

# ICDs Don't Save Women With Heart Failure

BY MARY ANN MOON

Implantable cardioverter defibrillators do not reduce all-cause mortality in women who have advanced heart failure, unlike in men, according to a meta-analysis.

"ICDs are being implanted in hundreds of thousands of women without substantial evidence of benefit, apparently based on the assumption that, to para-

phrase the old saying, 'What's good for the gander is good for the goose,'" Dr. Rita F. Redberg said in an accompanying editorial (*Arch. Intern. Med.* 2009;169:1460-1).

This finding is particularly concerning because a "recent analysis of the National Cardiovascular Data Registry found that women have a 70% higher risk of major adverse events after ICD implantation than do men," noted Dr. Redberg, editor of the journal and director of

women's cardiovascular services at the University of California, San Francisco.

Dr. Hamid Ghanbari and his associates at Providence Hospital in Southfield, Mich., pooled data from five randomized, controlled clinical trials that compared ICD implantation with medical therapy and included 934 women along with 3,810 men. Men who had heart failure with reduced left ventricular ejection fraction showed a significant decrease in

all-cause mortality when they were given an ICD rather than medical therapy to prevent sudden cardiac death.

In contrast, women did not show a mortality benefit, either in the combined data or in any of the five individual trials, Dr. Ghanbari and his colleagues said (*Arch. Intern. Med.* 2009;169:1500-6).

Neither Dr. Ghanbari nor Dr. Redberg reported any financial conflicts of interest. ■

## Valturna (aliskiren and valsartan, USP) Tablets

Initial U.S. Approval: 2009

BRIEF SUMMARY: Please see package insert for full prescribing information.

### WARNING: AVOID USE IN PREGNANCY

When pregnancy is detected, discontinue Valtorna as soon as possible. When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin-aldosterone system can cause injury and death to the developing fetus. [See Warnings and Precautions (5.1)].

### 1 INDICATIONS AND USAGE

Valturna is indicated for the treatment of hypertension.

#### Add-on Therapy

A patient whose blood pressure is not adequately controlled with aliskiren alone or valsartan (or another angiotensin receptor blocker) alone may be switched to combination therapy with Valtorna.

#### Replacement Therapy

Valturna may be substituted for the titrated components.

#### Initial Therapy

Valturna may be used as initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals.

The choice of Valtorna as initial therapy should be based on an assessment of potential benefits and risks.

Patients with Stage 2 hypertension are at a relatively high risk for cardiovascular events (such as strokes, heart attacks, and heart failure), kidney failure, and vision problems, so prompt treatment is clinically relevant. The decision to use a combination as initial therapy should be individualized and should be shaped by considerations such as baseline blood pressure, the target goal, and the incremental likelihood of achieving goal with a combination compared to monotherapy. Individual blood pressure goals may vary based upon the patient's risk.

Data from the high-dose multifactorial study [see Clinical Studies (14) in the full prescribing information] provide estimates of the probability of reaching a target blood pressure with Valtorna compared to aliskiren or valsartan monotherapy. The figures below provide estimates of the likelihood of achieving systolic or diastolic blood pressure control with Valtorna 300/320 mg, based upon baseline systolic or diastolic blood pressure. The curve of each treatment group was estimated by logistic regression modeling. The estimated likelihood at the right tail of each curve is less reliable because of a small number of subjects with high baseline blood pressures.

Figure 1: Probability of Achieving Systolic Blood Pressure (SBP) <140 mmHg in Patients at Endpoint

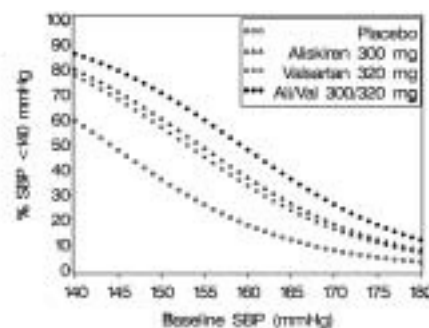


Figure 2: Probability of Achieving Diastolic Blood Pressure (DBP) <90 mmHg in Patients at Endpoint

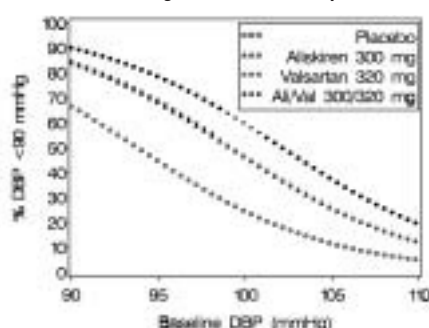


Figure 3: Probability of Achieving Systolic Blood Pressure (SBP) <130 mmHg in Patients at Endpoint

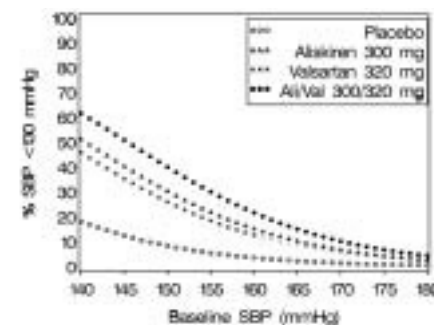
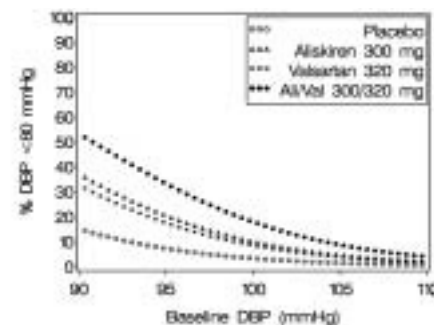


Figure 4: Probability of Achieving Diastolic Blood Pressure (DBP) <80 mmHg in Patients at Endpoint



At all levels of baseline blood pressure, the probability of achieving any given diastolic or systolic goal is greater with the combination than for either monotherapy. For example, the mean baseline SBP/DBP for patients participating in this multi-factorial study was 154/100 mmHg. A patient with a baseline blood pressure of 154/100 mmHg has about a 51% likelihood of achieving a goal of <140 mmHg (systolic) and 46% likelihood of achieving <90 mmHg (diastolic) on aliskiren alone, and the likelihood of achieving these goals on valsartan alone is about 47% (systolic) and 47% (diastolic). The likelihood of achieving these goals on Valtorna rises to about 62% (systolic) and 60% (diastolic). The likelihood of achieving these goals on placebo is about 28% (systolic) and 25% (diastolic) [see Dosage and Administration (2) and Clinical Studies (14) in the full prescribing information].

### 4 CONTRAINDICATIONS

None.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Fetal/Neonatal Morbidity and Mortality

Valturna can cause fetal harm when administered to a pregnant woman. If this drug is used during pregnancy, or if a patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus.

Drugs that act directly on the renin-angiotensin-aldosterone system can cause fetal and neonatal morbidity and death when administered to pregnant women. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus [see Use in Specific Populations (8.1)]. In several dozen published cases, use of ACE inhibitors during the second and third trimesters of pregnancy was associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. In addition, first trimester use of ACE inhibitors has been associated with birth defects in retrospective data.

#### 5.2 Head and Neck Angioedema

##### Aliskiren

Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with aliskiren and has necessitated hospitalization and intubation. This may occur at any time during treatment and has occurred in patients with and without a history of angioedema with ACE inhibitors or angiotensin receptor antagonists. If angioedema involves the throat, tongue, glottis or larynx, or if the patient has a history of upper respiratory surgery, airway obstruction may occur and be fatal. Patients who experience these effects, even without respiratory distress, require prolonged observation since treatment with antihistamines and corticosteroids may not be sufficient to prevent respiratory involvement. Prompt