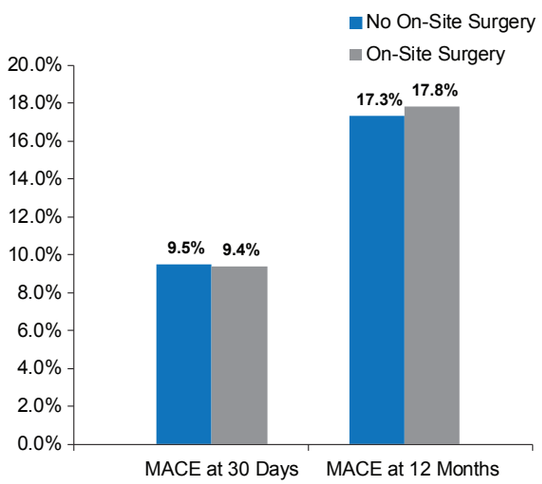
The primary efficacy endpoint of death, MI , stroke, or repeat revascularization at 12 months did not differ across groups—17.3% for sites without on-site surgery compared with 17.8% for sites with surgical services available (p<0.001 for noninferiority; Figure 1). Seven patients (0.25%) randomized to sites without surgery required transfer to a hospital for emergency surgery of whom none died.

Figure 1. Primary Safety and Efficacy Endpoints



MACE=major adverse cardiac events.

There was also no difference between groups in occurrence of secondary endpoints of target lesion revascularization, target vessel revascularization, and stent thrombosis at either 30 days or 12 months, and major vascular complications at 30 days (Table 1).

Table 1. Occurrence of Secondary Endpoints

	No On-Site Surgery (n=2774)	On-Site Surgery (n=917)	Relative Risk 95% CI	p Value
Target-lesion revascularization (%)†				
At 30 days	1.3	1.4	0.98 (0.51-1.88)	1.00
At 12 months	4.9	5.0	1.00 (0.70-1.43)	1.00
Target-vessel revascularization (%)†				
At 30 days	1.5	1.5	1.03 (0.56-1.92)	1.00
At 12 months	5.6	5.4	1.05 (0.75-1.48)	0.86
Stent thrombosis (%)				
At 30 days	0.6	0.8	0.75 (0.31-1.81)	0.48
At 12 months	1.1	2.1	0.55 (0.30-1.02)	0.07
Major vascular complications at 30 days	1.5	1.5	1.04 (0.56-1.92)	1.00

†Ischemia-driven.

PCI performed at hospitals in Massachusetts without cardiac surgery on site was noninferior to PCI performed with cardiac surgery on site with respect to the 30-day safety and 12-month effectiveness endpoints, Dr. Jacobs concluded. These data suggest that PCI can be safely performed at hospitals without surgery on site and could be an acceptable option for patients if the facility and individual operators have the requisite amount of experience.

ASTRONAUT Study: Aliskiren Does Not Improve Postdischarge Outcomes in Patients Hospitalized for Chronic Heart Failure

Written by **Wayne Kuznar**

Aliskiren in addition to standard therapy does not reduce cardiovascular (CV) death or heart failure (HF) rehospitalization in patients hospitalized for HF with reduced left ventricular ejection fraction (LVEF). Mihai Gheorghiade, MD, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA, presented data from the Six Months Efficacy and Safety of Aliskiren Therapy on Top of Standard Therapy, on Morbidity and Mortality in Patients With Acute Decompensated Heart Failure trial [ASTRONAUT; Gheorghiade M et al. *JAMA* 2013].

Despite the availability of several evidenced-based therapies for the treatment of patients hospitalized with HF, postdischarge mortality is as high as 14% and rehospitalization within 60 to 90 days is ~30% [Gheorghiade M et al. *JAMA* 2006]. The ASTRONAUT trial tested the hypothesis that the direct renin inhibitor, aliskiren, may improve postdischarge outcomes for patients hospitalized with HF when initiated during hospitalization and continued post discharge [Gheorghiade M et al. *Eur J Heart Fail* 2011].

In the international Phase 3, double-blind, placebo-controlled ASTRONAUT trial, 1639 patients hospitalized with HF were randomized to receive either 150 mg (increased to 300 mg as tolerated) of aliskiren or placebo daily along with standard therapy [Gheorghiade M et al. *JAMA* 2013]. Patients were eligible if they had an LVEF ≤40%, B-type natriuretic peptide (BNP) ≥400 pg/mL or N-terminal pro-BNP ≥1600 pg/mL at admission, and a systolic blood pressure ≥110 mm Hg for at least 6 hours.

The study drug was continued for a median 11.3 months after discharge, and 1615 patients were included in the final efficacy analysis cohort. The primary endpoint was CV death or rehospitalization for HF within 6 months. CV death or rehospitalization for HF within 12 months was the key secondary endpoint.

No significant difference was observed between the aliskiren and placebo treatment groups for the primary endpoint of CV death or HF rehospitalization within 6 months (24.9% vs 26.5%; HR, 0.92; 95% CI, 0.76 to 1.12; p=0.41). In addition, no significant difference was observed for the key secondary endpoint of CV death or rehospitalization for HF within 12 months in the patients receiving aliskiren compared with those receiving placebo (35.0% vs 37.3%; HR, 93; 95% CI, 0.79 to 1.09; p=0.36).

There was a significant treatment interaction for all-cause mortality dependent upon the presence of diabetes. Specifically, patients with diabetes receiving aliskiren had a significantly higher rate of all-cause mortality (HR, 1.64; 95% CI, 1.15 to 2.33) within 12 months of randomization compared with patients without diabetes (HR, 0.69; 95% CI, 0.50 to 0.94; p for interaction <0.001). There was a similar treatment interaction for CV death or rehospitalization for HF within 12 months with diabetic patients receiving aliskiren experiencing a higher rate of CV death or HF rehospitalization (HR, 1.16; 95% CI, 0.91 to 1.47) compared with patients without diabetes (HR, 0.80; 95% CI, 0.64 to 0.99; p for interaction=0.03). Although this interaction was statistically significant suggesting heterogeneity in the impact of aliskiren versus placebo among diabetic and nondiabetic subjects for all-cause mortality and CV death/HF rehospitalization, this finding must be interpreted cautiously given the inherent statistical limitations.

The rates of hyperkalemia, renal impairment or renal failure, and hypotension were all more commonly observed in subjects receiving aliskiren versus placebo (Table 1).

Dr. Gheorghiade concluded that the data from the ASTRONAUT trial demonstrate that when added to contemporary medical therapy for patients with systolic dysfunction hospitalized for HF, there was no clinical benefit to the addition of aliskiren. The impact of aliskiren among different patient populations, particularly the tendency toward worse outcomes in patients with diabetes, who are hospitalized for HF warrants further study.

Table 1. Summary of Adverse Events by Treatment Group

	Number (%)			
	Aliskiren	Placebo	Aliskiren vs Placebo, RR (95% CI)	p Value
Hyperkalemia[a]	169 (20.9)	142 (17.5)	1.19 (0.98-1.46)	0.09
Renal impairment or renal failure[b]	134 (16.6)	98 (12.1)	1.37 (1.08-1.75)	0.01
Hypotension[c]	138 (17.1)	102 (12.6)	1.36 (1.07-1.72)	0.01

[a] Includes hyperkalemia and increased blood potassium level.

[b] Includes abnormal results from renal function test, acute renal failure, decreased urine output, increased blood creatinine level, acute prerenal failure, renal impairment, renal failure, decreased glomerular filtration rate, and increased blood urea concentration.

[c] Includes decreased blood pressure, postural dizziness, hypotension, orthostatic hypotension, and procedural hypotension.

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