

## MULTINATIONAL CLINICAL STUDIES

EVIDENCE has a long history of high recruitment rates in cardio-vascular multinational trial. Below are examples of the multinational trials conducted by EVIDENCE; the results of these trials were published in well known international journals, including JAMA, the Lancet, the New England Journal of Medicine, Circulation and the European Heart Journal:

- **EMIP** (European Myocardial Infarction Project), sponsored by European Union and GlaxoSmithKline: Evidence has recruited 577 patients in 21 Russian and Latvian sites within 21 month (1.3 pts per site per month). Other CROs have recruited 4,892 patients in 142 European sites within 28 month (1.2 pts per site per month). The results of this trial were published in N Eng J Med 1993; 329 (6): 383-389: Pre-hospital thrombolytic therapy in patients with suspected acute myocardial infarction.
- **ESPRIM** (European Study of Prevention of Infarct with Molsidomine): EVIDENCE demonstrated the highest recruitment rates: 643 patients were recruited in 7 sites in Russia and 232 patients in 1 site in Latvia (average rate of recruitment by EVIDENCE 6.7 pts/site/month). In comparison, 3,374 patients were recruited by other CROs in 109 sites (1.0 pts/site/month). Published: The ESPRIM trial: short-term treatment of acute myocardial infarction with molsidomine. Lancet 1994; 344(8915):91-97.
- **EMIP-FR** (European Myocardial Infarction Project - Free Radicals): 6,247 patients were recruited in 79 sites by EVIDENCE (2.3 pts/site/month). In comparison, 13,370 patients were recruited by other CROs in 314 sites (0.9 pts/site/month); the results were published in Eur Heart J 2000; 21(18):1537-46: Effect of 48-h intravenous trimetazidine on short- and long-term outcomes of patients with acute myocardial infarction, with and without thrombolytic therapy; A double-blind, placebo-controlled, randomized trial.
- **FRAX.I.S** (Fraxiparine in Ischemic Syndrome): 336 patients recruited by EVIDENCE in 13 sites (3.2 pts/site/month), and 3,132 patients recruited by other CROs in 166 sites (0.7 pts/site/month). Published: Comparison of two treatment durations (6 days and 14 days) of a low molecular weight heparin with a 6-day treatment of unfractionated heparin in the initial management of unstable angina or non-Q wave myocardial infarction: FRAX.I.S. (FRAXiparine in Ischaemic Syndrome). Eur Heart J 1999 Nov; 20(21):1553-62. HERO-2 (Hirulog in Early Reperfusion/Occlusion 2): started in 1998, finished in 2001. 7,391 patients recruited by EVIDENCE. Among them, 6,057 patients were recruited in 65 sites in Russia, 199 patients in 6 sites in Bielorrussia; 181 patients in 4 sites in Latvia and 1,153 patients in 9 sites in the Republic of Georgia. EVIDENCE recruitment rate was 3.6 pts/site/month compared to other CROs 0.7 pts/site/month. Results of this trial were published in Lancet 2001; 358(9296): 1855-1863: An open prospectively randomized comparison of Hirulog (Angiomax™) vs. Heparin in patients receiving aspirin and thrombolysis for treatment of AMI.
- **MAGIC** (Magnesium in Coronary Syndromes), started in 2000, finished in 2002. 5,651 patients recruited by EVIDENCE. Among them 4,423 patients were recruited in 53 sites in Russia, 565 patients in 8 sites in Georgia; and 627 patients in 23 sites in Bulgaria. EVIDENCE recruitment rate was 2.8 pts/site/month compared to other CROs 0.1 pts/site/month. Results of this study were published in The Lancet 2002; 360:1189-96: Early administration of intravenous magnesium to high-risk patients with acute myocardial infarction in the Magnesium in Coronaries (MAGIC) Trial: a randomized controlled trial.
- **CARISA** (Combination Assessment of Ranolazine in Stable Angina) started in June 2000 (EVIDENCE started in November 2000), finished in September 2001. 219 patients were

recruited by EVIDENCE in 21 sites (17 sites in Russia, 4 - in Georgia) during 5 months of recruitment period. EVIDENCE recruitment rate was 2.1 pts/site/month compared to other CROs 0.3 pts/site/month. Results of this trial were published in JAMA. 2004 Jan 21;291(3):309-16: Effects of ranolazine with atenolol, amlodipine, or diltiazem on exercise tolerance and angina frequency in patients with severe chronic angina: a randomized controlled trial.

- **ERICA** (Evaluation of Ranolazine in Chronic Angina), recruitment started in August 2004, completed in January 2005. 608 patients were recruited by EVIDENCE in 49 sites (28 sites/402 pts in Russia, 8 sites/114 pts in Georgia; 2 sites/7 pts in Romania; 11 sites/85 pts in Bulgaria). EVIDENCE' average recruitment rate was 2 pts/site/month (2.4 pts/site/month in Russia and Georgia). Study drug was approved by FDA in February 2006.