Hypertension (STITCH) trial evaluated an algorithm designed for use in the family practice setting to combat the growing "epidemic" of nonadherence to guideline-based antihypertensive regimens.

The STITCH trial included 45 practices treating 2,104 patients in southwestern Ontario, Canada. Practices were randomly assigned to implement the Canadian Hypertension Education Program (CHEP) (n=27) or STITCH (n=18) treatment algorithm for the management of hypertension. The STITCH algorithm featured four steps:

- Initiate treatment with one-half tablet of the lowest dose of a fixed-dose combination
  - Angiotensin-converting enzyme-inhibitor (ACE-I)/diuretic or angiotensin-receptor blocker (ARB)/diuretic
- Increase the combination dose
  - Instruct patients to take the full tablet, then up-titrate to higher fixed doses
- Add a calcium channel blocker
- Add an alpha-blocker, beta-blocker, or spironolactone

The primary endpoint was the proportion of patients who were treated to target BP levels: <140/90 mm Hg and <130/80 mm Hg for patients with and without diabetes, respectively. At 6 months, significantly more patients in the STITCH group (64.8%) than in the CHEP group (52.7%) achieved BP targets (p=0.026). This represents an absolute benefit of 12% in favor of the STITCH algorithm (95% CI, 1.5-22.4%).

Systolic and diastolic BP levels improved in both groups, though the improvement was significantly greater among patients treated according to the STITCH practices. In the STITCH and CHEP groups, systolic BP dropped by 23 mm Hg and 18 mm Hg, respectively (p=0.002), whereas diastolic BP fell by 10 mm Hg and 8 mm Hg, respectively (p=0.03).

In practices assigned to the STITCH protocol, physicians were able to implement fixed-dose combination therapy in the majority (85%) of patients. By comparison, only 15% of patients in the CHEP group were treated with fixed-dose combination therapy (p<0.001).

"This simplified approach, which can be taught and used in busy family practices, resulted in better blood pressure control with less overall drug use," Prof. Feldman concluded. "The STITCH protocol may be a paradigm for the management of a range of chronic diseases that show poor control rates."

Rosuvastatin Offers No Significant Benefit for Older Patients with Heart Failure

Rosuvastatin was found to have no significant benefit in the prevention of cardiovascular (CV) death, myocardial infarction (MI), or stroke in symptomatic older patients with systolic heart failure (HF) of ischemic etiology in the Controlled Rosuvastatin Multinational (CORONA) trial. However, statin therapy was associated with significantly fewer hospitalizations and significantly decreased levels of low-density lipoprotein (LDL) compared with placebo.

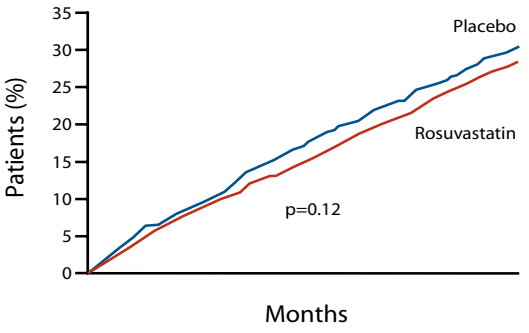
Assuming that rosuvastatin reduced the risk of acute atherothrombotic events, our results suggest that the major etiology of CV deaths in these older patients with advanced systolic HF may be a primary electrical event related to ventricular dilatation and scarring and not to an atherothrombotic event, said Åke Hjalmarson, MD, PhD, Göteborg University, Sweden, who reported on the study.

CORONA enrolled 5,011 patients (24% women) with systolic HF of ischemic etiology. The mean age was 73 years. All patients were receiving optimal HF therapy. After a placebo run-in phase of 2-4 weeks, patients were randomly assigned to a daily dose of 10 mg of rosuvastatin (2,514 patients) or to placebo (2,497 patients). The median follow-up was 2.7 years.

Baseline mean LDL levels decreased from 137 mg/dL to 76 mg/dL after 3 months of treatment with rosuvastatin but did not change significantly in the placebo group (136 -> 138 mg/dL). Rosuvastatin also had a significant effect on the level of high-sensitivity C-reactive protein; the level decreased from 3.1 mg/L to 2.1 mg/L after 3 months of treatment; this 32% decrease compared with a 5% increase in the placebo group (from 3.0 mg/L at baseline to 3.3 mg/L at 3 months; p<0.001).

Dr. Hjalmerson reported that the incidence of the primary endpoint, a composite of CV death, nonfatal MI, or nonfatal stroke did not differ significantly between the two groups (27.5% for rosuvastatin vs 29.3% for placebo, p=0.12) (Figure 1). He noted, "The study was powered to detect a mean relative risk reduction of 16%, but the reduction associated with rosuvastatin was only 8%."

Figure 1. Kaplan-Meier Estimates for the Primary Outcome, Death From Any Cause and Any Coronary Event.



No. at Risk							
Placebo	2497	2315	2156	2003	1851	1431	811
Rosuvastatin	2514	2345	2207	2068	1932	1484	855

Rosuvastatin also had no significant benefit in terms of the secondary endpoints of all-cause mortality (hazard ratio (HR) 0.95; p=0.31) or any coronary event (HR 0.92; p=0.18). Cardiovascular deaths accounted for 68% of the events, and post hoc analysis indicated that rosuvastatin reduced nonfatal events (MI or stroke) by 16% (10.6% for placebo vs 9.0% for rosuvastatin; p=0.05).

Rosuvastatin was associated with significantly fewer hospitalizations for all causes, as well as for CV causes and heart failure, but not for hospitalizations related to unstable angina or non-CV causes (Figure 2).

Figure 2. Patients Who Had at Least One Hospitalization, and the Total Number of Hospitalizations.

Variable	Placebo (N=2,497)		Rosuvastatin (N=2,514)		Hazard Ratio (95% CI)	p Value
	No.	Event Rate	No.	Event Rate		
For any cause						
Patients	1,523	38.0	1,489	35.6	0.94 (0.88-1.01)	0.09
Hospitalizations	4,074		3,694			0.007
For a cardiovascular cause						
Patients	1,164	25.0	1,104	22.9	0.92 (0.85-0.99)	0.04
Hospitalizations	2,564		2,193			<0.001
For worsening heart failure †						
Patients	669	12.3	622	11.3	0.91 (0.82-1.02)	0.11
Hospitalizations	1,299		1,109			0.01
For unstable angina						
Patients ‡	71	1.2	65	1.1	0.91 (0.66-1.27)	0.56
Hospitalizations	90		74			0.30
For noncardiovascular cause						
Patients	840	16.5	839	16.2	0.98 (0.89-1.08)	0.72
Hospitalizations	1,510		1,501			

* The event rate is the number of events per 100 patient-years of follow-up.
† The numbers of patients who died from any cause or were hospitalized for worsening heart failure were 1,116 in the placebo group (20.5 per 100 patient-years) and 1,064 in the rosuvastatin group (19.2 per 100 patient-years), with a hazard ratio for the rosuvastatin group of 0.94 (95% CI, 0.86-1.02; p=0.12).
‡ These numbers do not include five patients (three in the placebo group and two in the rosuvastatin group) who were deemed to have unstable angina by the outcome adjudication committee, since the events occurred during a hospitalization but were not the cause of the hospital admission.

Lastly, rosuvastatin did not improve patients' perception of health status, as assessed by the New York Heart Association class of heart failure or by the McMaster Overall Treatment Evaluation questionnaire, both of which were prespecified tertiary outcomes.

Previous studies have suggested that low lipid levels may be harmful in patients with heart failure, but there was no evidence of harm associated with rosuvastatin in CORONA. Rosuvastatin was well tolerated, and in fact, more patients discontinued placebo than rosuvastatin because of adverse events (302 vs 241; p=0.004). Importantly, the rates of ALT elevation and muscle-related side effects were similar between groups.

Several potential explanations have been raised for why rosuvastatin failed to meet the primary endpoint despite prior promising studies with other statins, including competing risks for events that were not modifiable by a statin; a patient population that had high comorbidity; mandated use of optimal, evidence-based treatments for heart failure; and differences in pleiotropic effects between statins (or doses). Further large, prospective studies are needed to answer the questions raised by the CORONA trial and to better delineate the role for statin therapy for patients with systolic heart failure.

The findings of this study have been published: [Kjekshus et al. NEJM 2007;357:2248-2261].

Final Results of the ILLUMINATE Trial

The final results of the ILLUMINATE trial comparing the cholesteryl ester transfer protein (CETP) inhibitor torcetrapib plus atorvastatin with atorvastatin alone in patients at high risk for cardiovascular disease showed that the rates of major cardiovascular events and all-cause mortality were higher with the addition of torcetrapib. The study had been prematurely terminated in December 2006 because of a significant excess of deaths and cardiovascular events in the group randomized to torcetrapib plus atorvastatin.

ILLUMINATE included 15,067 patients at high risk for cardiovascular disease. The study was preceded by a run-in period of 4-10 weeks of treatment with atorvastatin and lifestyle interventions to achieve a low-density lipoprotein (LDL) level of <100 mg/dL. Patients were then randomly assigned to either torcetrapib plus atorvastatin (7,533 patients) or matching placebo plus atorvastatin (7,534 patients).

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