Rosuvastatin in the Prevention of Stroke Among Men and Women With Elevated Levels of C-Reactive Protein

Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER)

Brendan M. Everett, MD, MPH; Robert J. Glynn, ScD; Jean G. MacFadyen, BA; Paul M Ridker, MD, MPH

Background—Prior primary prevention trials of statin therapy that used cholesterol criteria for enrollment have not reported significant decreases in stroke risk. We evaluated whether statin therapy might reduce stroke rates among individuals with low levels of cholesterol but elevated levels of high-sensitivity C-reactive protein.

Methods and Results—In Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER), 17,802 apparently healthy men and women with low-density lipoprotein cholesterol levels ≤130 mg/dL and high-sensitivity C-reactive protein levels ≥2.0 mg/L were randomly allocated to rosuvastatin 20 mg daily or placebo and then followed up for the occurrence of a first stroke. After a median follow-up of 1.9 years (maximum, 5.0 years), rosuvastatin resulted in a 48% reduction in the hazard of fatal and nonfatal stroke as compared with placebo (incidence rate, 0.18 and 0.34 per 100 person-years of observation, respectively; hazard ratio 0.52; 95% confidence interval, 0.34 to 0.79; \(P=0.002\)), a finding that was consistent across all examined subgroups. This finding was due to a 51% reduction in the rate of ischemic stroke (hazard ratio, 0.49; 95% confidence interval, 0.30 to 0.81; \(P=0.004\)), with no difference in the rates of hemorrhagic stroke between the active and placebo arms (hazard ratio, 0.67; 95% confidence interval, 0.24 to 1.88; \(P=0.44\)).

Conclusion—Rosuvastatin reduces by more than half the incidence of ischemic stroke among men and women with low levels of low-density lipoprotein cholesterol levels who are at risk because of elevated levels of high-sensitivity C-reactive protein.

Clinical Trial Registration—clinicaltrial.gov. Unique identifier: NCT00239681.

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Key Words: inflammation ■ lipids ■ prevention ■ stroke ■ trials

Hyperlipidemia is a well-established risk factor for cardiovascular disease, but its association with coronary heart disease is much stronger than its association with stroke.1–4 In prior primary prevention trials that used elevated cholesterol levels as criteria for entry, statin therapy has not demonstrated a reduction in stroke risk.5–7 Among patients with established vascular disease or diabetes, however, statin therapy has proven remarkably effective, reducing the risk of stroke by 19% to 48%.8–14

Clinical Perspective on p 150

High-sensitivity C-reactive protein (hsCRP) is an inflammatory biomarker that independently predicts future stroke and improves cardiovascular risk classification, regardless of low-density lipoprotein cholesterol (LDL-C) level.4,15–19 Because of this association and because statin therapy reduces hsCRP levels, we hypothesized that statin therapy would reduce stroke risk in patients with low levels of cholesterol but elevated levels of hsCRP.20 Furthermore, we hypothesized that the lowest risk of stroke would be observed among those who achieved the lowest levels of LDL-C or hsCRP after initiation of statin therapy.

Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) investigated whether treatment with rosuvastatin 20 mg daily compared with placebo would decrease the rate of first major cardiovascular events. Here, we report the impact of rosuvastatin compared with placebo on incident stroke, a component of the primary end point and a prespecified secondary end point of JUPITER.
Methods

Trial Design
JUPITER was a randomized, double-blind, placebo-controlled multicenter trial conducted at 1315 sites in 26 countries. The study protocol and population are described in detail elsewhere.21,22 Briefly, men ≥50 years of age and women ≥60 years of age who were eligible for the trial if they did not have a history of cardiovascular disease or diabetes and if they had an LDL-C level <130 mg/dL (3.4 mmol/L) and an hsCRP ≥2.0 mg/L.

Eligible subjects who provided informed consent were randomized to either rosuvastatin 20 mg daily or matching placebo. Lipid levels and hsCRP were measured at randomization and every year thereafter. The 17,802 participants randomized to rosuvastatin or placebo were included in the intention-to-treat analysis of the risk of incident stroke. To address the effect of reductions in hsCRP and LDL-C on stroke risk, we used baseline and 1-year hsCRP and LDL-C concentrations in 15,548 participants (87% of the total) for whom data were available.

End Points
Stroke (fatal or nonfatal) was a predefined end point of the JUPITER trial. An end-points committee blinded to randomized treatment assignment confirmed an incident stroke if there were unequivocal signs of a focal or global neurological deficit with sudden onset and duration >24 hours. Computed tomography or magnetic resonance imaging scans, as well as other clinical reports, were used to classify stroke types as hemorrhagic, atheroembolic, thromboembolic, or other. Fatal strokes were confirmed if they met the criteria for nonfatal strokes or if the diagnosis was specifically stated in the hospital discharge record, death certificate, or postmortem autopsy examination. Transient ischemic attacks (TIAs) were reported by local site investigators but were not confirmed by the end-points committee.

Statistical Analysis
Analyses of the effect of random allocation to rosuvastatin on incident stroke were performed on an intention-to-treat basis. Cox proportional-hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for the comparison of event rates in the 2 treatment groups. Subgroup analyses were performed according to the presence or absence of major cardiovascular risk factors. To measure the net clinical benefit of rosuvastatin when the combined effects on cerebral and coronary events were considered, we also fitted a proportional-hazards model with the first occurrence of stroke or other major cardiovascular event (nonfatal or fatal) as a composite outcome and estimated differences in risk and the number needed to treat for absolute measures of treatment efficacy.23

For the analysis of achieved LDL-C and incident stroke, on the basis of prior work in JUPITER and in the Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 (PROVE IT-TIMI 22) and Aggrastat-to-Zocor (Astatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 (PROVE IT-TIMI 22) and Aggrastat-to-Zocor (A

Results
Baseline characteristics of the JUPITER populations are shown in Table 1. No significant differences in baseline characteristics were observed between the rosuvastatin and placebo groups.

At the time of study termination (median follow-up, 1.9 years; maximal follow-up, 5 years), 33 strokes had occurred in the rosuvastatin group compared with 64 strokes in the placebo group (Table 2). The incidence rates of stroke were 0.18 and 0.34 per 100 person-years of follow-up in the rosuvastatin and placebo groups, respectively (HR for rosuvastatin, 0.52; 95% CI, 0.34 to 0.79; P = 0.002; Table 2 and Figure 1). A similar benefit of rosuvastatin was observed for nonfatal strokes, which made up 88 of the 97 strokes observed (HR, 0.52; 95% CI, 0.33 to 0.80; P = 0.003). Most strokes were categorized as ischemic, with incidence rates of 0.12 and 0.25 per 100 person-years in the rosuvastatin and placebo groups, respectively (HR, 0.49; 95% CI, 0.30 to 0.81; P = 0.004; Table 2 and Figure 1).

The rates of hemorrhagic stroke were 0.03 and 0.05 per 100 person-years in the rosuvastatin and placebo groups, respectively. The risk of hemorrhagic stroke was similar in both groups, with an HR of 0.67 (95% CI, 0.24 to 1.88; P = 0.44) in the rosuvastatin group compared with the placebo group. TIAs were observed with similar frequency in the 2 treatment groups (HR, 0.93; 95% CI, 0.56 to 1.56; P = 0.79).

The projected number needed to treat for 5 years to prevent 1 stroke was 123. When stroke was excluded from the primary cardiovascular end point of myocardial infarction, stroke, unstable angina, revascularization, and cardiovascular death, the number needed to treat to prevent 1 event was projected to be 31 at 5 years. When stroke was included, as it was in the primary end point of the JUPITER trial, the number needed to treat at 5 years was 25, a 19% decrease.

There was no evidence of heterogeneity in any subgroup evaluated (P ≥ 0.09 for each interaction; Figure 2). Rosuvastatin offered a similar benefit across sex and ethnicity groups and to those with and without traditional risk factors for stroke, including subjects who were older (>70 years of age), were smokers, had hypertension, reported a family history of
premature stroke, or had a Framingham stroke risk score >10%. The benefits of rosuvastatin were also observed in the subgroups that would otherwise be considered at low risk, including those with a body mass index <25 kg/m², without the metabolic syndrome, with a Framingham stroke or coronary heart disease risk score ≤10, with low levels of LDL-C (≤100 mg/dL), with normal levels of HDL-C (≥40 mg/dL among men, ≥50 mg/dL among women), and with normal triglyceride levels (<150 mg/dL). Likewise, the effects of rosuvastatin were similarly beneficial among those with a baseline hsCRP level ≥5.0 mg/L and those with baseline hsCRP levels <5.0 mg/L (P for interaction=0.35).

We also evaluated whether the magnitude in reduction of LDL-C or hsCRP was directly related to the magnitude of clinical benefit observed, as was observed for the primary end point of JUPITER.26 As reported previously, after 12 months of therapy, rosuvastatin reduced the median LDL-C by 50% (55 versus 110 mg/dL) and the median hsCRP by 37% (2.2 versus 3.5 mg/L) compared with placebo.22 However, achieved LDL-C and hsCRP levels were only weakly correlated (r=0.10), as were the percentage reduction in LDL-C and percentage reduction in hsCRP (r=0.15).26

As shown in Table 3, in a subcohort of 15 548 individuals with baseline and 1-year follow-up blood samples available for analysis, the greatest reduction in stroke risk with rosuvastatin was observed among those who reached an LDL-C goal of <70 mg/dL. In a similar manner, the greatest reduction in stroke risk with rosuvastatin was observed among those who reached an hsCRP goal of <2 mg/L. For both LDL-C and hsCRP, these effects persisted after adjustment for a wide range of baseline characteristics.

Although none of the 3 prior primary prevention trials of statin therapy individually demonstrated a statistically significant reduction in stroke, all suggested trends toward net benefit. The characteristics of JUPITER, WOSCOPS, AFCAPS/TexCAPS, and MEGA are presented in Table 4. In an updated random-effects meta-analysis including the JUPITER data described here, a net 25% reduction in stroke risk was observed (relative risk [RR], 0.75; 95% CI, 0.57 to 0.99; P=0.03; Figure 3). Aside from a small increase in physician-reported diabetes in the rosuvastatin group (270 versus 216; P=0.01), adverse events were similar in the 2 arms of the trial and are the same as those reported previously.22

### Discussion

In this randomized trial of apparently healthy men and women with elevated levels of hsCRP but low levels of LDL-C, rosuvastatin reduced the incidence of stroke by 48%. This reduction in stroke risk was consistent across all subgroups evaluated, including those customarily considered to be at low risk, such as women, nonsmokers, those with Framingham coronary heart disease scores or stroke scores ≤10%, and those without hypertension at baseline. No effect on hemorrhagic stroke was observed.

Although no significant effects of statin therapy on stroke were observed in the WOSCOPS, MEGA, or AFCAPS/TexCAPS primary prevention trials, all suggested a trend toward net benefit. In fact, we observe a nonsignificant 14% reduction in stroke risk with statin therapy (RR, 0.86; 95% CI, 0.66 to 1.10; P=0.23) in a random-effects meta-analysis using data from these 3 trials. When that analysis is updated with data from JUPITER, statin therapy in primary prevention is associated with a net 25% reduction in stroke risk (RR, 0.75; 95% CI, 0.57 to 0.97; P=0.03; Figure 3) without any evidence of heterogeneity (P=0.24). Thus, although there is
no evidence of heterogeneity between trials, the results of JUPITER must be included in the meta-analysis to observe a statistically significant reduction in stroke in a primary prevention population.

Given the net benefit of statin therapy observed in our updated meta-analysis, it is possible that any apparent differences between JUPITER and each of the prior trials may simply reflect the play of chance. However, the larger relative

<table>
<thead>
<tr>
<th>End Point</th>
<th>Rosuvastatin (n=8901)</th>
<th>Placebo (n=8901)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients, n</td>
<td>Rate per 100 Person-Years</td>
</tr>
<tr>
<td>Any stroke</td>
<td>33</td>
<td>0.18</td>
</tr>
<tr>
<td>Nonfatal stroke</td>
<td>30</td>
<td>0.16</td>
</tr>
<tr>
<td>Fatal stroke</td>
<td>3</td>
<td>0.02</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>23</td>
<td>0.12</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>6</td>
<td>0.03</td>
</tr>
<tr>
<td>Unknown stroke</td>
<td>4</td>
<td>0.02</td>
</tr>
<tr>
<td>TIA</td>
<td>28</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Table 2. Outcomes According to Study Group
and absolute benefits observed within JUPITER could also reflect the fact that, unlike the prior trials that used elevated lipid levels as entry criteria, JUPITER targeted those with elevated levels of hsCRP, which in several populations is more closely associated with incident stroke than elevated LDL-C.3,4,15,17,28 JUPITER also used a more potent statin regimen than was used in any of the prior trials. Thus, actively treated participants had greater LDL-C and hsCRP reductions. In JUPITER, we observed a 47-mg/dL reduction in LDL-C and a 48% reduction in stroke risk, or a 39% relative reduction in the risk of stroke per 1-mmol/L reduction in LDL-C. In contrast, assignment to pravastatin in WOSCOPS and MEGA was associated with a 41- and 29-mg/dL reduction in LDL-C, respectively, and no significant reduction in the risk of stroke. Statins are generally thought to be equally efficacious per unit of LDL-C reduction, and the Cholesterol Treatment Trialists’ Collaborative meta-analysis of previous primary and secondary prevention statin trials reported a 17% relative reduction in the risk of stroke for each 1-mmol/L (38.7-mg/dL) reduction in LDL-C.29 The summary RR from our meta-analysis of primary prevention trials is consistent with the result from the Cholesterol Treatment Trialists’ Collaborative, and the results of JUPITER, considered individually, are consistent with the results of trials of different statins conducted in higher-risk populations, including those with diabetes, hypertension, and pre-existing coronary or vascular disease.11–13,30

In our data, the lowest risk of stroke was observed among those assigned to rosuvastatin who achieved low levels of LDL-C or hsCRP. This observation is consistent with the association between the risk of the primary end point in JUPITER and achieved LDL-C and hsCRP levels and with prior observations in patients with acute coronary syndromes.24–26 Although none of the subjects enrolled in JUPITER would qualify for lipid-lowering therapy by Adult Treatment Panel III criteria,31 these data suggest that achieving a goal LDL-C of ≤100 mg/dL or a goal hsCRP of ≤2 mg/L is associated with the greatest reduction in stroke rates in the JUPITER primary prevention population.

In contrast to the results of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial, we observed no significant difference in the rates of hemorrhagic stroke between the 2 treatment arms in JUPITER.14

The results from JUPITER are consistent with results from...
Cholesterol and Recurrent Events (CARE), Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID), and Heart Protection Study (HPS) and with prior work suggesting that achieved LDL-C is not related to hemorrhagic stroke risk.11,30,32 The rates of TIA were similar in both arms of the trial. Although this finding differs from some prior reports such as those from SPARCL and HPS, our observations are consistent with those observed in other trials such as MEGA.

### Table 3. Achieved LDL-C and hsCRP and the Risk of Incident Stroke

<table>
<thead>
<tr>
<th>Event</th>
<th>Adjusted for Age, LDL, and CRP,†</th>
<th>Fully Adjusted</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>0.27 (0.15–0.57)</td>
<td>0.30 (0.15–0.58)</td>
<td>1.0</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>0.13 (0.09–0.19)</td>
<td>0.10 (0.09–0.18)</td>
<td>0.48 (0.29–0.81)</td>
</tr>
<tr>
<td>LDL &lt;70 mg/dL</td>
<td>0.08 (0.05–0.13)</td>
<td>0.06 (0.04–0.10)</td>
<td>0.84 (0.49–1.54)</td>
</tr>
<tr>
<td>LDL reduction &lt; 50%</td>
<td>0.23 (0.18–0.28)</td>
<td>0.22 (0.17–0.27)</td>
<td>0.84 (0.49–1.54)</td>
</tr>
<tr>
<td>LDL reduction ≥ 50%</td>
<td>0.02 (0.01–0.03)</td>
<td>0.02 (0.01–0.03)</td>
<td>0.10 (0.02–0.39)</td>
</tr>
<tr>
<td>hsCRP ≥ 2 mg/L</td>
<td>0.16 (0.13–0.20)</td>
<td>0.15 (0.12–0.18)</td>
<td>0.56 (0.31–1.02)</td>
</tr>
<tr>
<td>hsCRP reduction &lt; 50%</td>
<td>0.09 (0.06–0.12)</td>
<td>0.08 (0.05–0.11)</td>
<td>0.34 (0.15–0.57)</td>
</tr>
<tr>
<td>hsCRP reduction ≥ 50%</td>
<td>0.03 (0.02–0.05)</td>
<td>0.03 (0.02–0.05)</td>
<td>0.04 (0.01–0.08)</td>
</tr>
<tr>
<td>(P)</td>
<td>0.0007</td>
<td>0.0009</td>
<td></td>
</tr>
</tbody>
</table>

*Event rates are per 100 person-years of observation.
†Data are adjusted for age, baseline LDL-C, and baseline hsCRP.
‡Data are adjusted for age, baseline LDL-C and HDL-C, baseline hsCRP, blood pressure, sex, body mass index, smoking status, and parental history of premature stroke.

### Table 4. Comparison of the Baseline Characteristics Between JUPITER and Other Primary Prevention Trials of Statin Therapy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>JUPITER</th>
<th>WOSCOPS5</th>
<th>AFCAPS/TexCAPS6</th>
<th>MEGA7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size, n</td>
<td>17,802</td>
<td>6,595</td>
<td>6,605</td>
<td>7,730</td>
</tr>
<tr>
<td>Women, n</td>
<td>6,801</td>
<td>0</td>
<td>997</td>
<td>5,356</td>
</tr>
<tr>
<td>Current smoker, %*</td>
<td>16</td>
<td>44</td>
<td>12</td>
<td>21</td>
</tr>
<tr>
<td>Mean systolic BP, mm Hg</td>
<td>136</td>
<td>136</td>
<td>138</td>
<td>132</td>
</tr>
<tr>
<td>Duration (maximum), y</td>
<td>1.9 (5)</td>
<td>4.9</td>
<td>5.2</td>
<td>5.3</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>0</td>
<td>1</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Mean total cholesterol, mg/dL</td>
<td>183</td>
<td>272</td>
<td>221</td>
<td>242</td>
</tr>
<tr>
<td>Mean LDL-C, mg/dL</td>
<td>105</td>
<td>192</td>
<td>150</td>
<td>157</td>
</tr>
<tr>
<td>Mean HDL-C, mg/dL†</td>
<td>51</td>
<td>44</td>
<td>36</td>
<td>58</td>
</tr>
<tr>
<td>Median TG, mg/dL‡</td>
<td>118</td>
<td>164</td>
<td>158</td>
<td>126</td>
</tr>
<tr>
<td>Median hsCRP, mg/L</td>
<td>4.3</td>
<td>NA</td>
<td>1.6</td>
<td>NA</td>
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<tr>
<td>Intervention, mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pravastatin</td>
<td>40</td>
<td></td>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>Lovastatin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total strokes accrued, n¶</td>
<td>97</td>
<td>97</td>
<td>21</td>
<td>112</td>
</tr>
<tr>
<td>Rate in placebo arm, per 100 person-years</td>
<td>0.34</td>
<td>0.32</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.52 (0.34–0.79)</td>
<td>0.89 (0.53–1.51)</td>
<td>0.82 (0.33–2.08)</td>
<td>0.83 (0.57–1.21)</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; TG, triglycerides.
*The number reported for MEGA includes current and former smokers.
†In AFCAPS/TexCAPS, the mean HDL-C was 36 mg/dL for men and 40 mg/dL for women. The study had different HDL entry criteria for men and women.
‡Triglyceride levels for WOSCOPS are presented as the mean.
¶Total fatal and nonfatal strokes are included. AFCAPS/TexCAPS reported total strokes plus TIAs.
Risk of Stroke in Four Statin Primary Prevention Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Hazard Ratio (95% CI)</th>
<th>Statin Better</th>
<th>Placebo Better</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOSCOPS</td>
<td>0.89 (0.53-1.51)</td>
<td>0.50</td>
<td>0.75</td>
</tr>
<tr>
<td>AFCAPS/TexCAPS</td>
<td>0.82 (0.33-2.08)</td>
<td>0.75</td>
<td>0.75</td>
</tr>
<tr>
<td>MEGA</td>
<td>0.83 (0.57-1.21)</td>
<td>0.50</td>
<td>0.75</td>
</tr>
<tr>
<td>JUPITER</td>
<td>0.52 (0.34-0.79)</td>
<td>0.45</td>
<td>0.75</td>
</tr>
<tr>
<td>Summary</td>
<td>0.75 (0.57-0.97)</td>
<td>0.50</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Figure 3. Statins in the primary prevention of stroke. The results of random-effects meta-analysis of data from JUPITER and 3 other primary prevention trials are shown.5-7 The HRs and 95% CIs calculated in the meta-analysis, indicated by boxes and horizontal lines through the boxes, are shown for each trial. The dotted line marks the summary RR (0.75), and the solid line is drawn at 1.00. The size of each box is proportional to the information from each trial. There was no statistically significant evidence for heterogeneity (P=0.24).

CARE, and the Study of Pravastatin in the Elderly at Risk (PROSPER).7,11,14,30,33 The lack of association between statin therapy and rates of TIA in JUPITER may be due to a misclassification of nonvascular neurological events as TIA. However, the criteria used to distinguish a TIA from other neurological syndromes (including stroke) were the same in our study as they were in trials that have and have not shown a reduction in rates of TIA with statin therapy, making a systematic difference between JUPITER and the other trials unlikely.

The main strengths of our study include the large number of participants enrolled; the prospective, randomized, double-blind treatment assignment; and the prespecification of stroke as an end point. However, the trial was stopped early for evidence of benefit, so the long-term risks and benefits of high-dose statin use in this healthy population should be considered. Furthermore, the number of strokes in our analysis somewhat limits our ability to examine subgroups closely. This issue is particularly important in interpretations of the changes in stroke risk associated with achieved levels of LDL-C and hsCRP.

Conclusions

In this healthy population with normal cholesterol levels but elevated levels of hsCRP, random allocation to rosuvastatin was associated with a 48% reduction in the risk of incident stroke. The benefits of rosuvastatin were observed across all subgroups, including those at low risk for stroke, and we observed no increase in the risk of hemorrhagic stroke with active therapy.24

Source of Funding

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Disclosures

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**CLINICAL PERSPECTIVE**

Prior primary prevention trials of statin therapy that used cholesterol criteria for enrollment have not reported significant decreases in stroke risk with active statin therapy. Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) randomized 17,802 men and women without cardiovascular disease with low-density lipoprotein cholesterol levels <130 mg/dL and high-sensitivity C-reactive protein levels ≥2.0 mg/L to rosuvastatin 20 mg daily or placebo. Active therapy with rosuvastatin reduced overall stroke rates nearly by half (48%), largely because of a 51% reduction in ischemic stroke without an increase in the risk of hemorrhagic stroke. Aside from a small increase in the risk of physician-diagnosed diabetes in the rosuvastatin arm, adverse events were similar in the 2 treatment arms. An updated meta-analysis of data from JUPITER and data from prior primary prevention statin trials (West of Scotland Coronary Prevention Study, Air Force/Texas Coronary Atherosclerosis Prevention Study, and Management of Elevated Cholesterol in the Primary Prevention Group of Adult Japanese) revealed a statistically significant 25% reduction in the risk of stroke with active statin therapy in the primary prevention setting. Our data suggest that statin therapy prevents stroke in a primary prevention population with normal levels of low-density lipoprotein cholesterol but elevated levels of the inflammatory biomarker high-sensitivity C-reactive protein.
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