

Frequent Limb Movement Linked to LVH

BY ALICE GOODMAN

FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF CARDIOLOGY

NEW ORLEANS – Frequent periodic leg movements during sleep were associated with left ventricular hypertrophy in patients with restless legs syndrome, in a study presented at the meeting.

Moreover, patients who had sleep disturbance due to frequent periodic leg

movements and severe LVH were at increased risk for heart failure, recurrent hospitalizations, and death.

“We have known for a long time that LVH is a poor prognostic factor that increases the risk of cardiac events. What is new ... is that it appears that restless legs syndrome is another risk factor that may predispose patients to, and lead to more complications of, LVH,” Dr. Arshad Jahangir said at the meeting.

Dr. Jahangir, principal investigator in the study and professor of medicine at the Mayo Clinic in Scottsdale, Ariz., said that the findings need to be confirmed in larger studies. Also, it will be important to evaluate whether effective treatments for restless legs syndrome can prevent adverse outcomes associated with LVH.

Approximately 12 million Americans have restless legs syndrome. The condition is increasingly common with age

and is implicated in about one-third of all cases of insomnia. Up to 90% of patients also have periodic limb movement disorder. The mechanisms that drive the disorder are not fully understood, Dr. Jahangir said, but the sympathetic nervous system is involved and patients typically have increased heart rate and blood pressure.

The study enrolled 584 restless legs syndrome patients who underwent

Effient is indicated to reduce the rate of thrombotic CV events (including stent thrombosis) in UA/NSTEMI patients who are to be managed with PCI and in STEMI patients when managed with primary or delayed PCI.



REDUCTIONS IN THROMBOTIC CV EVENTS IN TRITON-TIMI 38 INCLUDING HIGH-RISK PATIENTS SUCH AS THOSE WITH DIABETES^{**†,‡}

The reduction in the primary composite endpoint of CV death, nonfatal MI, or nonfatal stroke in patients with diabetes treated with Effient plus ASA compared with Plavix plus ASA was consistent with those observed in the overall UA/NSTEMI and STEMI populations



^{*}As measured by reduction in the primary composite endpoint of CV death, nonfatal MI, or nonfatal stroke. [†]The LD of Effient was 60 mg followed by a 10-mg daily dose (plus ASA) and the loading dose of Plavix was 300 mg followed by a 75-mg daily dose (plus ASA). [‡]Relative risk reduction. [§]Absolute risk reduction.

- Difference in treatments was primarily driven by a significant reduction in nonfatal MIs, with no significant difference in CV death or nonfatal stroke¹
 - In the overall study population, approximately 40% of MIs occurred periprocedurally and were detected solely by changes in CK-MB
- In TRITON-TIMI 38, the LD of Plavix was delayed relative to the placebo-controlled trials that supported its approval for ACS
- TRITON-TIMI 38 was not designed or powered to demonstrate independent efficacy or safety in the diabetes subgroup

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.

overnight polysomnography studies. Patients were stratified according to frequency of leg movements during sleep: 45% had frequent leg movements, defined as a Periodic Movement Index [PMI] of more than 35 per hour, and 55% had infrequent leg movements, defined as a PMI of 35 or fewer movements per hour. Despite having a left ventricular ejection fraction of around 60% at baseline, the group with frequent periodic limb movements had a significantly higher left ventricular mass, mass index, and posterior wall thickness, indicating the presence of LVH.

At baseline, the groups with frequent versus infrequent periodic limb movements had similar clinical and echocardiographic parameters, and were comparable for the presence of cardiovascular risk factors, including hypertension, diabetes, heart failure, and renal dysfunction. Patients with frequent periodic limb movements were older (median age 67 vs. 61 years), more often male, had more atrial fibrillation (30% vs. 17%), and more underlying coronary heart disease than those with infrequent periodic limb movements.

The presence of severe LVH [defined as

left ventricular mass index >116 g/m²] and atrial fibrillation led to a significantly greater likelihood of heart failure, recurrent hospitalizations, and death over a mean follow-up of 3 years. Dr. Jahangir said that even in participants with frequent periodic limb movements and no atrial fibrillation, patients with severe LVH had a greater number of cardiac events.

Severe LVH was found in 37% of those with atrial fibrillation and 20% of those without it, suggesting that underlying electrical dysfunction and restless legs syndrome may act together to lead to adverse cardiovascular outcomes.

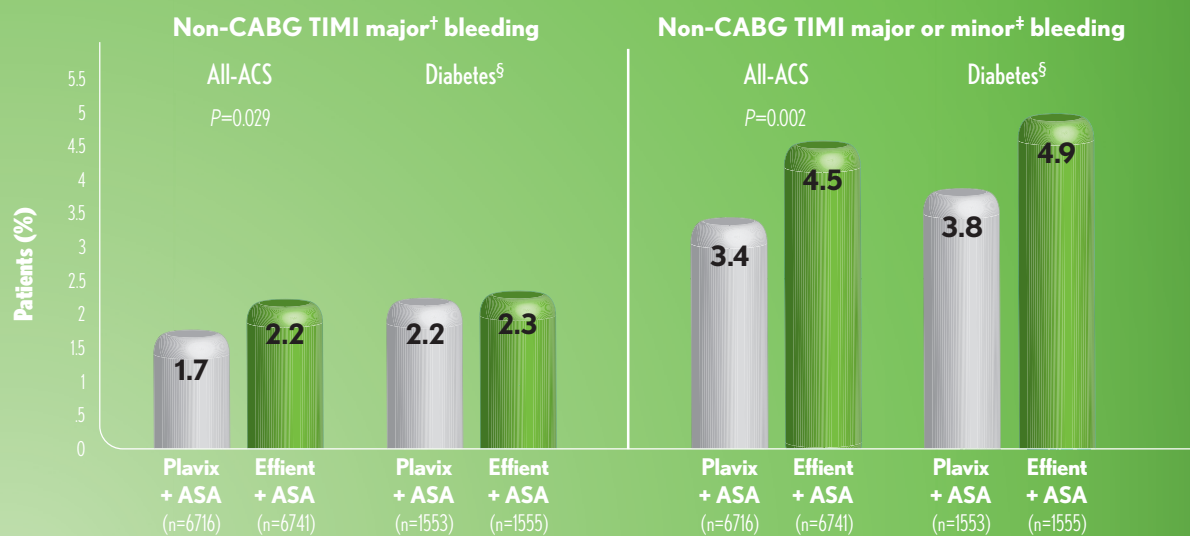
The study was funded by the National Heart, Lung, and Blood Institute and the Angel and Paul Harvey Cardiovascular Research Endowment to CardioGerontology Research Laboratory at Mayo Clinic Arizona. Dr. Jahangir had no relevant financial disclosures. ■

To see a video interview with Dr. Jahangir, scan this QR code or visit www.youtube.com/watch?v=qvm1sSQ9LdM&NR=1.



Effient
(prasugrel) tablets

NON-CABG-RELATED BLEEDING: TRITON-TIMI 38 ALL-ACS POPULATION, INCLUDING DIABETES SUBGROUP*1,4



*Observed event rates. [†]Intracranial hemorrhage or clinically overt bleeding associated with a fall in hemoglobin ≥ 5 g/dL. [‡]Clinically overt bleeding associated with a fall in hemoglobin of ≥ 3 g/dL but < 5 g/dL. [§]*P* value not provided because the trial was not designed to prospectively evaluate bleeding differences in subgroups.

- In TRITON-TIMI 38, overall rates of non-CABG TIMI major and non-CABG TIMI major or minor bleeding were significantly higher with Effient plus ASA compared with Plavix plus ASA[†]
- 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. Do not start Effient in patients likely to undergo urgent CABG[†]
- Patients at highest risk for non-CABG TIMI major or minor bleeding were those ≥ 75 years of age and/or those < 60 kg (132 lb)[†]
- 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[†]
 - Patients who experience a stroke or TIA while on Effient generally should have therapy discontinued

Please see Important Safety Information, including Boxed Warning regarding bleeding risk, on previous page. See also Brief Summary of Prescribing Information on subsequent pages.