

Effect of Telmisartan on Functional Outcome, Recurrence, and Blood Pressure in Patients With Acute Mild Ischemic Stroke

A PROFESS Subgroup Analysis

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Background and Purpose—High blood pressure (BP) is common in acute ischemic stroke and associated independently with a poor functional outcome. However, the management of BP acutely remains unclear because no large trials have been completed.

Methods—The factorial PROFESS secondary stroke prevention trial assessed BP-lowering and antiplatelet strategies in 20 332 patients; 1360 were enrolled within 72 hours of ischemic stroke, with telmisartan (angiotensin receptor antagonist, 80 mg/d, n=647) vs placebo (n=713). For this nonprespecified subgroup analysis, the primary outcome was functional outcome at 30 days; secondary outcomes included death, recurrence, and hemodynamic measures at up to 90 days. Analyses were adjusted for baseline prognostic variables and antiplatelet assignment.

Results—Patients were representative of the whole trial (age 67 years, male 65%, baseline BP 147/84 mm Hg, small artery disease 60%, NIHSS 3) and baseline variables were similar between treatment groups. The mean time from stroke to recruitment was 58 hours. Combined death or dependency (modified Rankin scale: OR, 1.03; 95% CI, 0.84–1.26; $P=0.81$); death: OR, 1.05; 95% CI, 0.27–4.04; and stroke recurrence: OR, 1.40; 95% CI, 0.68–2.89; $P=0.36$) did not differ between the treatment groups. In comparison with placebo, telmisartan lowered BP (141/82 vs 135/78 mm Hg, difference 6 to 7 mm Hg and 2 to 4 mm Hg; $P<0.001$), pulse pressure (3 to 4 mm Hg; $P<0.002$), and rate-pressure product (466 mm Hg.bpm; $P=0.0004$).

Conclusion—Treatment with telmisartan in 1360 patients with acute mild ischemic stroke and mildly elevated BP appeared to be safe with no excess in adverse events, was not associated with a significant effect on functional dependency, death, or recurrence, and modestly lowered BP. (*Stroke*. 2009;40:3541-3546.)

Key Words: acute stroke ■ blood pressure ■ ischemic stroke ■ outcome ■ randomized controlled trial ■ telmisartan

High blood pressure (BP) is present in 70% to 80% of patients with acute ischemic stroke^{6,7} and is associated independently with a poor outcome.^{7–10} However, there is a reluctance to lower a high BP because ischemic stroke is associated with focal attenuation of cerebral autoregulation. As a result, there is equipoise in whether high BP should be lowered (epidemiological evidence) or not (pathophysiological concerns).

Previous data on the effects of BP lowering on functional outcome in acute stroke are sparse and have given conflicting results. Trials of calcium channel blockers were ineffective overall,¹¹ and some studies reported them to be hazardous.^{12,13} The β -receptor antagonists were associated with a worse outcome in 1 trial.¹⁴ The ACCESS trial found that treatment with oral candesartan (angiotensin receptor antagonist [ARA]) was associated with reduced recurrent vascular

events at 1 year (secondary outcome) but had no effect on functional outcome at 3 months (primary outcome) or BP over the course of the first 7 days of treatment.¹⁵ A small trial of lisinopril or labetalol vs placebo suggested that case fatality (secondary outcome) was reduced in patients receiving antihypertensive therapy, although there was no effect on functional outcome (primary outcome).¹⁶ Few studies have assessed the effect of antihypertensive agents on cerebral blood flow (CBF),¹⁷ although some agents, eg, nitrates, are able to lower BP without adversely altering cerebral blood flow.¹⁸ Nevertheless, all of these studies enrolled <400 patients and no large trials have been completed in patients with acute ischemic stroke.

The Prevention Regimen for Effectively Avoiding Second Strokes (PROFESS) trial is the largest secondary stroke prevention study and compared, in a factorial design, telmis-

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artan (ARA) with placebo, and aspirin-extended release dipyridamole with clopidogrel, in preventing recurrent stroke.¹⁹ A key intention of the protocol was to recruit the patient at a time when the risk of recurrence was particularly high;¹⁹ 39.9% patients were recruited within 10 days of the index event.² Also, 1360 (6.7%) of patients were recruited within 72 hours of stroke onset, thereby providing the opportunity to assess, in a randomized design, the safety and efficacy of lowering blood pressure with telmisartan (on top of standard poststroke antihypertensive treatment) in patients with acute ischemic stroke.

Materials and Methods

The PROfESS trial protocol¹⁹ and primary results^{1,2} have been published. Briefly, PROfESS compared the effect of lowering BP with telmisartan (ARA, 80 mg daily) vs placebo, and combined aspirin (25 mg twice daily) and extended release dipyridamole (200 mg twice daily) vs clopidogrel (75 mg daily), in a 2×2 factorial design, in patients with recent ischemic stroke. Over 34 months, 20 332 patients were randomized from 695 centers in 35 countries and followed-up for a mean duration of 30 months. All patients received best medical care independent of treatment assignment; in particular, the PROfESS study protocol mandated that all patients with hypertension should be treated with an appropriate BP-lowering medication, excluding an ARA, with a target blood pressure of <140/90 mm Hg.

Inclusion Criteria

The aim of this PROfESS subgroup analysis, which was not prespecified in the statistical analysis plan, was to assess the safety and efficacy of lowering BP with telmisartan in patients with acute stroke. Patients were included if they were enrolled in the main trial and had been randomized within 72 hours of stroke onset. The time of 72 hours was chosen a priori to mirror the design of the ACCESS trial of candesartan, another ARA.¹⁵ Some PROfESS inclusion criteria are relevant specifically to assessment of BP management in acute stroke: ischemic stroke; symptoms persisting for >24 hours, or if <24 hours then CT or MRI evidence of a new stroke; hospitalization; age older than 55 years, or age 50 to 54 years if 2 additional vascular risk factors present; seated systolic BP (SBP) 121 to 180 mm Hg; seated diastolic BP ≤110 mm Hg; and neurologically stable. Similarly, relevant key exclusion criteria are: dysphagia preventing oral medication; severe dependency at time of randomization (modified Rankin Scale [mRS] >3); currently using or needing ARA; known severe renal insufficiency or renal artery stenosis; hyperkalemia; uncorrected volume or sodium depletion; known severe coronary artery disease or recent MI; and patients scheduled for carotid endarterectomy.

Hemodynamic Measures

SBP, diastolic BP, and heart rate (HR) were measured using a validated semiautomatic monitor (Omron 705CP).²⁰ Other hemodynamic variables were derived mathematically from BP and HR:

Pulse pressure=SBP−diastolic BP

SBP variability=SD of SBP/mean SBP

Rate pressure product (measure of cardiac work)=SBP×HR

Outcomes

The primary outcome in this post hoc subgroup analysis was functional outcome measured using the mRS at 30 days after randomization; a more conventional trial time of 90 days was not possible because mRS was not measured at this point. Secondary outcomes were studied at 7, 30, and 90 days (thereby mimicking the design of many acute stroke trials) and included hemorrhagic transformation of the infarct, cerebral edema, recurrent stroke, MI, composite vascular events (vascular death, nonfatal stroke, or MI), death, and serious adverse events. When possible, ordered categor-

ical outcomes were analyzed using ordinal statistical approaches.^{21,22} Tolerability was measured by adherence to therapy.

Analyses

Data are shown as the number of subjects (%) or mean (SD). Comparisons were performed with binary logistic regression (dichotomous data), ordinal logistic regression, or the Mann–Whitney *U* test (ordered categorical data), or multiple regression (continuous data). Statistical models were adjusted for prognostic covariates: baseline age, sex, severity, and SBP, and antiplatelet treatment assignment (aspirin/dipyridamole vs clopidogrel). OR (95% CI) are shown and statistical significance was set at *P*<0.05. Analyses were performed using SAS version 9.1.

Results

This subgroup analysis of the PROfESS trial^{1,2} examined the clinical usefulness of adding telmisartan vs placebo to standard poststroke antihypertensive treatment in 1360 patients (telmisartan 647, placebo 713) recruited within 72 hours of stroke onset (supplemental Figure I, available online at <http://stroke.ahajournals.org>). The mean time from stroke to recruitment was 58 hours, with the majority of patients recruited during the third day after stroke onset; treatment was started within 3 days of stroke in 853 patients (63%) and within 4 days in 1250 (92%). The characteristics of patients in this analysis were broadly similar to those of the whole trial (Table 1). The mean baseline BP was 147/84 mm Hg, and severity was mild with NIHSS=3. The treatment groups were similar for demographic, clinical, and hemodynamic measures (Table 1).

BP

In comparison with placebo, telmisartan lowered BP significantly by 6 to 7 mm Hg and 2 to 4 mm Hg over the 90 days (Table 2). Parallel reductions in pulse pressure and rate-pressure product were present. No effect on heart rate was seen.

Outcome

Combined death or dependency (mRS at 30 days after randomization, with adjustment for baseline covariates) did not differ whether analyzed as an ordinal outcome (ordered mRS categories: 0, 1, 2, 3, 4–6 to maintain proportionality)²¹ (OR, 1.03; 95% CI, 0.84–1.26; *P*=0.81; Figure 1) or with dichotomization of the data at the median (mRS 0–1 vs 2–6; OR, 1.00; 95% CI, 0.77–1.29; Table 3). No subgroups showed differential treatment effects (supplemental Figure II, available online at <http://stroke.ahajournals.org>).

The distribution of ordinal stroke events (fatal, dependent [mRS 2–5], independent [mRS 0,1], TIA, none)²² did not differ between the treatment groups (Mann–Whitney *U* test, *P*=0.42; Figure 2). Similarly, the time to recurrence did not differ between the treatment groups (log-rank test, *P*=0.40). Similarly, other events (ie, death, stroke recurrence, MI, and combined vascular events) did not differ between the treatment groups, whether measured at 7, 30, or 90 days (Table 3). There was no difference in the Mini-Mental State Examination at 30 days.

Serious Adverse Events

Serious adverse events were similar between telmisartan and control (Table 3; fatal, 5 vs 6; nonfatal, 45 vs 33). Selected serious adverse events relevant to stroke, BP-lowering, or

Table 1. Patient Characteristics at Enrollment

Characteristic	Telmisartan (N=647)	Placebo (N=713)	All Trial
Demographics			
Age, yr (SD)	66.8 (8.8)	67.1 (9.2)	66.1 (8.6)
Male (%)	420 (64.9)	464 (65.1)	13 022 (64.0)
Ethnicity (%)			
White	369 (57.0)	407 (57.0)	11 697 (57.5)
Asian	221 (34.2)	240 (33.7)	6660 (32.8)
Black	38 (5.9)	41 (5.8)	816 (4.0)
Other	19 (2.9)	25 (3.5)	1159 (5.7)
Clinical history			
Previous stroke/TIA (%)	160 (24.7)	184 (25.8)	4997 (24.6)
Atrial fibrillation (%)	10 (1.6)	14 (2.0)	540 (2.7)
Hypertension (%)	453 (70.0)	503 (70.6)	15 048 (74.0)
Hypertension, treated (%)	345 (53.3)	383 (53.7)	12 231 (60.1)
Diabetes mellitus (%)	176 (27.2)	198 (27.8)	5743 (28.3)
Hyperlipidemia (%)	264 (40.8)	283 (39.7)	9493 (46.7)
Left ventricular hypertrophy (%)	79 (12.5)	80 (11.6)	3167 (16.3)
Ischemic heart disease (%)	95 (14.7)	104 (14.6)	3304 (16.3)
Smoker, current (%)	158 (24.4)	178 (25.0)	4308 (21.2)
Antihypertensives (%)			
Angiotensin-converting enzyme inhibitor	204 (31.5)	206 (28.9)	7,519 (37.0)
Angiotensin receptor antagonist	20 (3.1)	24 (3.4)	1,059 (5.2)
Alpha-receptor antagonist	14 (2.2)	14 (2.0)	432 (2.1)
Beta-receptor antagonist	134 (20.7)	141 (19.8)	4231 (20.8)
Calcium channel blocker	113 (17.5)	166 (23.3)	4960 (24.4)
Diuretic	120 (18.6)	131 (18.4)	4261 (21.0)
Potassium sparing diuretic	13 (2.0)	10 (1.4)	307 (1.5)
Time from stroke, day			
0–1	73 (11.3)	99 (13.9)	...
1–2	239 (36.9)	257 (36.0)	...
2–3	335 (51.8)	357 (50.1)	...
Clinical details			
BP, mm Hg (SD)			
Systolic	146 (16.2)	147 (16.3)	144 (16.6)
Diastolic	84 (10.1)	84 (10.2)	84 (10.5)
Pulse pressure	62.4 (14.2)	63.1 (14.7)	60.3 (13.9)
Heart rate, bpm	72.8 (11.9)	73.1 (11.4)	73.2 (11.7)
Rate-pressure product, mm Hg.bpm	10 637 (2008)	10 747 (2028)	10 540 (2052)
Body mass index, kg.m ⁻² (SD)	26.9 (4.9)	26.8 (4.6)	26.8 (5.0)
TOAST classification (%)			
Large-artery atherosclerosis	129 (19.9)	156 (21.9)	5805 (28.6)
Cardioembolism	11 (1.7)	7 (1.0)	369 (1.8)
Small-artery occlusion	402 (62.1)	406 (56.9)	10 578 (52.0)
Other determined etiology	14 (2.2)	9 (1.3)	416 (2.1)
Undetermined etiology	91 (14.1)	135 (18.9)	3148 (15.5)
Missing	16 (0.1)
mRS (%)			
0 (no symptoms)	74 (11.4)	83 (11.6)	2853 (14.0)
1 (no significant disability)	219 (33.9)	279 (39.1)	7580 (37.3)
2 (slight disability)	182 (28.1)	191 (26.8)	5081 (25.0)
3 (moderate disability)	109 (16.9)	91 (12.8)	2891 (14.2)
4 (moderately severe disability)	63 (9.7)	69 (9.7)	1926 (9.5)
NIH Stroke Scale (SD)	2.9 (2.8)	3.1 (2.9)	2.8 (2.9)

Data for the whole trial are given for comparison. N (%) or mean (SD).

Table 2. Hemodynamic Effects on Treatment at Days 7, 30, and 90 After Enrollment

	Telmisartan (n=647)	Placebo (n=713)	Difference (95% CI)	P
Day 7				
Subjects (%)	479 (74.0)	542 (76.0)
SBP, mm Hg	135.3 (17.8)	141.4 (17.0)	6.1 (4.0, 8.2)	<0.0001
Diastolic BP, mm Hg	78.4 (10.8)	81.6 (11.0)	3.2 (1.8, 4.5)	<0.0001
Pulse pressure, mm Hg	56.8 (14.7)	59.7 (14.7)	2.9 (1.1, 4.7)	0.0017
Heart rate, bpm	74.3 (11.1)	74.2 (10.8)	-0.2 (-1.5, 1.2)	0.82
Rate-pressure product (SBP.HR)	10057 (1937)	10523 (2070)	466 (210, 723)	0.0004
Day 30				
Subjects (%)	612 (94.6)	674 (94.5)
N of nontrial antihypertensives (mean)	0.96 (1.03)	1.04 (1.03)	0.08 (0.99, 1.07)	0.14
0 (%)	271 (41.9)	267 (37.5)
1	203 (31.4)	231 (32.4)
2	117 (18.1)	151 (21.2)
3	42 (6.50)	50 (7.0)
4	14 (2.2)	12 (1.7)
5	0 (0)	2 (0.3)
SBP, mm Hg	135.7 (20.0)	142.6 (18.6)	6.9 (4.8, 9.0)	<0.0001
Diastolic BP, mm Hg	79.6 (11.9)	83.1 (11.2)	3.6 (2.3, 4.8)	<0.0001
Pulse pressure, mm Hg	56.2 (15.1)	59.5 (14.9)	3.3 (1.7, 5.0)	<0.0001
Day 90				
Subjects (%)	592 (91.5)	664 (93.1)
SBP, mm Hg	134.5 (19.9)	140.3 (19.0)	5.8 (3.6, 8.0)	<0.0001
Diastolic BP, mm Hg	79.2 (11.1)	81.5 (11.2)	2.4 (1.1, 3.6)	0.0002
Pulse pressure, mm Hg	55.3 (15.4)	58.7 (15.9)	3.5 (1.7, 5.2)	<0.0001

N (%) or mean (SD) with difference (95% CI). Comparisons by χ^2 test or *t* test.

treatment (telmisartan, placebo) included: hypotension (2 vs 2), syncope (1 vs 1), and falls (2 vs 1). No serious adverse events related to edema extension, cerebral hemorrhage, MI, or hyperkalemia were recorded over the 90 days.

Discussion

The aim of the present nonprespecified subgroup analysis was to investigate the safety, efficacy, and tolerability of

telmisartan when started in the acute phase of an ischemic stroke; 1360 patients were randomized within 72 hours of the onset of ischemia and data for these subjects form the basis of this report. In comparison with placebo, telmisartan did not alter functional outcome (assessed using the mRS) at 30 days or other outcomes, including stroke recurrence, MI, composite vascular outcome, or death, each at 90 days. Hence, these results mirror those seen across the main study, this being neutral, such that adding telmisartan to standard poststroke treatment did not reduce stroke recurrence at an average of 2.5 years in comparison with placebo.¹ Despite the fact that BP at baseline was reasonably well controlled (mean, 147/84 mm Hg), telmisartan further reduced it by 6 to 7 mm Hg and 2 to 4 mm Hg over the first 90 days after stroke; parallel reductions in pulse pressure and rate-pressure product were also seen.

Although telmisartan did not alter stroke recurrence in either this subgroup analysis or across the whole trial,¹ it is noteworthy that the direction of the point estimates were in opposite directions. In the main trial, a trend to reduction was apparent (HR, 0.95; 95% CI, 0.86–1.04; *P*=0.23); a post hoc analysis indicated that recurrence was nonsignificantly higher with telmisartan during the first 6 months of treatment (HR, 1.07; 95% CI, 0.92–1.25) and significantly lower thereafter (HR, 0.88; 95% CI, 0.78–0.99), with a significant treatment by time interaction (*P*=0.042).¹ As with short-term treatment in the main trial, a nonsignificant increase in the odds of

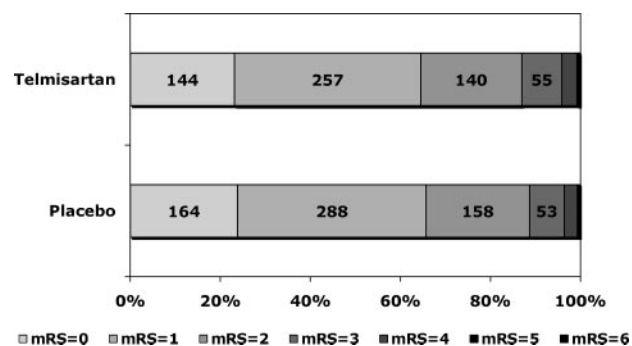


Figure 1. The mRS at day 30, comparison by Mann-Whitney *U*, *P*=0.55 (note: mRS=0, no symptoms; mRS=1, symptoms; mRS=2, slight disability but independent; mRS=3, moderate disability requiring some help; mRS=4, moderately severe disability requiring significant help with activities of daily living; mRS=5, dead; no patients had mRS=6). The numbers in the plot give the number of patients in each mRS class by treatment assignment.

Table 3. Cumulative Outcome and Safety at Days 7, 30, and 90 After Enrollment

	Telmisartan (n=647)	Placebo (n=713)	OR (95% CI)
7 Days			
Dropouts (%)*	0 (0.0)	1 (0.14)	...
Hemorrhagic transformation (%)	0 (0.0)	3 (0.42)	...
Cerebral edema (%)	0 (0.0)	0 (0.0)	...
Stroke recurrence (%)	4 (0.62)	5 (0.70)	0.88 (0.24, 3.31)
MI (%)	1 (0.15)	0 (0.0)	...
Combined vascular (%)	5 (0.77)	6 (0.84)	0.95 (0.28, 3.16)
Death (%)	0 (0.0)	1 (0.14)	...
SAE (%)	12 (1.85)	10 (1.40)	1.37 (0.59, 3.21)
30 Days			
Dropouts (%)†	4 (0.62)	2 (0.28)	3.98 (0.52, 30.2)
mRS (mean, SD)	1.3 (1.1)	1.3 (1.1)	...
mRS 0–1 vs 2–6 (%)‡	401 (64.5)	452 (65.7)	1.00 (0.77, 1.29)
Stroke recurrence (%)	13 (2.01)	8 (1.12)	1.89 (0.77, 4.62)
MI (%)	2 (0.31)	0 (0.0)	...
Combined vascular (%)	17 (2.63)	10 (1.40)	2.07 (0.93, 4.63)
Death (%)	4 (0.62)	2 (0.28)	...
SAE (%)	29 (4.48)	25 (3.51)	1.30 (0.75, 2.25)
Mini-Mental State Examination =30 (%)	190 (32.0)	207 (31.7)	1.02 (0.80, 1.31)
90 Days			
Dropouts (%)*	6 (0.93)	6 (0.84)	1.25 (0.36, 4.36)
Stroke recurrence (%)	17 (2.6)	14 (2.0)	1.40 (0.68, 2.89)
MI (%)	3 (0.5)	1 (0.1)	...
Combined vascular (%)	23 (3.6)	19 (2.7)	1.48 (0.78, 2.79)
Death (%)	5 (0.77)	6 (0.84)	1.05 (0.27, 4.04)
SAE (%)	50 (7.73)	39 (5.47)	1.43 (0.93, 2.22)

N (%) or mean (SD) with OR (95% CI). Comparison by binary logistic regression or multiple regression (continuous variables).

SAE indicates serious adverse events.

*Dropouts are patients lost to follow-up at the time point.

†Patients with no day 30 outcome data were excluded.

having a recurrent event was present in those patients who were enrolled during the acute phase.

The results of this subgroup analysis may be compared with previous studies of BP-lowering in acute ischemic stroke, especially those from the ACCESS trial,¹⁵ which also studied an oral ARA (candesartan) in patients with acute ischemic stroke within 72 hours of onset. However, the trials differed in several key respects: size (ACCESS was much smaller with 339 patients); time to recruitment (ACCESS had a mean time of 30 hours); BP inclusion criteria (ACCESS only included patients with severely elevated BP and had mean BP 189/99 mm Hg); presence of other antihypertensive agents (patients in ACCESS were not using any other BP drugs); stroke severity (the baseline severity is not reported in the ACCESS article but it is likely that the strokes will have been far more severe with significantly greater impairment); location (patients in ACCESS came from Germany only); length of treatment (comparison of candesartan with placebo

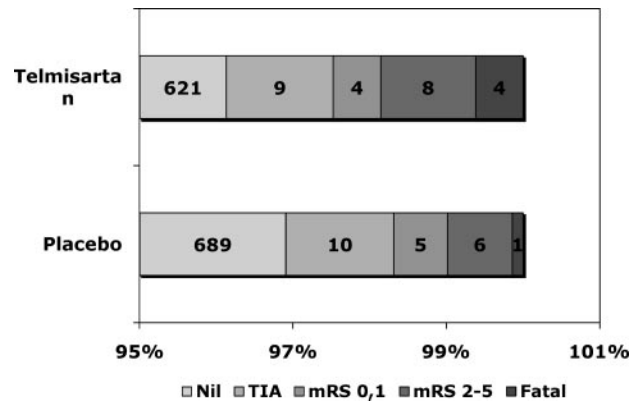


Figure 2. Ordinal stroke (recurrence and severity) at day 90, comparison by Mann–Whitney *U* test, *P*=0.42 (note: the majority of patients who did not have an event are not shown, and 3 patients with a recurrent stroke did not have a mRS recorded; the numbers of patients with each outcome are shown).

in ACCESS was only made for 7 days with patients in both treatment groups receiving candesartan thereafter for 1 year); effect of treatment on BP (candesartan did not alter BP in ACCESS); and results (the primary outcome, disability at 3 months, in ACCESS was neutral, although treatment with candesartan was associated with a significant reduction in a secondary outcome, comprising the cumulative 12-month mortality and vascular events).¹⁵

Taking the similarities and differences between ACCESS and PRoFESS, the apparent discrepancies in their results may simply reflect a false-positive finding in the small ACCESS trial. Additionally, the failure to show beneficial effects of telmisartan may reflect that patients had only mild hypertension and mild stroke. Nevertheless, this subgroup analysis of PRoFESS is the first to our knowledge to test whether it is safe for patients with acute mild stroke to have their BP actively lowered. Because chronic lowering of BP reduces stroke recurrence,^{23,24} the present results suggest it is safe to start such treatment acutely, particularly if based on an angiotensin-modifying drug. Further, it is possible that these results can be extrapolated to patients with TIA for which no trials have been performed to date and, possibly, none are likely.

Several caveats exist for this PRoFESS subgroup analysis. First, the results come from a subgroup of patients entered into a large secondary prevention trial such that patient characteristics reflect the inclusion criteria for a study of vascular prophylaxis rather than acute intervention. As a result, the trial was not designed to explicitly test the effect of lowering BP in acute stroke. Second, the inclusion criteria included neurological stability, which is usually absent in acute stroke, and means that no patients were recruited during the hyperacute phase (<6 hours of onset) of stroke. Third, the sample size was too small to reliably detect the effects of telmisartan on functional outcome or secondary prevention. The ongoing SCAST trial (<http://www.scast.no>) of candesartan in 2500 patients will extend the existing data from ACCESS and PRoFESS on lowering BP in acute ischemic stroke with ARA. Other large trials are also assessing the management of BP in acute stroke, including ENOS

(n=5000)³ in mixed ischemia/hemorrhage and INTERACT 2 (n=3000) in intracerebral hemorrhage.²⁵

In summary, this subgroup analysis of the PROfESS trial was neutral and did not identify any apparent beneficial or hazardous effects of telmisartan on functional outcome in patients with acute mild stroke. Nevertheless, the CI are wide and antihypertensive treatment might be beneficial or hazardous. The findings are relevant to patients with mild stroke (and possibly TIA) but do not apply to patients with moderate to severe stroke because no such patients were included. Several ongoing large trials are addressing this latter question, and the Cochrane Blood Pressure in Acute Stroke Collaboration systematic reviews^{4,5} will be updated to include the results of all of these. In the meantime, guidelines (such as those from the European Stroke Organisation²⁶) should not be changed until the results of these large randomized trials become available.

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Disclosure

Drs Yusuf, Sacco, and Diener were co-Chief Investigators of PROfESS; Drs Bath, Toni, Estol, and Roberts were members of the Trial Steering Committee, and Drs Martin and Palesch and Mr Cotton were biostatisticians supporting the trial. Boehringer Ingelheim sponsored and funded PROfESS, and reviewed and commented on the manuscript. Dr Bath is Chief Investigator of ENOS and BASC,³⁻⁵ a member of the SCAST Trial Steering Committee, and The Stroke Association Professor of Stroke Medicine.

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Effect of Telmisartan on Functional Outcome, Recurrence, and Blood Pressure in Patients With Acute Mild Ischemic Stroke: A PROfESS Subgroup Analysis

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