

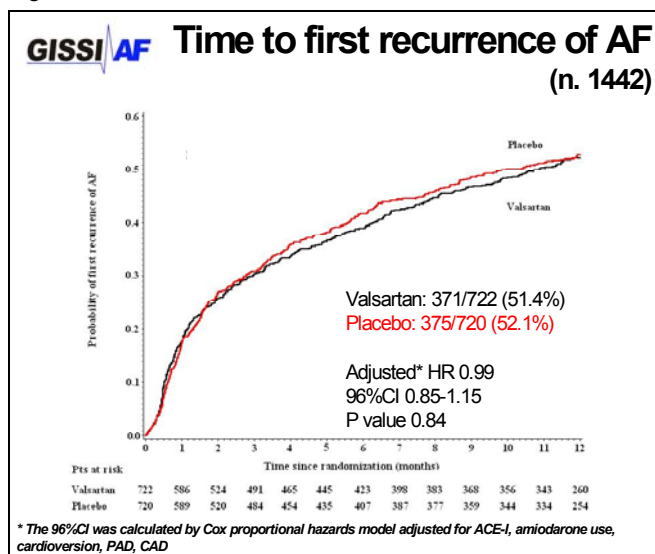
Authors: E. AGABITI-ROSEI - G. AMBROSIO - L. BADIMON - JP. BASSAND - A. BAYÉS DE LUNA - M.E. BERTRAND - E. CHAZOV - S. CHIERCHIA - J. CLELAND - D. CLEMENT - D. COKKINOS - N. DANCHIN - R. DIETZ - P. DOMINIAC - I. EDES - E. ERDMANN - R. FERREIRA - H.R.FIGULLA - W. FLAMENG - I. GRAHAM - G. JACKSON - W. 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.MLCZOCH - 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. RUZYLLO - 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

GISSI-AF trial

Atrial fibrillation (AF) is the most common clinical arrhythmia.¹ Antiarrhythmic drugs have limited efficacy in prevention of AF recurrences, and sometimes cause serious adverse reactions. The renin-angiotensin-aldosterone system (RAAS) plays a role in atrial remodeling. Several clinical studies showed the effects of ACE-I or ARBs on AF, either new onset (ie, primary prevention) or recurrent (ie, secondary prevention).² A trial of adequate size designed to test an ARB versus placebo in the prevention of AF recurrence appeared to be of great relevance due to the high incidence of this clinical condition despite the use of available treatments. The purpose of the GISSI-AF (Atrial Fibrillation) study was therefore to assess whether the addition of the ARB valsartan to established therapies could reduce the recurrence of AF in patients with a history of AF associated with cardiovascular diseases.³

GISSI-AF was a prospective, multicenter, randomized, double-blind, placebo-controlled study. Patients eligible for inclusion in the study were either sex, at least 40 years of age, with at least 2 ECG documented episodes of symptomatic AF in the previous 6 months, or successful cardioversion (electrical or pharmacological) between 14 days and 48 hours before randomization. Patients had to have a cardiovascular disorder or, in case of lone AF, a dilated left atrium. All prescribed treatments for AF or for the underlying cardiovascular diseases, including ACE-I, amiodarone and β -blockers were allowed. Valsartan or placebo were initiated at the dose of 80 mg daily for 2 weeks, then uptitrated to the maximal dosage of 320 mg daily and this regimen was continued until completion of follow-up at week 52.

Figure. Time to first recurrence of AF.



The study was designed with 2 co-primary end points: time to first recurrence of AF, and rate of patients with more than one episode of AF over the 1-year follow-up. From November 2004 to January 2007, 1442 patients were randomized by 114 centers: 722 were assigned to receive valsartan and 720 placebo. At 1-year follow-up, 51.4% (371/722) of patients in the valsartan group and 52.1% (375/720) of patients in the placebo group had had a recurrence of AF (HR 0.99; 96%CI 0.85-1.15, $P=0.84$) (Figure).⁴

After adjustment for all baseline variables, HR was 0.97, 96%CI [0.83-1.14], $P=0.73$. The coprimary end point, rate of patients with more than one episode of AF, occurred in 194/722 (26.9%) patients in the valsartan group and in 201/720 (27.9%) patients in the placebo group (OR 0.95; 99% CI 0.70-1.29, $p=0.66$). After adjustment for all baseline variables, OR 0.89, 99% CI (0.64 -1.23), $P=0.34$.

GISSI-AF was the largest randomized, prospective trial testing the effect of an ARB, valsartan, on AF recurrence in patients with history of AF associated with cardiovascular risk factors. It was a pragmatic trial, with broad selection criteria to mimic real clinical practice as much as possible. Against the wealth of strict experimental evidences, and the highly suggestive cumulative evidences generated in the post-hoc analyses of many clinical series, the addition of valsartan to recommended treatments for AF and for the underlying cardiovascular diseases, including ACE inhibitors and amiodarone, was generally well tolerated but did not reduce the rate of recurrence of AF over 1 year.

A neutral result extended to subgroups, in the presence of plausible expectations of a beneficial effect, prompts a reconsideration of the role of RAAS blockers in the secondary prevention of AF, while their role in primary prevention remains to be defined by specific trials.⁵

A. P. MAGGIONI – Florence, Italy
(Guest Author)

References: 1. Go AS et al. *JAMA*. 2001;285:2370-2375. 2. Healey JS et al. *J Am Coll Cardiol*. 2005;45:1832-1839. 3. Disertori M et al. *J Cardiovasc Med*. 2006;7:29-38. 4. GISSI-AF Investigators. *N Engl J Med*. 2009;360:1606-1617. 5. Gillis AM. *N Engl J Med*. 2009;360:1669-1671.

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