

Authors: E. AGABITI-ROSEI - G. AMBROSIO - L. BADIMON - JP. BASSAND - A. BAYÉS DE LUNA - M.E. BERTRAND - E. CHAZOV - S. CHIERCHIA - J. CLELAND - D. CLEMENT - D. COKKINOS - N. DANCHIN - R. DIETZ - P. DOMINIAK - I. EDES - E. ERDMANN - R. FERREIRA - H.R.FIGULLA - W. FLAMENG - I. GRAHAM - G. JACKSON - W. JANUSZEWICZ - J.C. KASKI - P. KEARNEY - W. KLEIN - F. KOLBEL - M. KOMAJDA - W. KÜBLER - J.L.LOPEZ-SENDON HENTSCHEL - G. MANCIA - W.J. MCKENNA - T. MEINERTZ - J.MLCZOCZ - D. MULCAHY - E. O'BRIEN - A. OTO - J. PAPP - W.J. PAULUS - J. POLONIA - I. PRÉDA - L.A. PROVIDENCIA - J. REID - W.J. REMME - W. RUZYLO - Z. SADOWSKI - P. SERRUYS - P. SLEIGHT - J. SOLER-SOLER - J. SOMERVILLE - P.G. STEG - H.A.J. STRUIJKER BOUDIER - B. SWYNGHEDAUW - L. TAVAZZI - M. TENDERA - P. TOUTOUZAS - A. VAHANIAN - J.L. VANOVERSCHELDE - J. WIDIMSKY - M. YACOB

## Angiotensin-converting enzyme inhibition for prevention of cardiovascular events after myocardial infarction

Over 30% of all-cause mortality in the Western world is linked to cardiovascular disease (CVD). Patients with coronary artery disease (CAD)—particularly those who have suffered a myocardial infarction (MI)—represent a high-risk group regarding future cardiac events. Lifestyle changes, including smoking cessation, reduced alcohol intake, diet, and regular exercise, are known to be effective in reducing the risk of future events. In patients with a history of MI, pharmacological treatment can also contribute significantly to improve prognosis. Agents known to improve prognosis in these patients include  $\beta$ -blockers, antiplatelets, eplerenone, statins, and angiotensin-converting enzyme inhibitors (ACEI). This article focuses on the role of ACEI in secondary cardiovascular disease prevention in post-MI patients.

### ACEI in post MI patients

The European Society of Cardiology (ESC) expert consensus guidelines indicate that oral ACEIs are beneficial in acute MI patients when administered within 36 hours of the initiation of the event. Patients considered to benefit the most are those with anterior MI and impaired ejection fraction (EF) or mild-to moderate heart failure.<sup>1</sup> It is recommended that patients with clinical evidence for heart failure or asymptomatic left ventricular dysfunction should receive long-term treatment with an ACEI. Similarly, patients with diabetes appear to benefit from the long term administration of ACEI. The guidelines also state that if treatment is initiated early, a low dose should be administered in the first instance, which can be increased gradually over the following 48 hours with careful assessment of blood pressure levels and renal function.<sup>1</sup> ACEI are also beneficial when used later in MI patients, as reported by a meta-analysis of late ACEI intervention trials (>48 hours after acute MI).<sup>2</sup> After 2.6 years of ACEI therapy, mortality and risk of reinfarction and heart failure were reduced in the ACEI-treated group. Moreover, in a large meta-analysis of over 100 000 patients, 30-day mortality was reduced from 7.6% in the placebo group to 7.1% in the ACEI group, with most of the benefit observed during the first week following the MI.<sup>2</sup> The study suggested that ACEI may have a role in both the early management of MI and the late phase of MI, but only in high risk groups.

### ACEI in ST-elevation MI (STEMI) and NSTEMI patients

The recent update<sup>3</sup> of the ACC/AHA guidelines is of relevance in this context, as ACE inhibitor treatment is recommended for all STEMI patients who are not at a low risk, and in these patients the treatment should be continued indefinitely. Low-risk patients are defined as those with a normal left ventricular EF and controlled risk factors. Interestingly, for these lower-risk patients, the new guidelines consider

ACE inhibitor therapy to be a reasonable indication. Early therapy with an oral ACE inhibitor is also indicated for NSTEMI patients with clinical signs of heart failure or EF <40%.<sup>4</sup> ARBs are recommended as an alternative to ACEI in patients who are intolerant to the latter.<sup>3,4</sup>

### ACEI in high-risk groups with or without an MI

The ESC guidelines suggest that long-term treatment with ACEI is beneficial also in patients without heart failure, if these subjects have CVD or diabetes and other risk factors.<sup>2</sup> The PREAMI<sup>5</sup> (Perindopril Remodelling in Elderly with Acute Myocardial Infarction) study in elderly patients with a previous MI but preserved left ventricular EF ( $\geq 40\%$ )<sup>1</sup> showed a reduced risk of (composite end point) death, cardiac remodeling, and hospitalization with heart failure (38%;  $P < 0.001$ ). HOPE,<sup>6</sup> EUROPA,<sup>7</sup> and PEACE<sup>8</sup> assessed whether ACEI treatment reduces major cardiovascular events in patients with cardiovascular disease. HOPE and EUROPA suggested a beneficial effect of ACEI treatment. In EUROPA, patients receiving perindopril had significantly fewer cardiovascular events across all subgroups examined, namely those with or without previous MI, hypertension and noncoronary vascular disease. PEACE<sup>8</sup>, however, did not show beneficial effects with the use of trandolapril despite the inclusion of patients comparable to those in HOPE and EUROPA. The reasons for the different results in these trials are not fully understood.

**Conclusion.** Based on recent guidelines recommendations it seems appropriate to start all STEMI and NSTEMI patients on oral ACEI treatment and decide at a later stage whether or not treatment should be continued indefinitely. ARBs represent an alternative for patients who are intolerant to ACEI.

**J. C. KASKI and D. FERNANDEZ-BERGES**  
 London, UK

**References:** 1. The Task Force on ACE-inhibitors of the European Society of Cardiology. *Eur Heart J.* 2004;25:1454-1470. 2. ACE inhibitor myocardial infarction collaborative group. *Circulation.* 1998;97:2202-2212. 3. Antman EM et al. *J Am Coll Cardiol.* 2008;51:210-47. 4. Anderson J et al. *J Am Coll Cardiol.* 2007;50:e1. 5. Ferrari R. *Arch Intern Med.* 2006;166:659-666. 6. Yusuf S et al. *N Engl J Med.* 2000; 342:145-153. 7. Fox KM et al. *Lancet.* 2003;362:782-788. 8. The PEACE trial investigators. *N Engl J Med.* 2004;351:2058-2068.

All texts for *The European Cardiologist - Journal by Fax* are available on our website: [www.servier.com](http://www.servier.com)

In the event of any questions, or if you wish to receive the referenced publications, please contact fax n° 01 55 72 75 02

Medical service from Serdia Pharmaceuticals  
 Makers of

**COVERSYL**<sup>®</sup>  
 PERINDOPRIL *once daily*

**NATRILIX** *SR*  
 1 TABLET DAILY

**FLAVEDON** *MR*  
 2 tablets daily

SERDIA PHARMACEUTICALS (INDIA) PVT. LTD.  
 Serdia House, Off Dr. S.S. Rao Road, Parel, Mumbai 400 012.  
 Under Licence from: Les Laboratoires Servier, France. Visit us at: [www.serdia-pharma.com](http://www.serdia-pharma.com)

