SUPPLEMENTAL MATERIAL

Rosuvastatin slows progression of carotid intima-media thickness: the METEOR-China randomized controlled study

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Key inclusion criteria

Participants with only hypertension (defined as blood pressure ≥140/90 mm Hg or on antihypertensive treatment) and age as ischemic cardiovascular disease (ICVD) risk factors and participants without hypertension who had ≥3 other ICVD risk factors (including age) must have had fasting LDL-C (low-density lipoprotein cholesterol) levels ≥120 mg/dL (3.1 mmol/L) and <160 mg/dL (4.1 mmol/L). Participants without hypertension who had <3 other ICVD risk factors (including age) must have had fasting LDL-C levels ≥120 mg/dL (3.1 mmol/L) and <190 mg/dL (4.9 mmol/L); triglyceride levels <500 mg/dL (5.65 mmol/L) at visit 1 (week −6); high-density lipoprotein cholesterol levels ≤60 mg/dL (1.6 mmol/L) at visit 1; and maximum CIMT ≥1.2 mm and <3.5 mm at any location in the carotid ultrasound scans conducted at both visit 2 (week −4) and visit 3 (week −2).
Key exclusion criteria

History of coronary artery or any other atherosclerotic disease; history of diabetes mellitus; uncontrolled hypertension; use of any lipid-lowering drugs in the year prior to visit 1 or lipid-metabolism altering supplements within 2 weeks of visit 1; active liver disease or hepatic dysfunction defined as alanine aminotransferase, aspartate aminotransferase, or bilirubin $\geq 1.5 \times$ upper limit of normal; serum creatine kinase $> 3 \times$ upper limit of normal at visit 1; and serum creatinine $> 2.0$ mg/dL (177 µmol/L) during the screening period.
**Figure S1.** Difference between rosuvastatin and placebo in annualized rate of change and 95% CIs for the primary and secondary CIMT end points, mixed-effects model (per protocol analysis set)

12 carotid sites: near and far walls of the right and left CCA, carotid bulb, and the ICA.

Per protocol analysis set included 224 patients from the rosuvastatin arm and 232 from the placebo arm.

CCA, common carotid artery; CIMT, carotid intima-media thickness; ICA, internal carotid artery; MeanMax, mean of the maximum; MeanMean, mean of the mean.
### Table S1. Site list

| Site name                                                                 | Principal investigator |
|---------------------------------------------------------------------------|------------------------|
| The PLA General Hospital of People's Liberation Army (301 Hospital)       | Yundai Chen            |
| Beijing Tiantan Hospital, Capital Medical University                      | Yongjun Wang           |
| Beijing Friendship Hospital                                               | Hongwei Li             |
| Jishuitan Hospital                                                        | Hongtao Hu             |
| The People's Hospital of Liaoning Province                                | Zhanquan Li            |
| Nanfang Hospital of Nanfang Medical University                            | Shiping Cao            |
| Guangdong Provincial Chinese Medicine Hospital                            | Yefeng Cai             |
| Xiangya Second Hospital                                                   | Daoquan Peng           |
| The First Affiliated Hospital of Jinan University                          | Yaogao Fu              |
| The First Affiliated Hospital of Xi'an Jiaotong University                | Zuyi Yuan              |
| The First Affiliated Hospital, Sun Yat-sen University                     | Yugang Dong            |
| Hospital and University Name                                      | Name           |
|-----------------------------------------------------------------|----------------|
| Zhongda Hospital, Southeast University                           | Genshan Ma     |
| Ningbo No. 2 Hospital                                            | Wenke Hong     |
| The Second Affiliated Hospital of Guangzhou Medical University   | En Xu          |
| TEDA International Cardiovascular Hospital                      | Huimin Li      |
| Shanghai Yangpu District Central Hospital                       | WenHua Yue     |
| Wuhan Union Hospital                                             | Bo Hu          |
| Peking University Third Hospital                                 | Xiaogang Li    |
| Shanghai Tongji Hospital                                         | Zhiyu Nie      |
| Third Affiliated Hospital of the Third Military Medical University of PLA | Yanjiang Wang |
| The First Affiliated Hospital of Nanchang University              | Zeqi Zheng     |
| The Affiliated Hospital of Bengbu Medical College                | Ningru Zhang   |
| The First Affiliated Hospital of Wenzhou Medical University      | Xu Zhang       |
| The First Affiliated Hospital of Harbin Medical University       | Lu Fu          |
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| Zhongshan Hospital, Fudan University | Weiguo Fu |
|--------------------------------------|-----------|

Table S2. CONSORT 2010 checklist

| Section/Topic       | Item # | Checklist item                                                                 | Reported on page # of accepted manuscript |
|---------------------|--------|-------------------------------------------------------------------------------|-------------------------------------------|
| Title and abstract  | 1a     | Identification as a randomised trial in the title                             | 1                                         |
|                     | 1b     | Structured summary of trial design, methods, results, and conclusions         | 3                                         |
| Introduction        | 2a     | Scientific background and explanation of rationale                            | 6                                         |
| Background and      | 2b     | Specific objectives or hypotheses                                             | 6                                         |
| objectives          |        |                                                                                |                                            |
| Methods             | 3a     | Description of trial design (such as parallel, factorial) including allocation ratio | 7                                         |
|                     | 3b     | Important changes to methods after trial commencement (such as eligibility criteria), with reasons | Not applicable |
| Participants        | 4a     | Eligibility criteria for participants                                          | 8; (1–2 in supplemental material)         |
|                     | 4b     | Settings and locations where the data were collected                           | 7; (Table S1 on page 6 in supplemental material) |
| Interventions       | 5      | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | 8                                         |
| Outcomes            | 6a     | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | 8–9                                      |
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|   |   |
|---|---|
| 6b | Any changes to trial outcomes after the trial commenced, with reasons |
|   | Not applicable as no changes were made |
| Sample size | 7a | How sample size was determined |
|   | 7b | When applicable, explanation of any interim analyses and stopping guidelines |
| Randomisation: | 8a | Method used to generate the random allocation sequence |
|   | 8b | Type of randomisation; details of any restriction (such as blocking and block size) |
|   | 9  | Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned |
|   | 10 | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions |
| Blinding | 11a | If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how |
|   | 11b | If relevant, description of the similarity of interventions |
| Statistical methods | 12a | Statistical methods used to compare groups for primary and secondary outcomes |
|   | 12b | Methods for additional analyses, such as subgroup analyses and adjusted analyses |
|   | 11–12 | 12 (Table S4 on page 12 in supplemental material) |
| Results | Participant flow (a diagram is strongly recommended) | For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome |
|   | 13a | Figure 1; 31 |
|   | 13b | For each group, losses and exclusions after randomisation, together with reasons |
|   | 13 | Figure 1; 31 |
| Recruitment | 14a | Dates defining the periods of recruitment and follow-up |
|   | 14b | Why the trial ended or was stopped |
|   | 13 | Not applicable |
| Baseline data | 15 | A table showing baseline demographic and clinical characteristics for each group |
|   | Table 1; 34 |
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| Section        | Details                                                                 | Page Range                           |
|----------------|-------------------------------------------------------------------------|-------------------------------------|
| Numbers analysed | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups | 12; Table 2; 36                      |
| Outcomes and estimation | For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) | Table 2; 36                          |
| Ancillary analyses | For binary outcomes, presentation of both absolute and relative effect sizes is recommended | Not applicable                      |
| Ancillary analyses | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory | 13–14                               |
| Ancillary analyses | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory (Table S4 on pages 11–12 in supplemental material) |                                      |
| Harms           | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) | 15–16                               |
| Harms           | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) (Tables S5–S7 on pages 13–21 in supplemental material) |                                      |
| Discussion      | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses | 19                                  |
| Generalisability | Generalisability (external validity, applicability) of the trial findings | 19                                  |
| Interpretation  | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence | 17–19                               |
| Other information | Registration number and name of trial registry | 4                                   |
| Other information | Where the full trial protocol can be accessed, if available | 4                                   |
| Other information | Sources of funding and other support (such as supply of drugs), role of funders | 20                                  |
Table S3. Summary of annualized rate of change (slope) in mm/y for the rosvastatin-treated participants by time-weighted averages for the pre-specified LDL-C subgroups

| Subgroup category                        | Summary statistic | Rosuvastatin 20 mg/d (N=272) |
|------------------------------------------|-------------------|-------------------------------|
| % change from baseline in LDL-C          |                   |                               |
| ≥ mean (−15.4%)                          | n                 | 70                            |
|                                           | Slope mean (SE)   | 0.0060 (0.00574)              |
|                                           | Slope 95% CI      | (−0.0053, 0.0172)             |
| < mean (−15.4%)                          | n                 | 190                           |
|                                           | Slope mean (SE)   | 0.0030 (0.00383)              |
|                                           | Slope 95% CI      | (−0.0045, 0.0105)             |
| On-treatment LDL-C                       |                   |                               |
| ≥ mean (113.4 mg/dL)                     | n                 | 58                            |
|                                           | Slope mean (SE)   | 0.0056 (0.00614)              |
|                                           | Slope 95% CI      | (−0.0064, 0.0176)             |
| < mean (113.4 mg/dL)                     | n                 | 202                           |
|                                           | Slope mean (SE)   | 0.0029 (0.00372)              |
|                                           | Slope 95% CI      | (−0.0044, 0.0102)             |

Note: The annualized rate of change (mm/y) of max CIMT of the 12 carotid artery sites was estimated from the mixed model for primary end point analysis using data only from participants in the subgroup.

CI, confidence interval; ITT, intent to treat; LDL-C, low-density lipoprotein; SE, standard error.
Table S4. Analysis of percentage change from baseline to final visit in lipid, lipoprotein, and apolipoprotein values, ANCOVA (ITT analysis) set

| LS mean Percent change* | Final visit (LOCF) | Time-weighted average† |
|-------------------------|--------------------|------------------------|
|                         | Rosuvastatin 20 mg/d | Placebo | Rosuvastatin 20 mg/d vs placebo \(95\%\text{ CI}\) | P value | Rosuvastatin 20 mg/d | Placebo | Rosuvastatin 20 mg/d vs placebo \(95\%\text{ CI}\) | P value |
|                         | (N=272) | (N=271) | (N=272) | (N=271) | (N=272) | (N=271) | (N=272) | (N=271) |
| LDL-C (mg/dL) | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 |
| −26.5 (1.70) | 9.0 (1.73) | −35.5 (−40.2, −30.7) | <0.001 | −34.9 (1.28) | 4.6 (1.30) | −39.5 (−43.1, −35.9) | <0.001 |
| TC (mg/dL) | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 |
| −20.6 (1.01) | 1.3 (1.03) | −21.9 (−24.7, −19.0) | <0.001 | −24.0 (0.80) | 1.5 (0.81) | −25.5 (−27.7, −23.2) | <0.001 |
| HDL-C (mg/dL) | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 |
| 5.5 (0.94) | 0.5 (0.96) | 5.0 (2.4, 7.6) | <0.001 | 7.1 (0.74) | 3.4 (0.75) | 3.7 (1.6, 5.7) | <0.001 |
| TG (mg/dL) | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 |
| −7.3 (2.58) | 12.4 (2.62) | −19.7 (−26.9, −12.4) | <0.001 | −9.1 (2.09) | 9.4 (2.12) | −18.4 (−24.3, −12.6) | <0.001 |
| Non–HDL-C (mg/dL) | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 |
| −27.7 (1.34) | 1.8 (1.37) | −29.5 (−33.3, −25.7) | <0.001 | −32.6 (1.07) | 1.2 (1.09) | −33.8 (−36.8, −30.8) | <0.001 |
| Non–HDL-C/HDL-C | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 | n=260 | n=252 |
| −28.5 (1.64) | 3.2 (1.66) | −31.8 (−36.3, −27.2) | <0.001 | −34.3 (1.29) | −0.4 (1.31) | −33.9 (−37.5, −30.3) | <0.001 |
| ApoB† (mg/dL) | n=210 | n=214 | NA | NA | n=210 | n=214 | NA | NA |
| −24.2 (1.31) | 1.9 (1.30) | −26.1 (−29.7, −22.5) | <0.001 | NA | NA | NA | NA |
| ApoA-I† (mg/dL) | n=210 | n=214 | NA | NA | n=210 | n=214 | NA | NA |
| 3.2 (0.78) | 1.0 (0.78) | 2.2 (0.02, 4.4) | 0.047 | NA | NA | NA | NA |
| ApoB/ApoA-I ratio | n=210 | n=214 | NA | NA | n=210 | n=214 | NA | NA |
| −25.1 (1.45) | 1.6 (1.44) | −26.8 (−30.8, −22.8) | <0.001 | NA | NA | NA | NA |
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For each lipid, lipoprotein and apolipoprotein, participant numbers, percentage change from baseline, and SE (shown in parentheses) by treatment group are presented. The percentage change from baseline difference between rosuvastatin 20 mg/d and placebo groups and 95% CI with corresponding P value are reported. Baseline is the last result collected prior to the first dose of study treatment.

The time-weighted average value is defined as the value multiplied by the number of days since the last assessment, summed for all observations, and divided by the sum of days between all visits.

LS mean, LS mean difference, SE, and CI were obtained using the ANCOVA model for the percentage change from baseline values at the end of treatment with treatment as a fixed effect and baseline value as a covariate.

Includes measurements on or before 10 days after the date of last dose of study treatment.

The LDL-C result is based on converted values. All LDL-C values collected on or after March 8, 2018 were converted from third-generation reagent to second-generation reagent results.

ApoA-I, apolipoprotein A-I; ApoB, apolipoprotein B; ANCOVA, analysis of covariance; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LOCF, last observation carried forward; LSmean, least squares mean; NA, not applicable; Non-HDL-C, non-high-density lipoprotein cholesterol; SE, standard error; TC, total cholesterol; TG, triglycerides.
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**Table S5.** Annualized changes from baseline values to the end of the treatment period (week 104) in MeanMax CIMT of the 12 carotid artery sites by subgroups (ITT analysis set)

| Subgroup category | Rosuvastatin 20 mg/d (N=272) | Placebo (N=271) | Comparison between groups |
|-------------------|-------------------------------|-----------------|--------------------------|
|                   | Annualized rate of change from baseline (mm/y) | Estimated mean (SE) | 95% CI | Estimated mean (SE) | 95% CI | Estimated mean difference (SE) | 95% CI | Statistics for interaction*/ estimated mean difference (95% CI) | P value |
| Age (y)           |                               |                 |          |                 |         |                                |        |                                           |        |
| <65               | 234                           | 1.0955 (0.01416) | (1.0677, 1.1234) | 227 | 1.0984 (0.01474) | (1.0695, 1.1274) | −0.0029 (0.01657) | (−0.0354, −0.0297) | 0.0055 (−0.0198, 0.0307) | 0.672 |
| ≥65               | 38                            | 1.1502 (0.03051) | (1.0903, 1.2102) | 44 | 1.1840 (0.02797) | (1.1290, 1.2389) | −0.0338 (0.03969) | (−0.1117, 0.0442) |                                           |        |
| Sex               |                               |                 |          |                 |         |                                |        |                                           |        |
| Men               | 126                           | 1.1584 (0.01752) | (1.1240, 1.1929) | 113 | 1.1740 (0.01841) | (1.1378, 1.2102) | −0.0155 (0.02238) | (−0.0595, 0.0284) | 0.0059 (−0.0235, 0.0117) | 0.513 |
| Women             | 146                           | 1.0631 (0.01690) | (1.0299, 1.0963) | 158 | 1.0584 (0.01621) | (1.0266, 1.0903) | 0.0046 (0.01997) | (−0.0346, 0.0439) |                                           |        |
| BMI (kg/m²)       |                               |                 |          |                 |         |                                |        |                                           |        |
| <28               | 241                           | 1.1076 (0.01384) | (1.0804, 1.1348) | 240 | 1.1220 (0.01375) | (1.0950, 1.1490) | −0.0145 (0.01576) | (−0.0454, 0.0165) | −0.0141 (−0.0416, 0.0134) | 0.316 |
| ≥28               | 31                            | 1.1266 (0.03209) | (1.0635, 1.1896) | 31 | 1.0489 (0.03301) | (0.9841, 1.1138) | 0.0776 (0.04430) | (−0.0094, 0.1647) |                                           |        |
| ICVD risk category|                               |                 |          |                 |         |                                |        |                                           |        |
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### Table 1: Annualized Rate of Change

| Subgroup category | Rosuvastatin 20 mg/d (N=272) | Placebo (N=271) | Comparison between groups |
|-------------------|-------------------------------|-----------------|---------------------------|
|                   | n                | Estimated mean (SE) | 95% CI     | n                | Estimated mean (SE) | 95% CI     | Estimated mean difference (SE) | 95% CI | Statistics for interaction*/estimates mean difference (95% CI) | P value |
| <5%               | 196              | 1.0957 (0.01475)   | (1.0667, 1.1246) | 195              | 1.1109 (0.01474)   | (1.0820, 1.1399) | −0.0152 (0.01744) | (−0.0495, 0.0190) | −0.0159 (−0.0353, 0.0035) | 0.108 |
| ≥5% to <10%       | 76               | 1.1346 (0.02119)   | (1.0929, 1.1762) | 76               | 1.1091 (0.02118)   | (1.0675, 1.1507) | 0.0255 (0.02852) | (−0.0305, 0.0815) | 0.0298 (0.0090, 0.0506) | 0.005 |
| Hypertension history status | | | | | | | | | | |
| History of hypertension | 57              | 1.1331 (0.02863)   | (1.0769, 1.1894) | 68               | 1.1203 (0.02740)   | (1.0665, 1.1742) | 0.0128 (0.03135) | (−0.0488, 0.0744) | 0.0298 (0.0090, 0.0506) | 0.005 |
| No history of hypertension | 215             | 1.1008 (0.01812)   | (1.0652, 1.1364) | 203              | 1.1090 (0.01938)   | (1.0710, 1.1471) | −0.0082 (0.01700) | (−0.0416, 0.0252) | 0.0181 (−0.0019, 0.0382) | 0.076 |
| Smoking status | | | | | | | | | |
| Never | 194              | 1.1098 (0.01549)   | (1.0794, 1.1403) | 212              | 1.1055 (0.01515)   | (1.0757, 1.1353) | 0.0043 (0.01726) | (−0.0296, 0.0382) | 0.0181 (−0.0019, 0.0382) | 0.076 |
| Current/former | 78               | 1.1125 (0.02283)   | (1.0677, 1.1574) | 59               | 1.1445 (0.02590)   | (1.0936, 1.1954) | −0.0320 (0.02982) | (−0.0905, 0.0266) | 0.0181 (−0.0019, 0.0382) | 0.076 |

Comparisons of the annualized rate of change are based on a multilevel mixed-effects model, which is fitted to Max CIMT value for each site over 104 weeks with randomized treatment group, time, subgroup, treatment-by-subgroup interaction, treatment-by-time interaction, time-by-subgroup interaction, and treatment-by-time-by-subgroup interaction. ICVD risk stratification, carotid artery site, center, sex, and scan reader are fixed effects. Random effects within the model are the intercept and slope for individual patients. Time in the model is a continuous measure and is the interval in years from date of randomization to date of CIMT measurement and its effect is linear.

*Statistical significance of the maximum CIMT annualized rate of change (slope) between rosuvastatin and placebo was evaluated using a treatment by time by subgroup interaction term in the model. Estimated mean difference, 95% CI, and P values are provided.
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BMI, body mass index; CIMT, carotid intima-media thickness; ICVD, ischemic cardiovascular disease; SE, standard error.
Table S6. Adverse events leading to discontinuation of investigational treatment, by system organ class and preferred term (safety analysis set)

| System organ class/Preferred term | Number (%) of participants* |
|----------------------------------|-----------------------------|
|                                  | Rosuvastatin 20 mg/d (N=272) | Placebo (N=268) |
| Participants with an AE leading to discontinuation of treatment† | 28 (10.3) | 25 (9.3) |
| Metabolism and nutrition disorders | 8 (2.9) | 1 (0.4) |
| Diabetes mellitus | 6 (2.2) | 1 (0.4) |
| Type 2 diabetes mellitus | 2 (0.7) | 0 |
| Investigations | 6 (2.2) | 7 (2.6) |
| Alanine aminotransferase increased | 1 (0.4) | 0 |
| Apolipoprotein A-I decreased | 1 (0.4) | 0 |
| Aspartate aminotransferase increased | 1 (0.4) | 0 |
| Blood creatine kinase increased | 1 (0.4) | 1 (0.4) |
| Blood glucose increased | 1 (0.4) | 4 (1.5) |
| Electrocardiogram ST-T change | 1 (0.4) | 0 |
| Hematocrit decreased | 1 (0.4) | 0 |
| Low-density lipoprotein increased | 1 (0.4) | 0 |
| Electrocardiogram ST-T segment abnormal | 0 | 1 (0.4) |
| Electrocardiogram T wave inversion | 0 | 1 (0.4) |
| Low-density lipoprotein abnormal | 0 | 1 (0.4) |
| Cardiac disorders | 3 (1.1) | 8 (3.0) |
| Bundle branch block left | 1 (0.4) | 0 |
| Coronary artery disease | 1 (0.4) | 1 (0.4) |
| Palpitations | 1 (0.4) | 0 |
| Acute myocardial infarction | 0 | 2 (0.7) |
| Angina pectoris | 0 | 2 (0.7) |
| Angina unstable | 0 | 1 (0.4) |
| Defect conduction intraventricular | 0 | 1 (0.4) |
| System organ class/Preferred term | Number (%) of participants* |
|----------------------------------|-----------------------------|
|                                  | Rosuvastatin 20 mg/d (N=272) | Placebo (N=268) |
|                                  |                             |                 |
| Sinus bradycardia                | 0                           | 1 (0.4)         |
| Ventricular extrasystoles        | 0                           | 1 (0.4)         |
| Nervous system disorders         |                             |                 |
| Cerebral infarction              | 2 (0.7)                     | 0               |
| Cerebral artery stenosis         | 1 (0.4)                     | 0               |
| Carotid artery occlusion         | 0                           | 1 (0.4)         |
| Hepatobiliary disorders          |                             |                 |
| Hepatic function abnormal        | 2 (0.7)                     | 0               |
| Infections and infestations      |                             |                 |
| Pneumonia                        | 1 (0.4)                     | 0               |
| Urinary tract infection          | 1 (0.4)                     | 0               |
| Hepatitis viral                  | 0                           | 1 (0.4)         |
| Neoplasms benign, malignant and unspecified (including cysts and polyps) | 2 (0.7) | 2 (0.7) |
| Lung neoplasm malignant          | 1 (0.4)                     | 0               |
| Thyroid cancer                   | 1 (0.4)                     | 0               |
| Breast cancer metastatic         | 0                           | 1 (0.4)         |
| Colon cancer                     | 0                           | 1 (0.4)         |
| Renal and urinary disorders      |                             |                 |
| Proteinuria                      | 2 (0.7)                     | 4 (1.5)         |
| Blood and lymphatic system disorders | 1 (0.4) | 0 |
| Anemia                           | 1 (0.4)                     | 0               |
| Gastrointestinal disorders       |                             |                 |
| Abdominal distension             | 1 (0.4)                     | 0               |
| Dyspepsia                        | 1 (0.4)                     | 0               |
| Gastroesophageal reflux disease  | 1 (0.4)                     | 0               |
| General disorders and administration site conditions | 1 (0.4) | 0 |
| Chest pain                       | 1 (0.4)                     | 0               |
| Musculoskeletal and connective tissue disorders | 1 (0.4) | 0 |
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| System organ class/Preferred term | Number (%) of participants* |
|----------------------------------|-----------------------------|
|                                  | Rosuvastatin 20 mg/d (N=272) | Placebo (N=268) |
| Back pain                        | 1 (0.4)                     | 0 |
| Pain in extremity                | 1 (0.4)                     | 0 |
| Psychiatric disorders            | 1 (0.4)                     | 0 |
| Insomnia                         | 1 (0.4)                     | 0 |
| Vascular disorders               | 1 (0.4)                     | 1 (0.4) |
| Hypertension                     | 1 (0.4)                     | 0 |
| Arteriosclerosis                 | 0                            | 1 (0.4) |

*Number (%) of participants with AEs, sorted in decreasing frequency of SOC and PT (rosuvastatin 20 mg/d group).
†Action taken, study drug permanently stopped.
Participants with multiple AEs leading to discontinuation are counted once for each SOC/PT.
Includes AEs with an onset date on or after the date of first dose up to and including 10 days following the date of last dose of study treatment.
AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities version 21.0; PT, preferred term; SOC, system organ class.
Table S7. Adverse events with a frequency of ≥2% (safety analysis set)

| System organ class/preferred term                              | Number (%) of participants* |           |
|---------------------------------------------------------------|-----------------------------|-----------|
|                                                               | Rosuvastatin 20 mg/d (N=272) | Placebo (N=268) |
| Participants with any AE                                     | 230 (84.6)                  | 208 (77.6) |
| Infections and infestations                                  | 101 (37.1)                  | 109 (40.7) |
| Nasopharyngitis                                              | 52 (19.1)                   | 56 (20.9)  |
| Upper respiratory tract infection                            | 49 (18.0)                   | 55 (20.5)  |
| Bronchitis                                                   | 6 (2.2)                     | 7 (2.6)    |
| Pharyngitis                                                  | 6 (2.2)                     | 7 (2.6)    |
| Pneumonia                                                    | 6 (2.2)                     | 2 (0.7)    |
| Periodontitis                                                | 5 (1.8)                     | 10 (3.7)   |
| Urinary tract infection                                      | 5 (1.8)                     | 8 (3.0)    |
| Investigations                                               | 57 (21.0)                   | 39 (14.6)  |
| Blood glucose increased                                      | 24 (8.8)                    | 18 (6.7)   |
| Protein urine present                                       | 16 (5.9)                    | 9 (3.4)    |
| Blood creatine kinase increased                              | 11 (4.0)                    | 7 (2.6)    |
| Alanine aminotransferase increased                           | 8 (2.9)                     | 2 (0.7)    |
| Blood cholesterol decreased                                  | 7 (2.6)                     | 0          |
| Aspartate aminotransferase increased                         | 6 (2.2)                     | 2 (0.7)    |
| Blood triglycerides increased                                | 4 (1.5)                     | 6 (2.2)    |
| Gastrointestinal disorders                                   | 54 (19.9)                   | 47 (17.5)  |
| Toothache                                                    | 23 (8.5)                    | 15 (5.6)   |
| Abdominal discomfort                                         | 11 (4.0)                    | 8 (3.0)    |
| Abdominal pain upper                                         | 11 (4.0)                    | 7 (2.6)    |
| Diarrhea                                                     | 7 (2.6)                     | 10 (3.7)   |
| Gastritis                                                    | 6 (2.2)                     | 5 (1.9)    |
| Chronic gastritis                                            | 5 (1.8)                     | 7 (2.6)    |
| Musculoskeletal and connective tissue disorders              | 33 (12.1)                   | 28 (10.4)  |
| Back pain                                                    | 12 (4.4)                    | 9 (3.4)    |
| Pain in extremity                                            | 9 (3.3)                     | 5 (1.9)    |
| System organ class/preferred term                              | Rosuvastatin 20 mg/d (N=272) | Placebo (N=268) |
|---------------------------------------------------------------|------------------------------|-----------------|
| Arthralgia                                                   | 8 (2.9)                      | 13 (4.9)        |
| Myalgia                                                       | 8 (2.9)                      | 4 (1.5)         |
| Nervous system disorders                                     | 33 (12.1)                    | 23 (8.6)        |
| Dizziness                                                    | 14 (5.1)                     | 16 (6.0)        |
| Hypoesthesia                                                 | 9 (3.3)                      | 3 (1.1)         |
| Headache                                                     | 7 (2.6)                      | 7 (2.6)         |
| Cerebral infarction                                          | 6 (2.2)                      | 0               |
| Vascular disorders                                           | 20 (7.4)                     | 21 (7.8)        |
| Hypertension                                                 | 20 (7.4)                     | 21 (7.8)        |
| Respiratory, thoracic and mediastinal disorders              | 17 (6.3)                     | 22 (8.2)        |
| Cough                                                        | 14 (5.1)                     | 15 (5.6)        |
| Oropharyngeal pain                                           | 4 (1.5)                      | 8 (3.0)         |
| Cardiac disorders                                            | 11 (4.0)                     | 9 (3.4)         |
| Palpitations                                                 | 7 (2.6)                      | 3 (1.1)         |
| Angina pectoris                                              | 4 (1.5)                      | 6 (2.2)         |
| Renal and urinary disorders                                  | 10 (3.7)                     | 12 (4.5)        |
| Proteinuria                                                  | 10 (3.7)                     | 12 (4.5)        |
| General disorders and administration site conditions         | 9 (3.3)                      | 13 (4.9)        |
| Pyrexia                                                      | 6 (2.2)                      | 7 (2.6)         |
| Chest pain                                                   | 4 (1.5)                      | 6 (2.2)         |
| Hepatobiliary disorders                                      | 9 (3.3)                      | 4 (1.5)         |
| Hepatic function abnormal                                    | 9 (3.3)                      | 4 (1.5)         |
| Psychiatric disorders                                        | 9 (3.3)                      | 4 (1.5)         |
| Insomnia                                                     | 9 (3.3)                      | 4 (1.5)         |
| Metabolism and nutrition disorders                           | 6 (2.2)                      | 1 (0.4)         |
| Diabetes mellitus                                            | 6 (2.2)                      | 1 (0.4)         |
| Skin and subcutaneous tissue disorders                       | 6 (2.2)                      | 1 (0.4)         |
| Urticaria                                                    | 6 (2.2)                      | 1 (0.4)         |
Supplemental Material for METEOR-China

*Number (%) of participants with AEs, sorted in decreasing frequency of SOC and PT (rosuvastatin 20 mg/d group). Includes AEs with an onset date on or after the date of first dose up to and including 10 days following the date of last dose of study treatment.

AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities version 21.0; PT, preferred term; SOC, system organ class.
Table S8. Ischemic cardiovascular adverse events, by system organ class and preferred term (safety analysis set)

| System organ class / Preferred term                       | Rosuvastatin 20 mg/d (N=272) | Placebo (N=268) |
|-----------------------------------------------------------|------------------------------|-----------------|
| Any ischemic cardiovascular event                         | 15 (5.5)                     | 12 (4.5)        |
| Nervous system disorders                                  |                              |                 |
| Cerebral infarction                                       | 6 (2.2)                      | 0               |
| Cerebral artery stenosis                                 | 1 (0.4)                      | 0               |
| Cerebral ischemia                                         | 1 (0.4)                      | 0               |
| Cerebrovascular accident                                 | 1 (0.4)                      | 0               |
| Cerebrovascular insufficiency                             | 1 (0.4)                      | 0               |
| Transient ischaemic attack                               | 0                            | 1 (0.4)         |
| Cardiac disorders                                         |                              |                 |
| Angina pectoris                                           | 4 (1.5)                      | 6 (2.2)         |
| Coronary artery disease                                  | 3 (1.1)                      | 1 (0.4)         |
| Arteriosclerosis coronary artery                          | 1 (0.4)                      | 2 (0.7)         |
| Myocardial ischemia                                       | 1 (0.4)                      | 0               |
| Acute myocardial infarction                              | 0                            | 2 (0.7)         |
| Angina unstable                                           | 0                            | 1 (0.4)         |

* Number (%) of participants with AEs, sorted in decreasing frequency of preferred term (rosuvastatin group).

Note: Includes adverse events with an onset date on or after the date of first dose up to and including 10 days following the date of last dose of study medication. Ischemic events are identified by preferred term. Preferred terms are: Angina pectoris, Angina unstable, Arteriosclerosis coronary artery, Coronary artery disease, Acute myocardial infarction, Myocardial infarction, Myocardial ischemia, Cerebral artery stenosis, Cerebral infarction, Cerebral ischemia, Cerebrovascular accident, Cerebrovascular insufficiency and Transient ischemic attack. AE, adverse event.
Table S9. Comparison of baseline characteristics of the participants from the global METEOR and METEOR-China studies

|                      | Global METEOR | METEOR-China |
|----------------------|--------------|--------------|
|                      | Rosuvastatin 40 mg/d (N=702) | Placebo (N=282) | Rosuvastatin 20 mg/d (N=272) | Placebo (N=271) |
| Age (y), mean (SD)   | 57 (6.2)     | 57 (6.0)     | 59.0 (5.2)                  | 59.7 (5.0)     |
| Women, n (%)         | 281 (40.0)   | 115 (40.8)   | 146 (53.7)                 | 158 (58.3)     |
| BMI, mean (kg/m²) (SD)| 27.1 (4.0)   | 27.5 (4.0)   | 25.0 (2.6)                 | 24.7 (2.7)     |
| Impaired renal function,* n (%) | 122 (19) | 37 (15) | 67 (24.6) | 105 (38.7) |
| Hypertension, n (%)  | 138 (20)     | 58 (21)      | 57 (21.0)                  | 68 (25.1)      |
| LDL-C (mg/dL), mean (SD) | 155 (24.1) | 154 (24.2) | 135.0 (22.5)              | 137.9 (24.4)  |
| Mean of maximum CIMT, mean (SD), mm | | | |
| 12 Carotid artery sites | 1.15 (0.19) | 1.17 (0.20) | 1.11 (0.17) | 1.10 (0.18) |
| Common carotid artery sites | 1.01 (0.17) | 1.02 (0.18) | 1.06 (0.18) | 1.04 (0.17) |
| Carotid bulb sites | 1.39 (0.28) | 1.41 (0.28) | 1.35 (0.27) | 1.34 (0.27) |
| Internal carotid artery sites | 1.06 (0.27) | 1.06 (0.28) | 0.90 (0.22) | 0.90 (0.24) |
| Mean of mean CIMT, mean (SD), mm | | | |
| Common carotid artery sites | 0.76 (0.12) | 0.76 (0.12) | 0.78 (0.12) | 0.77 (0.11) |

*Defined as creatinine clearance of 80 mL/min or less.
BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; CIMT, carotid intima-media thickness; SD, standard deviation.