Safety And Efficacy Of Sitagliptin Plus Granulocyte-colony Stimulating Factor In Patients Suffering From Acute Myocardial Infarction - Sitagrami Trial

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Aims: G-CSF based stem cell mobilization in combination with an inhibition of DPP-IV (Sitagliptin) after acute myocardial infarction (MI) lead to increased homing of bone marrow derived stem cells to the injured myocardium via the SDF1/CXCR4 axis, reduced remodelling, enhanced ejection fraction (EF) and survival. Therefore we initiated a phase III, multi-centre, randomised, double-blind and placebo-controlled efficacy and safety trial hypothesizing an absolute treatment effect of 3.5% of left ventricular EF 6 months after MI applying G-CSF/Sitagliptin (SITAGRAMI trial; EudraCT Number: 2007-003941-34; www.clinicaltrials.gov; Reg.Nr: NCT00650143).
Methods and Results: The last of the 174 patients was enrolled in July 2012. All suffered from large MI (mean creatine kinase elevation 3081+ 2106 U/l) undergoing successful percutaneous coronary intervention within 24 hours. After stratified (diabetes y/n; sex) randomisation in a 1:1 ratio, patients were treated with either placebo or G-CSF (10µg/kg/d)) over a period of 5 days together with an oral dose of 100 mg Sitagliptin daily for 4 weeks. Magnetic resonance imaging (MRI) was performed at screening visit and after 6 months, additional clinical follow-ups were scheduled at 6 weeks and 12 months. In the final analysis (power 80%), the Placebo group showed an absolute mean change in left ventricular EF of 4.6% (SD 7.9%) corresponding to the improvement reported by the REPAIR-AMI study. We will present primary endpoint data assessing the change of left and right ventricular EF by means of MRI from screening to 6 months of follow-up. Secondary endpoints comprised regional cardiac function, cardiac volumes, myocardial perfusion and extent of non-viable myocardium. Furthermore, we assessed peripheral blood CD34, CD34/KDR and CD34/CD26 positive cells, the occurrence of major adverse cardiac events (death, myocardial infarction, CABG, re-intervention), in stent restenosis, and de novo stenosis using angiography .
Conclusion: Final results of this first in men clinical trial using pharmacological stem cell mobilization in combination with SDF-1 related enhanced homing of CXCR4+ bone marrow-derived cells in order to induce myocardial regeneration after myocardial infarction will be reported.

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