Established 1994

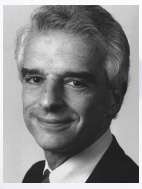
*Vascular Biology in Clinical Practice*™

VOLUME 7 · NUMBER 1

A CME MONOGRAPH SERIES
PUBLISHED UNDER
THE AUSPICES OF THE
VASCULAR BIOLOGY
WORKING GROUP℠

# ACE INHIBITION IN CAD PATIENTS:

## *Expanding the Reach of Cardioprotection*



EDITOR IN CHIEF

**Carl J. Pepine, MD**
*University of Florida*
*College of Medicine*
*Gainesville, Florida*

CONTRIBUTING EDITOR

**Willem J. Remme, MD, PhD**
*Carol Davila University*
*Bucharest, Romania*
*Sticares Cardiovascular Research Institute*
*Rotterdam-Rhoon, The Netherlands*

SPONSORED BY
UNIVERSITY OF FLORIDA
COLLEGE OF MEDICINE

*Vascular Biology in Clinical Practice*™
Established 1994

## EDUCATIONAL GOALS

**On successful completion of this continuing education activity, you should have a clear understanding of the following:**

- Role of angiotensin II in the development of coronary artery disease
- The rationale for angiotensin-converting enzyme (ACE) inhibition for improving cardiovascular mortality and morbidity in patients with coronary artery disease
- Results of recent clinical trials extending the benefit of ACE inhibition to nearly all patients with stable coronary artery disease and without heart failure or left ventricular dysfunction

## ACCREDITATION

The University of Florida College of Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

## CREDIT

The University of Florida College of Medicine designates this educational activity for a maximum of 1 category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

This continuing education activity was planned and produced in accordance with ACCME essentials. As of November 14th, 2005, this monograph is approved for 24 months (through November 14th, 2007).

## DISCLOSURES

The University of Florida Office of Continuing Medical Education has a conflict of interest policy that requires course faculty to disclose whether or not they have financial interest or affiliations with organizations with a direct or substantial interest in the subject matter of their presentations. It is not assumed that these financial interests or affiliations will have an adverse impact on the data presented in this monograph. They simply are noted here to fully inform the readers. The following information was received.

Dr Pepine has a financial relationship/affiliation for grant support for research, CME, consultant and/or Speakers Bureau programs with Abbott Laboratories, AstraZeneca, Aventis Pharmaceuticals Inc, Berlex Laboratories Inc, Millennium Pharmaceuticals Inc, CV Therapeutics Inc, King Pharmaceuticals Inc, Pfizer Inc, and Wyeth Pharmaceuticals. He has no employment, stock ownership, stock options, patents, or royalties with any pharmaceutical or medical device company.

Dr Remme has a financial relationship/affiliation for grant support for research, consultant, and/or Speakers Bureau programs with Abbott Laboratories, Chiesi Pharmaceuticals Inc, CV Therapeutics Inc, Guidant Corp, Medtronic Inc, Novartis, Pfizer Inc, Roche, and Servier. He has no employment, stock ownership, stock options, patents, or royalties with any pharmaceutical or medical device company.

## DISCLAIMER

The editorial contents of this monograph express the views of the individual contributors and do not necessarily reflect the views or recommendations of the University of Florida College of Medicine, Carol Davila University, Sticares Cardiovascular Research Institute, CV Therapeutics Inc, or the publisher. The reader is advised to consult the full prescribing information for all medications prior to use.

Supported by an educational grant from CV Therapeutics, Inc.



# ACE INHIBITION IN CAD

Activation of the renin-angiotensin-aldosterone system (RAAS) is a major contributor to the development of coronary artery disease (CAD) and an important therapeutic target. RAAS inhibition with angiotensin-converting enzyme (ACE) inhibition (ACEI) is a key component of secondary prevention in current treatment guidelines (Table 1).[1-3]

**Table 1. ACC/AHA and ACP Recommendations for ACEI in Secondary Prevention**[1-3]

| Patient population | Recommendations | Level of evidence |
|---|---|---|
| ST-elevation MI | All patients at discharge | A |
| Unstable angina/ non–ST-elevation MI | Patients with chronic heart failure, LV dysfunction (EF <40%), hypertension, or diabetes | A |
| Chronic stable angina | All symptomatic patients | A |
| | Asymptomatic patients | |
| | CAD with systolic dysfunction | A |
| | Diabetes with CAD | A |
| | Diabetes without CAD | B |

Clinical trials initially demonstrated the benefit of ACEI in selected groups of patients with recent myocardial infarction (MI), left ventricular (LV) dysfunction, or heart failure.[4] More recently, the benefits of ACEI were shown in stable CAD patients without heart failure or LV dysfunction in the Heart Outcomes Prevention Evaluation (HOPE) study in high-risk patients.[5] These benefits were confirmed in the EUropean trial on Reduction Of cardiac events with Perindopril in stable coronary Artery disease (EUROPA), which showed that ACEI can have a vasculoprotective effect in a broad spectrum of patients at lower risk than those enrolled in the HOPE study.[6] As much has been written about the HOPE trial since its publication in 2000, this monograph will discuss the recent EUROPA study and its relevance for clinical practice.

*EUROPA…showed that ACEI can have a vasculoprotective effect in a broad spectrum of patients at lower risk than those enrolled in the HOPE study.*

## Effects of ACEI: Ang II vs bradykinin

ACE generates angiotensin (Ang) II from its relatively inactive precursor, Ang I. Ang II promotes atherosclerosis and related events by increasing oxidative stress, inflammation, endothelial dysfunction, neurohormonal and cytokine activation, apoptosis, and fibrinolytic imbalance.[7,8] Ang II interacts with hypercholesterolemia

to accelerate atherosclerosis. In a hyperlipidemic environment, Ang II is generated locally and increases atherosclerotic plaque development through the $AT_{1A}$ receptor.[9]

**Effects of bradykinin:** ACE is identical to kininase II, an enzyme that degrades bradykinin. In many respects, bradykinin has a counteracting effect on the adverse

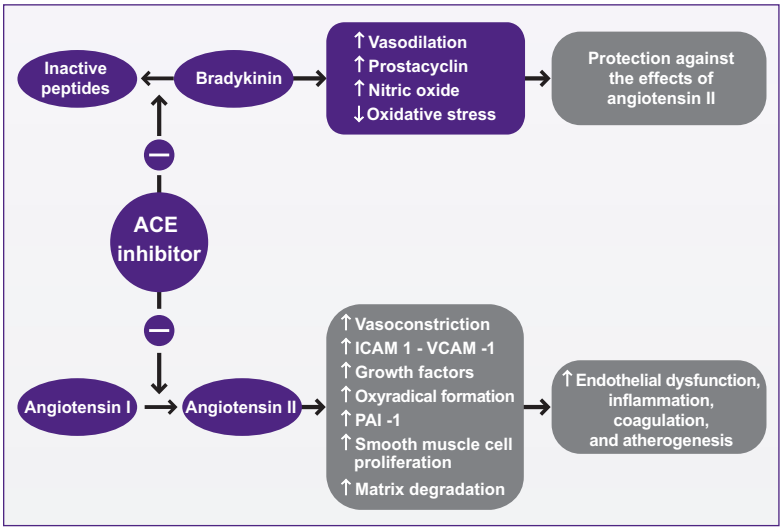



**Figure 1. The atherosclerosis-promoting actions of Ang II and protective effects of bradykinin.**[10]

actions of Ang II (Figure 1).[10] Bradykinin stimulates generation of vasodilators (nitric oxide, endothelium-hyperpolarizing factor, and prostacyclin) that improve endothelial function and promote fibrinolytic balance by increasing tissue plasminogen activator.[11]

ACEI acts by dual pathways to blunt Ang II production and prevent bradykinin degradation. The increased availability of endogenous bradykinin probably explains much of the cardiovascular benefit of ACEI.

The rationale for ACEI is based on extensive cardioprotective effects that influence pathophysiologic processes at all stages of CAD (Table 2).[8]

**Table 2. Vasculoprotective Effects of ACEI: Potential Mechanisms**[8]

| | |
|---|---|
| Antiatherosclerotic: ↓ neointima formation | ↓ Ischemia-induced neurohormonal activation |
| ↑ Endothelial function | Antihypertensive: ↓ BP |
| Prevent plaque rupture | ↓ LV hypertrophy |
| Enhance fibrinolysis | Prevent progressive LV dilatation in LV dysfunction and HF |
| Modulate cytokine activity | Bradykinin-induced vasorelaxation |
| ↓ Inflammation | ↑ eNOS |
| ↓ Oxidative stress | |

eNOS = endothelial cell nitric oxide synthase

**Effect on endothelial function:** The PERindopril-Thrombosis-Inflammation Endothelial dysfunction and Neurohormonal activation Trial (PERTINENT), a substudy of EUROPA, suggests that ACEI improves endothelial function by increasing bradykinin.[12] Endothelial cell nitric oxide synthase (eNOS) was increased in human umbilical-vein endothelial cells incubated with serum from patients treated with perindopril for 1 year. Plasma studies showed that perindopril increased bradykinin and reduced Ang II and von Willebrand factor, a marker of endothelial dysfunction. The only significant correlation observed was between bradykinin and eNOS upregulation, suggesting that in CAD patients, ACEI increases bradykinin, which in turn upregulates eNOS activity, increasing nitric oxide levels and improving endothelial dysfunction.

**Antiatherosclerotic effects:** In the Study to Evaluate Carotid Ultrasound changes in patients treated with Ramipril and vitamin E (SECURE), a HOPE substudy, ACEI lowered the rate of atherosclerotic progression.[13] Patients receiving ramipril 10 mg daily received maximum benefit, whereas ramipril 2.5 mg showed only a trend toward benefit despite similar effects on blood pressure (BP). A high dose was needed for antiatherosclerotic effects (eg, perindopril 8 mg). In a study of diabetic hyperlipidemic mice, perindopril inhibited atherosclerosis and overexpression of aortic ACE, connective tissue growth factor, and vascular cell adhesion molecule-1.[14]

**ACEI, Ang II, and obesity:** Ang II is implicated in obesity-induced cardiac remodeling and ischemia/reperfusion injury.[15] In obese insulin-resistant mice, ACEI prevented coronary perivascular fibrosis and collagen deposition potentially by impeding Ang II-mediated upregulation of plasminogen activator inhibitor-1 (PAI-1) and transforming growth factor-beta-1.[16] Treatment also blocked c-Jun NH(2)-terminal kinase (JNK) activation, which was upregulated in the left ventricle. JNK may be a mediator of obesity-related cardiac dysfunction.

## Extending use of ACEI to lower-risk patients

The HOPE study demonstrated that long-term treatment with ramipril 10 mg daily reduced major vascular events by 22% in high-risk patients ≥55 years of age with vascular disease or diabetes and another major CAD risk factor. Subsequently, the EUROPA study extended the observations in HOPE by showing that ACEI can have a vascular-protective effect in patients irrespective of risk profile or LV function.

**Table 3. EUROPA vs HOPE: A Comparison of Patients' Baseline Characteristics**

| | EUROPA[6] (N = 12,218) | HOPE[5] (N = 9297) |
|---|---|---|
| Mean age (years) | 60 | 66 |
| Female (%) | 15 | 27 |
| Coronary artery disease (%) | 100 | 80 |
| MI (%) | 65 | 53 |
| Peripheral vascular disease (%) | 7 | 43 |
| Stroke (%) | 3 | 11 |
| Hypertension (%) | 27 | 47 |
| Diabetes (%) | 12 | 39 |
| Hypercholesterolemia (%) | 63 | 66 |
| Baseline medication | | |
| Antiplatelet drugs (%) | 91 | 76 |
| Beta-blockers (%) | 63 | 39 |
| Lipid-lowering drugs (%) | 58 | 28 |

A comparison of baseline characteristics in HOPE and EUROPA patients, such as age, rates of diabetes and hypertension, and use of concomitant cardioprotective drugs, indicates that HOPE patients were a higher-risk group (Table 3).[5,6] Annual rates of major CV events in the placebo groups were 40% to 80% higher in HOPE versus EUROPA.

EUROPA enrolled 12,218 patients aged ≥18 years without clinical heart failure but with CAD documented by previous MI >3 months before screening, coronary revascularization >6 months before screening, or evidence of stenosis (≥70% narrowing of ≥1 coronary artery), or, for men, a positive stress test with a history of chest pain. The mean age of patients was 60 years and >30% were <55 years of age. Use of concomitant therapy was high: 92% were taking platelet inhibitors, 63% were taking beta-blockers, and 58% were taking lipid-lowering drugs, which increased to 69% at 3 years. Patients were randomized to treatment with perindopril 8 mg daily (n = 6110) or placebo (n = 6108). Mean follow-up was 4.2 years.[6]

**ACEI benefits are observed in all patients:** Perindopril significantly reduced the primary outcome of CV mortality, nonfatal MI, or cardiac arrest by 20% (P = 0.0003), with event rates of 8% in the perindopril group vs 9.9% with placebo. Benefits began to appear at 1 year and gradually increased throughout the trial (Figure 2). Perindopril was associated with reductions in all primary and secondary outcomes, although not all reached statistical significance. Reductions in hospital admissions for heart failure (39%; P = 0.002) and MI (24%; P < 0.001) were highly significant.[6]

The beneficial effect of perindopril was consistent across all predefined subgroups, including all age groups, patients with or without hypertension, diabetes, or previous MI, as well as in patients taking other cardioprotective therapies (Figure 3).

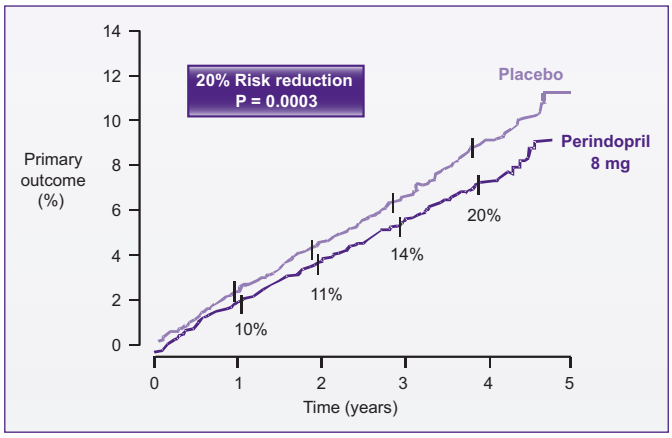



**Figure 2. EUROPA: Primary outcome of CV death, nonfatal MI, and resuscitated cardiac arrest.[6]**

**Outcomes are not dependent on BP reduction:** The reduction in CV events in EUROPA was greater than expected for the BP reduction achieved with perindopril (mean 5/2 mm Hg). Further analysis of EUROPA data shows that prevention of CV events did not depend on BP and its reduction.[18] Major CV events decreased among patients at all levels of baseline BP. Patients with substantial BP reduction, as well as those whose BP was unchanged during the run-in phase when all patients received perindopril, had similar reductions in the primary outcome (20% vs 18%, respectively).

**Risk reductions in diabetic patients:** In the PERindopril SUbstudy in coronary Artery disease and DiabEtes (PERSUADE), the diabetic substudy of EUROPA

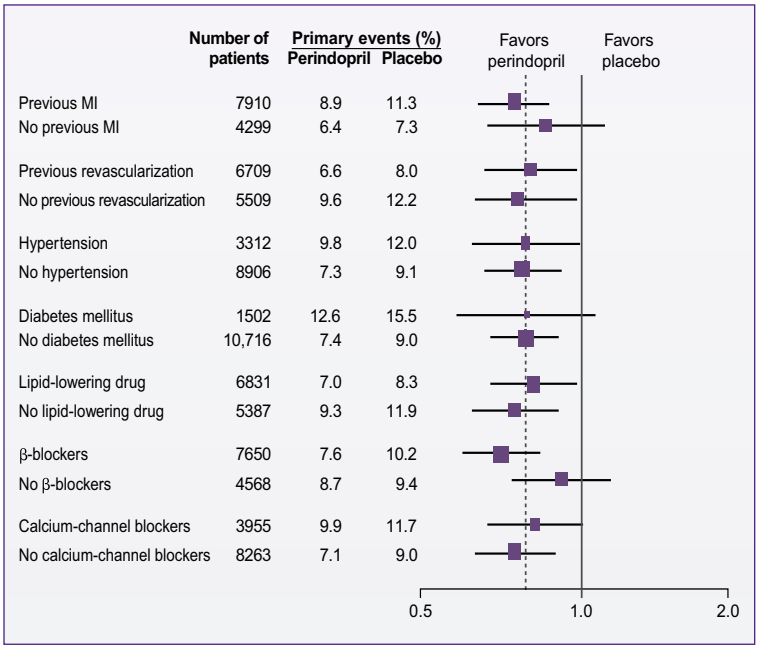



**Figure 3. EUROPA reported benefits in a broad range of patients and on top of other recommended therapies.** Primary event = CV death, nonfatal MI, resuscitated cardiac arrest. Square's size is proportional to subgroup population. Dashed line indicates overall relative risk.[6]

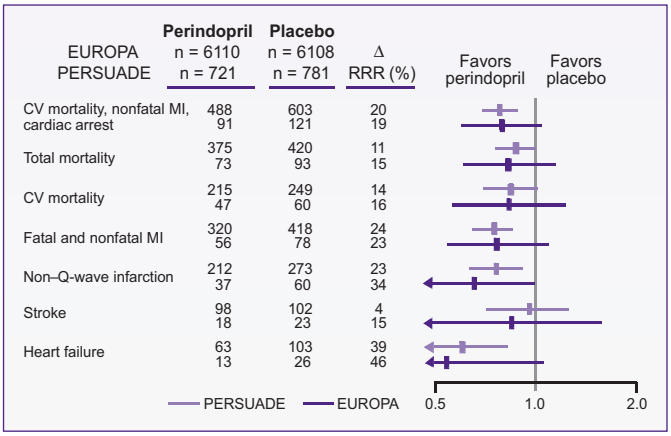



**Figure 4. PERSUADE showed similar benefits in patients with diabetes as in the overall EUROPA study.[18]**

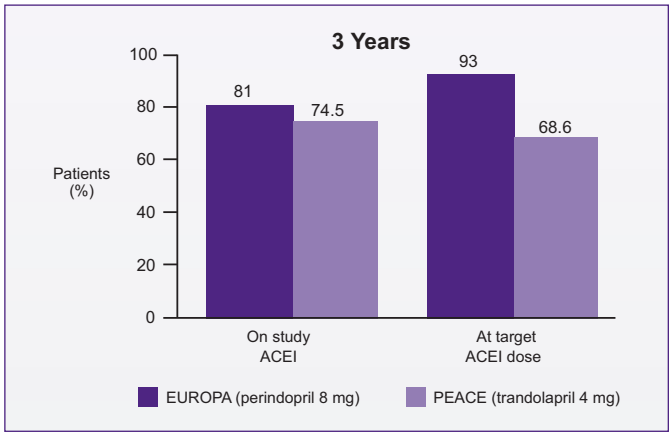



**Figure 5. EUROPA vs PEACE: Differences in compliance.[5,22]**

(N =1502), perindopril reduced the primary outcome by 19% (P = 0.13), which was similar to the 20% reduction in the main EUROPA study.[18] Results showed a trend toward benefit in secondary outcomes that was comparable to EUROPA (Figure 5). Absolute benefits were greater because of higher event rates in the diabetes subgroup. PERSUADE results are consistent with positive effects of ACEI previously reported in MICRO-HOPE, the diabetic substudy of HOPE, thereby extending the benefits of ACEI to lower-risk patients with diabetes.[19]

**Consistent benefits of ACEI:** EUROPA demonstrates that, independent of age, sex, or presence/absence of diabetes or hypertension, ACEI reduces CV morbidity and mortality in CAD patients with preserved LV function in addition to other recommended therapies. Risk reductions were comparable to HOPE even though EUROPA patients had a higher rate of other cardioprotective therapy. Both studies demonstrated benefits after 1 year of treatment and in patients at all levels of risk.[20,21]

**The challenge of PEACE is answered**. In contrast, the Prevention of Events with Angiotensin Converting Enzyme inhibition (PEACE) trial reported that treatment with trandolapril 4 mg did not lower the risk of CV mortality, MI, or the need for revascularization in low-risk CAD patients with normal or near-normal LV function who were already receiving state-of-the art therapy (N = 8290).[22] Although the results of PEACE raised questions about the benefit of ACEI in well-managed patients,[23] the totality of clinical trial evidence clearly indicates that ACE inhibitors have shown significant benefits in stable CAD patients.[24,25] Compliance rates in the ACE inhibitor arm of the PEACE study suggest that patients were undertreated—at 3 years only 68.6% were taking the study medication at the target dose vs 93% of EUROPA patients (Figure 5).

**Are all ACE inhibitors interchangeable?** The clinical benefits shown with perindopril 8 mg and ramipril 10 mg do not necessarily indicate a class effect. Although ACE inhibitors share main actions, agents differ structurally and pharmacologically, and dose is important.[26] Perindopril and ramipril are strongly lipophilic, potentially an important property in atherosclerotic plaque penetration. Effectiveness should not be confused with a mechanism of action, that is, surrogate efficacy, such as BP reduction.[23] Effective dosage for treating patients with CAD may not be the same as for patients with hypertension. The 8-mg dose of perindopril used in EUROPA was chosen to increase the potential for achieving BP-independent cardioprotective effects.[27]

## Clinical Summary

- Clinical practice guidelines recommend use of ACEI as secondary-preventive therapy for patients with CAD with or without LV dysfunction or heart failure.[1-3]
- Benefits of ACEI have been shown in stable CAD patients at all levels of risk and in addition to other state-of-the-art therapy.[5,7,24,25]
- All ACE inhibitors may not have comparable effects for all indications. When making therapeutic decisions, consider agents at doses proven to be safe and effective in clinical trials.[26]
- Both perindopril and ramipril reduce the risk of CV events in stable CAD patients without heart failure or LV dysfunction.[5,6]
  - Ramipril has proven efficacy in CAD patients ≥55 years of age
  - Perindopril has proven efficacy in CAD patients ≥18 years of age

## References


1. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al; American College of Cardiology; American Heart Association. Committee on the Management of Patients With Unstable Angina. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction—summary article: A report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients With Unstable Angina). *J Am Coll Cardiol.* 2002;40:1366-1374.
2. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, et al; American College of Cardiology; American Heart Association Task Force on Practice Guidelines. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction–Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction). *Circulation.* 2004;110:588-636.
3. Snow V, Barry P, Fihn SD, Gibbons RJ, Owens DK, Williams SV, et al; American College of Physicians; American College of Cardiology Chronic Stable Angina Panel. Primary care management of chronic stable angina and asymptomatic suspected or known coronary artery disease: A clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2004;141:562-567.
4. Flather MD, Yusuf S, Køber L, Pfeffer M, Hall A, Murray G, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: A systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. *Lancet*. 2000;355:1575-1581.
5. Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med*. 2000;342:145-153.
6. The EURopean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: Randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). *Lancet.* 2003;362:782-788.
7. Weir MR, Dzau VJ. The renin-angiotensin-aldosterone system: A specific target for hypertension management. *Am J Hypertens*. 1999;12:205S-213S.
8. Remme WJ. Reconsidering the management of all coronary artery disease patients: Importance of the EUROPA trial. *Eur Heart J*. 2003;5(suppl):E23-E30.
9. Daugherty A, Rateri DL, Lu H, Inagami T, Cassis LA. Hypercholesterolemia stimulates angiotensin peptide syntheses and contributes to atherosclerosis through the AT1A receptor. *Circulation*. 2004;110:3849-3857.
10. Ferrari R. Angiotensin-converting enzyme inhibition in cardiovascular disease: Evidence with perindopril. *Exp Rev Cardiovasc Ther*. 2005;3:15-29.
11. Pretorius N, Rosenbaum D, Vaughan DE, Brown NJ. Angiotensin-converting enzyme inhibition increases human vascular tissue-type plasminogen activator release through endogenous bradykinin. *Circulation.* 2003;107:579-585.
12. Ferrari R. PERTINENT: PERindopril-Thrombosis, InflammatioN, Endothelial dysfunction and Neurohormonal activation Trial. A subanalysis of EUROPA. Available at: www.Europa-trial.org Accessed July 2005.
13. Lonn E, Yusuf S, Dzavik V, Doris C, Yi Q, Smith S, et al. Effects of ramipril and vitamin E on atherosclerosis. The study to evaluate carotid ultrasound changes in patients treated with ramipril and vitamin E (SECURE). *Circulation*. 2001;103:919-925.
14. Candido R, Jandeleit-Dham KA, Cao Z, Nesteroff SP, Burns WC, Trigg SM, et al. Prevention of accelerated atherosclerosis by angiotensin-converting enzyme inhibition in diabetic apolipoprotein E-deficient mice. *Circulation.* 2002;106:246-253.
15. du Toit EF, Nabben M, Lochner A. A potential role for angiotensin II in obesity induced cardiac hypertrophy and ischaemic/reperfusion injury. *Basic Res Cardiol*. 2005;100:346-354.
16. Zaman AK, Fujii S, Goto D, Furumoto T, Mishima T, Nakai Y, et al. Salutary effects of attenuation of angiotensin II on coronary perivascular fibrosis associated with insulin resistance and obesity. *J Mol Cell Cardiol*. 2004;37:525-535.
17. Remme WJ. Prevention of cardiovascular events by perindopril in patients with stable coronary disease does not depend on blood pressure and its reduction: Results from the EUROPA Study. *Circulation*. 2004;110(suppl):III-628. Available at www.europa-trial.org Accessed September 2005.
18. Daly CA, Fox KM, Remme WJ, Bertrand ME, Ferrari R, Simoons ML. The effect of perindopril on cardiovascular morbidity and mortality in patients with diabetes in the EUROPA study: results from the PERSUADE substudy. *Eur Heart J*. 2005;26:1369-1378.
19. HOPE Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: Results of the HOPE study and MICRO-HOPE substudy. *Lancet.* 2000;355:253-259.
20. Vantrimpont P, Goedhart DM, Bertrand ME, Deckers JW, Ferrari R, Fox KM et al. Risk assessment and risk reduction by perindopril in patients with stable coronary artery disease. *Circulation*. 2004;110(suppl):III-546.
21. HOPE/HOPE-TOO Study Investigators. Long-term effects of ramipril on cardiovascular events and on diabetes. Results of the HOPE study extension. *Circulation*. 2005;112:1339-1346.
22. The PEACE Trial Investigators. Angiotensin-converting-enzyme inhibition in stable coronary artery disease. *N Engl J Med*. 2004;351:2058-2068.
23. Pitt B. ACE inhibitors for patients with vascular disease without left ventricular dysfunction–May they rest in PEACE? *N Engl J Med*. 2004;351:2115-2116.
24. Pepine CJ, Probstfield JL. A HOPE for PEACE? Update on the role of ACE inhibition in CAD patients. In: *Vascular Biology in Clinical Practice: A CME monograph*. University of Florida College of Medicine. Gainesville, Fla; 2004(6)3.
25. Yusuf S, Pogue J. ACE inhibition in stable coronary artery disease. *N Engl J Med.* 2005;352:937-939.
26. Furberg CD, Pitt B. Are all angiotensin-converting enzyme inhibitors interchangeable? *J Am Coll Cardiol*. 2001;37:1456-1460.
27. Sica DA. EUROPA: Has anything new been learned with angiotensin-converting enzyme inhibitors? *J Clin Hypertens*. 2004;6:91-95.


## Self-Assessment Questions

*Please check the appropriate answer for each question on the Answer Key.*
*Instructions for obtaining CME credit are provided on the back of the Answer Key.*

1. The increased availability of bradykinin probably explains much of the cardiovascular benefit of ACE inhibition.
   a. True  b. False

2. In the EUROPA study, major cardiovascular events decreased among patients at all levels of baseline blood pressure.
   a. True  b. False

3. The PERSUADE and EUROPA studies had comparable reductions in the primary outcome. What were the respective risk reductions?
   a. 19% vs 22%  b. 21 vs 23%  c. 19% vs 20%

4. At what point in the HOPE and EUROPA studies did the benefit of ACE inhibitor therapy become evident?
   a. 3 years  b. 2 years  c. 1 year

5. The 8-mg dose of perindopril used in EUROPA, which was relatively high, was selected to enhance the potential for achieving blood pressure–independent cardioprotective effects.
   a. True  b. False

Established 1994

*Vascular Biology in Clinical Practice*™

# ACE INHIBITION IN CAD PATIENTS:

## *Expanding the Reach of Cardioprotection*

## Answer Key

Please check the correct box for each question. There is only 1 correct response for each question.

1. [A] [B]
2. [A] [B]
3. [A] [B] [C]
4. [A] [B] [C]
5. [A] [B]

## Activity Evaluation

Your input will help us improve our educational activities. Please rate this monograph in the following areas:

| | Excellent | | | | Poor |
|---|---|---|---|---|---|
| Quality of monograph | 5 | 4 | 3 | 2 | 1 |
| Relevance to practice | 5 | 4 | 3 | 2 | 1 |
| Value of content | 5 | 4 | 3 | 2 | 1 |
| Readability and presentation | 5 | 4 | 3 | 2 | 1 |
| Usefulness of illustrations | 5 | 4 | 3 | 2 | 1 |
| | **Agree** | | | | **Disagree** |
| Importance to physicians | 5 | 4 | 3 | 2 | 1 |
| Increased my knowledge | 5 | 4 | 3 | 2 | 1 |
| Did not promote particular product or company | 5 | 4 | 3 | 2 | 1 |

Overall rating of monograph (5 = excellent; 1 = poor): _____

Does the monograph cover the stated educational goals? Yes _____ No _____

If no, what areas were not covered?

_____

_____

Would you read monographs on other topics as a form of continuing education? Yes _____ No _____

If yes, what topics would you like to learn about?

_____

_____

What form of educational activity do you find most useful?

_____

It took me _____ hour(s) and _____ minutes to read the monograph and complete the self-assessment questions.

Sponsored by
UNIVERSITY OF FLORIDA
College of Medicine

UF-P-05-38-942 11/05


*Vascular Biology in Clinical Practice*™

# ACE INHIBITION IN CAD PATIENTS:

## *Expanding the Reach of Cardioprotection*

## INSTRUCTIONS FOR OBTAINING CONTINUING MEDICAL EDUCATION CREDIT

To obtain a certificate for 1 category 1 credit toward the Physician's Recognition Award of the American Medical Association (AMA) for completing the activity ***ACE inhibition in CAD patients: Expanding the Reach of Cardioprotection,*** please complete the Self-Assessment Questions, fill out the correct answers on the Answer Key, and mail the Activity Evaluation and Answer Key with a $15.00 processing fee (checks made payable to University of Florida) to:

Office of Continuing Medical Education
University of Florida College of Medicine
PO Box 100233
Gainesville, FL 32610-0233

**Telephone:** (352) 265-8081

**Fax:** (352) 265-8082

### For All Continuing Medical Education Respondents:

This is to attest that I have participated in the University of Florida College of Medicine monograph, ***ACE inhibition in CAD patients: Expanding the Reach of Cardioprotection.*** I have successfully reviewed all the materials and answered the Self-Assessment Questions. I understand that a certificate for 1 category 1 credit toward the AMA Physician's Recognition Award will be mailed to me upon receipt of this form, provided I receive a passing score of 70% or higher. I also understand that a $15.00 processing fee is required for me to receive credit. This fee may be paid by check or credit card.

Name _____
(First Name) (Last Name)

Street Address _____

City _____ State _____ ZIP Code _____

Telephone _____ Specialty _____

Signature _____ Date _____

MasterCard or Visa Card number _____ Expiration Date _____

Cardholder's name and address if different from above:

_____

_____

Sponsored by
UNIVERSITY OF FLORIDA
College of Medicine

UF-P-05-38-942 11/05