerenone, there was a 46% reduction in the primary end point of death from cardiovascular causes or heart failure hospitalization, compared with those who took placebo.

Data Source: Subanalysis of high-risk groups and follow-up analyses of the phase III EMPHASIS-HF trial.

Disclosures: Pfizer sponsored the trial. Dr. Pitt reports financial relationships with several firms excluding Pfizer. His coauthors report similar relationships including employment with Pfizer.

closed, Dr. Bertram Pitt reported at the congress.

“Overall efficacy, no matter where we looked, was about the same, and we had the same safety,” he told reporters.

EMPHASIS-HF (Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure) was stopped prematurely last spring after eplerenone in addition to standard therapy demonstrated a 37% (hazard ratio, 0.63) improvement over placebo in the primary end point of death from cardiovascular causes or heart failure hospitalization in 2,637 patients with mild New York Heart Association class II systolic heart failure (N. Engl. J. Med. 2011;364:11-21).

Among 1,597 patients who remained on double-blind therapy after study, the primary end point occurred in 21% on eplerenone and 29% on placebo (HR, 0.66), a significant difference, said Dr. Pitt of the University of Michigan, Ann Arbor.

Repeat hospitalization for heart failure was significantly reduced with eplerenone (rate ratio, 0.62).

“This suggests, to us at least, that this is going to have important cost implications and quality of life implications, as well as important implications on survival, since we know that heart failure hospitalization relates to target-organ damage and survival,” he said.

The benefits of eplerenone were particularly compelling in elderly patients and those with diabetes and renal dysfunction, three high-risk populations in whom clinicians are hesitant to use adjuvant aldosterone blockade because of fears of inducing hyperkalemia, Dr. Pitt said. He pointed out that recent head-to-

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IMPORTANT SAFETY INFORMATION

WARNING: BLEEDING RISK

Effient® (prasugrel) can cause significant, sometimes fatal, bleeding.

Do not use Effient in patients with active pathological bleeding or a history of transient ischemic attack or stroke.

In patients ≥75 years of age, Effient is generally not recommended, because of the increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk situations (patients with diabetes or a history of prior myocardial infarction [MI]) where its effect appears to be greater and its use may be considered.

Do not start Effient in patients likely to undergo urgent coronary artery bypass graft surgery (CABG). When possible, discontinue Effient at least 7 days prior to any surgery.

Additional risk factors for bleeding include:

- body weight <60 kg
- propensity to bleed
- concomitant use of medications that increase the risk of bleeding (eg, warfarin, heparin, fibrinolytic therapy, chronic use of nonsteroidal anti-inflammatory drugs [NSAIDs])

Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, percutaneous coronary intervention (PCI), CABG, or other surgical procedures in the setting of Effient.

If possible, manage bleeding without discontinuing Effient. Discontinuing Effient, particularly in the first few weeks after acute coronary syndrome, increases the risk of subsequent cardiovascular events.

References: 1. Wright RS, Anderson JL, Adams CD, et al. *Circulation*. 2011;123:2022-2060. 2. Wright RS, Anderson JL, Adams CD, et al. *J Am Coll Cardiol*. 2011;57:1920-1959. 3. Kushner FG, Hand M, Smith SC Jr, et al. *Circulation*. 2009;120:2271-2306. 4. Kushner FG, Hand M, Smith SC Jr, et al. *J Am Coll Cardiol*. 2009;54:2205-2241.



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kalemia. Despite this, the positive results remain applicable, Dr. Pitt said in an interview.

Among elderly patients at least 75 years old, the benefit on the primary end point with eplerenone reached 34%.

Significant benefits were also observed in patients with a left ventricular ejection fraction less than 30% and with a median systolic blood pressure of less than 123 mm Hg.

As seen in the overall EMPHASIS-HF cohort, the benefits of eplerenone were accompanied by a significant increase in the incidence of serum potassium greater

than 5.5 mmol/L in each of the high-risk subgroups.

However, there were no significant increases in the incidence of serum potassium above 6 mmol/L, hospitalization leading to treatment discontinuation, hospitalization for/or deaths due to hyperkalemia, or hospitalizations for worsening renal function, Dr. Pitt said.



Invited discussant Dr. Piotr Ponikowski, with the 4th Military Hospital in Wroclaw, Poland, highlighted as important the benefits of eplerenone in people with diabetes and the reduction in repeat hospitalizations. He noted that up to 50% of heart failure patients are rehospitalized and these visits are associated with significant costs and reduced

This is going to have important implications in terms of cost, quality of life, and survival.

DR. PITT

quality of life and mortality. Still, aldosterone antagonists remain underutilized in heart failure patients in Europe as well as the United States.

Physicians frequently question whether clinical trial data are real, consistent, and clinically meaningful, he said. "With the presented data, we can now say that the answer to all these questions is 'yes.'"

View a video interview with Dr. Pitt with the QR code, or by visiting ecardiologynews.com.



CONTRAINDICATIONS

- Effient is contraindicated in patients with active pathological bleeding, such as from a peptic ulcer or intracranial hemorrhage (ICH), or a history of transient ischemic attack (TIA) or stroke, and in patients with hypersensitivity to prasugrel or any component of the product

WARNINGS AND PRECAUTIONS

- Patients who experience a stroke or TIA while on Effient generally should have therapy discontinued. Effient should also be discontinued for active bleeding and elective surgery
- Premature discontinuation of Effient increases risk of stent thrombosis, MI, and death
- Thrombotic thrombocytopenic purpura (TTP), a rare but serious condition that can be fatal, has been reported with Effient, sometimes after a brief exposure (<2 weeks), and requires urgent treatment, including plasmapheresis

ADVERSE REACTIONS

- Bleeding, including life-threatening and fatal bleeding, is the most commonly reported adverse reaction

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