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# Letters to the Editor: CHARM - the Answer to all Questions - two Years Later?

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# Letters to the Editor

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## CHARM – the Answer to all Questions – two Years Later?

Treatment of chronic heart failure (CHF) has been under investigation for many years, but many questions have remained unanswered: the value of Ang II receptor blockade itself, the question of combined ACE inhibitor and Ang II receptor-blocking therapy and the effect of "triple blockade" with β-blockers in addition. CHARM has clarified the matter and can be seen as a landmark study in the context of CHF treatment.

The treatment of CHF has not been resolved in a satisfactory manner as yet. Too many patients still die within the first three years after the onset of symptoms, costs constantly rise. While we have plenty of evidence concerning the positive effects of ACE inhibitors or Ang II receptor blockers (e.g. STRECH, Val-Heft) and β-blockers (e.g. CIBIS II, COPERNICUS), some questions remain, e.g. which is better: ACE inhibitors or Ang II receptor blockers, or the combination?

CHARM (Candesartan in Heart Failure – Assessment of Reduction in Mortality and Morbidity [1]): this study recruited 7061 patients and these have been subdivided into 3 groups:

- *CHARM-alternative:* heart failure patients with reduced LVEF < 40 % who did not tolerate ACE inhibitors (n = 2028): treatment with candesartan improved cardiovascular hospitalisation or mortality by 7 % versus placebo equalling a relative risk reduction of 23 %.
- *CHARM-added:* CHF patients already on ACE inhibitors (n = 2548) who received candesartan in addition showed an additional benefit (4 % less hospitalisations and 4 % less cardiovascular deaths).
- *CHARM-preserved:* patients with a still reasonable LV function (LVEF > 40 %; n = 3023) did not benefit as far as cardiovascular mortality has been concerned, but showed less hospitalisation (2.4 %; p = 0.047).
- *CHARM-overall:* summarising the three arms of the study one can be confident about a 12 % reduction in cardiovascular mortality (p = 0.006) and a reduction in hospitalisation rate leading to a risk reduction for the primary cumulative end point by 16 % (p = 0.0001). Interestingly, candesartan also reduced the risk to develop type II diabetes by 22 %.

CHARM is a landmark study which will largely influence therapeutic strategies for CHF. On the other hand, we have learned from the Danish arm of the IMPROVEMENT study that only 20 % of NYHA III patients and just 15 % of NYHA IV patients receive adequate therapy with ACE inhibitors and β-blockers despite ample evidence for their benefit. Compliance and adequate treatment through the physician still appear to be the real problem, causing more cardiovascular deaths than necessary. Very likely, CHARM will not change this.

**References:**

1. Pfeffer MA, Swedberg K, Granger CB, Held P, McMurray JJ, Michelson EL, Olofsson B, Ostergren J, Yusuf S, Pocock S; CHARM Investigators and Committees. Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-Overall Programme. Lancet 2003; 362: 759–66.

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