Quick Statin Use After Stroke Cuts Mortality

BY MITCHEL L. ZOLER

FROM THE INTERNATIONAL STROKE CONFERENCE

LOS ANGELES – Starting or maintaining acute stroke patients on a statin during their initial hospitalization was linked with a dramatic improvement in 1-year survival in a retrospective review of medical records for more than 12,000 U.S. patients.

On the basis of the finding, Kaiser Permanente of Northern California will issue a revised order set that will recommend to physicians that they start acute stroke patients on 80 mg simvastatin as soon as possible on the first day of their hospitalization, Dr. Alexander C. Flint reported at the conference.

"Based on results from the SPARCL [Stroke Prevention by Aggressive Reduction in Cholesterol Levels] trial, pretty much everyone in the stroke community believes that patients who have had an ischemic stroke should be treated with high-dose statin to prevent a second stroke (N. Engl. J. Med. 2006; 355:549-59).

'In our study, the question wasn't whether to treat, but the timing. ... You should start the statin on day 1.'

DR. FLINT

In our study, the question wasn't whether to treat, but the timing. What our results say is that you should not wait until the patient is discharged or is an outpatient, but that you should start the statin on day 1," Dr. Flint said in an interview.

The data he reported showed that stroke patients who started on a statin during their acute-phase hospitalization had a 15% absolute reduced rate of death during the first year following their stroke, compared with patients who did not start on a statin and did not receive a statin prior to their stroke (Stroke 2011;42:e-42-110).

After adjustment for several possible confounding factors, including age, sex, race and ethnicity, year of stroke, and comorbidities such as hypertension and diabetes, stroke patients who started on a statin while hospitalized had a statistically significant, 45% lower relative risk of death during the subsequent year, compared with patients who did not receive a statin.

The study involved 12,689 patients who received care from Kaiser Permanente of Northern California and had an ischemic stroke during 2000-2007. The total included 3,749 patients who were on steady statin treatment for at least 3 months before their stroke, and 8,940 patients who were not receiving a statin at all before their stroke.

Of the 3,749 patients who were on a statin before their stroke, most (3,280, or 87%) continued to receive a statin during their hospitalization. And among the 8,940 who did not receive regular statin treatment before their stroke, 3,013 (34%) began statin treatment while hospitalized.

Patients who received a statin prior to their stroke but did not continue while hospitalized had a statistically significant 15% relative reduction in their mortality during the following year, compared with patients who never received a statin.

The key element for mortality protection appeared to be treatment while hospitalized. Relative mortality reduction compared with non–statin users was 41% among patients who were on a statin both before their stroke and while hospitalized, and 45% among those who started on a statin while hospitalized, said Dr. Flint, a neurointensivist and stroke specialist at Kaiser Redwood City (Calif.).

Patients who received a statin before their stroke but discontinued the drug once hospitalized had the worst outcomes, with a mortality rate that was 2.5 times as high as that of patients who never received a statin.

Further analysis highlighted the importance of an early start to statin treatment in hospitalized patients, and also showed a dose-response relationship. Patients who received at least 60 mg of

Effient® (prasugrel) is indicated to reduce the rate of thrombotic cardiovascular (CV) events (including stent thrombosis) in patients with acute coronary syndrome (ACS) who are to be managed with percutaneous coronary intervention (PCI) as follows: [1] patients with unstable angina (UA) or non–ST-elevation myocardial infarction (NSTEMI); [2] patients with ST-elevation myocardial infarction (STEMI) when managed with primary or delayed PCI.

VITALS

Major Finding: Stroke patients who started on a statin during their acute-phase hospitalization had a 15% absolute reduced rate of death at 1 year, compared with patients never treated with a statin.

Data Source: Review of 12,689 patients enrolled in Kaiser Permanente of Northern California who had an acute ischemic stroke during 2000-2007.

Disclosures: Dr. Flint reported having no relevant disclosures.

their statin daily either before hospitalization or both before and during hospitalization had a significantly lower mortality rate, compared with patients who took less than 60 mg/day. Dr. Flint noted that about 70% of patients received lovastatin, and about 20% received simvastatin.

Regarding timing, patients who either began on a statin for the first time or restarted their treatment on their first hospitalized day had a significantly lower 1-year mortality, compared with patients who did not start or restart their statin until their third day in hospital.

Dr. Flint also reported an additional analysis that had been run to determine whether patients' survival prognosis drove their statin treatment instead of their statin treatment's driving their survival.

To do this, he looked at patterns of care at each of the 17 Kaiser Permanente of Northern California hospitals that were involved in the study. This "grouped treatment analysis" demonstrated that although the survival prognosis of patients who were withdrawn from prior statin treatment while hospitalized played some role in the relationship, it was unable to explain all of the survival effect, indicating that statin treatment itself during hospitalization played a significant role in subsequent survival.

The strong impact that early statin treatment during stroke hospitalization has on long-term survival probably depends on the pleiotropic effects of statins. The timing makes it less likely that the effect of statins on lipid levels can explain the observed survival benefits, Dr. Flint said. ■

Effient plus aspirin (ASA) provided

STRONGER PROTECTION

vs Plavix® (clopidogrel bisulfate) plus ASA against thrombotic cardiovascular (CV) events (including stent thrombosis)

- In the overall UA/NSTEMI population, event rates* for Effient plus ASA and Plavix plus ASA were 9.3% and 11.2%, respectively (1.9% ARR†; *P*=0.002). In the overall STEMI population, event rates for Effient plus ASA and Plavix plus ASA were 9.8% and 12.2%, respectively (2.4% ARR; *P*=0.02)[1,2]
- Difference in treatments was primarily driven by a significant reduction in nonfatal myocardial infarctions (MIs), with no significant difference in CV death or nonfatal stroke[1]
  - In the overall study population, approximately 40% of MIs occurred periprocedurally and were detected solely by changes in CK-MB
- 52% RRR‡ in stent thrombosis in the all-ACS population with Effient plus ASA vs Plavix plus ASA (1.1% vs 2.2%; 1.1% ARR; *P*<0.0001)[3]
- TRITON-TIMI 38 was a head-to-head study comparing Effient (60-mg loading dose [LD], followed by 10-mg once-daily maintenance dose) plus ASA with Plavix (300-mg LD, followed by a 75-mg once-daily maintenance dose) plus ASA in 13,608 patients with ACS managed with PCI (median duration 14.5 months)
  - In TRITON-TIMI 38, the LD of Plavix was delayed relative to the placebo-controlled trials that supported its approval for ACS

For more information, please visit EffientHCP.com or Effientconferences.com.

SELECTED SAFETY, INCLUDING SIGNIFICANT BLEEDING RISK

Effient can cause significant, sometimes fatal, bleeding. In TRITON-TIMI 38, overall rates of non-CABG TIMI major or minor bleeding were significantly higher with Effient plus ASA (4.5%) compared with Plavix plus ASA (3.4%). In patients who underwent CABG (n=437), the rates of CABG-related TIMI major or minor bleeding were 14.1% with Effient plus ASA and 4.5% with Plavix plus ASA.

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.

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

Please see Brief Summary of Prescribing Information on subsequent pages.

*As measured by reduction in the primary composite endpoint of CV death, nonfatal MI, or nonfatal stroke.
†Absolute risk reduction.
‡Relative risk reduction.

Effient® (prasugrel) tablets