2 SYNOPSIS

Name of Sponsor/Company: Universitätsklinikum Hamburg-Eppendorf	**Individual Study Table Referring to Part of the Dossier**	**(For National Authority Use only)**
Name of Finished Product: Ranexa©	**Volume:**	
Name of Active Ingredient: Ranolazine	**Page:**	
Study Title	Reduction of Ischemic Myocardium with Ranolazine-Treatment IN patients with acute myocardial Ischemia – RIMINI-Pilot-Trial	
Principal Investigator	Prof. Dr. med. Stefan Blankenberg	
Study center	Universitätsklinikum Hamburg-Eppendorf Universitäres Herzzentrum Martinistr. 52, 20246 Hamburg	
Protocol No.	RIMINI-Pilot (Sponsor), CTC11599 (CRO)	
EudraCT-No.	2013-000030-35	
Study Period	Study Initiation Date: 17JUN2013 Study Close Out Date: 17SEP2015	
Phase of development	Phase II (proof of concept)	
Primary Objective	Area of ischemic myocardium/cm² (longitudinal strain, radial/circumferential strain) after 42 days treatment with Ranolazine	
Secondary Objectives	• Level of cardiac markers (NT-pro-BNP, Troponine, CK, Copeptin) after 42 days treatment with Ranolazine • Incidence of cardiac complications (i.e. ventricular tachycardia, re-infarction, rehospitalisation for revascularization) A statistical evaluation of secondary endpoints was not performed, because no relevant changes in cardiac marker levels or relevant incidences occurred.	
Methodology	Single center, randomized, controlled two-armed open-label clinical trial. Patients were randomized either to Ranolazine-Treatment or to the control-group without additional medication. The cardiology specialist performing speckle-tracking echocardiography was blinded to the treatment regime of the patient undergoing examination.	
Number of subjects	A total of 20 patients with acute coronary syndrome and proof of myocardial dyskinesia were enrolled.	
Indication	CAD with acute ischemia and myocardial dysfunction	
Main criteria for inclusion	- Proof of acute cardiac ischemia by elevated serum Troponine T-hs levels > 14 pg/nl - Proof of myocardial dyskinesia with functional echocardiography	

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	("speckle tracking") - Stable angina pectoris >/= CCS II in patient history - Stabilized (i.e. normalized vital parameters) patients after coronary angioplasty or angiography - Coronary angioplasty or angiography not older than 48 hours - Written informed consent - Established standard therapy for coronary artery disease (i.e. Beta-Blocker, ACE-Inhibitor or AT1-Inhibitor, ASS, Clopidogrel, Statins)	
Test product, dose and mode of administration, batch no.	Ranolazine was administered as one tablet orally twice a day. Dosage started with 500mg bid and was increased to 750mg bid after seven days of treatment as described in the Summary of Product Characteristics.	
Duration of treatment	42 days	
Reference product, dose and mode of administration, batch no.	Control-Group without additional medication	
Criteria for evaluation Efficacy and Safety	For primary endpoint myocardial wall movement disorders evaluation via strain rate measurements using speckle tracking echocardiography. Safety were evaluated in terms of vital signs, 12-lead ECG, physical examination and clinical laboratory at the screening and the follow-up investigation. Adverse events were monitored at all study visits. The safety evaluation was based upon the review of the individual values (potentially clinically important abnormalities) and descriptive statistics (summary tables, graphics).	
Statistical methods	Analysis between Ranolazine treatment and no additional treatment was carried out using paired t-test. Non-parametric Mann-Whitney test was used for data that are not normally distributed. Categorical parameters was analyzed using χ^2 and exact Fisher's test.	
Efficacy Results	Ranolazine can safely be administered in acute myocardial infarction additionally to standard medical therapy. No safety issues occurred during the course of the clinical trial. Treatment with Ranolazine did not improve strain rates significantly compared to control treatment. A grouping of strain rates of segments by supplying coronary arteries did not alter this evaluation.	

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	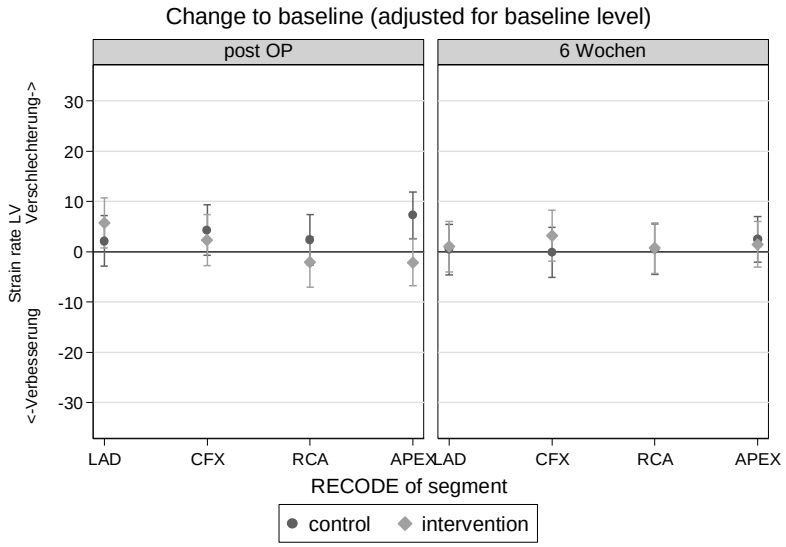	
Safety Results	A total of 21 AEs in 11 subjects with 12 different AE terms were reported. 18 AEs were of mild and 3 events of moderate intensity. None of the AEs was suspected to be related to the study medication. During this clinical trial 2 serious adverse events occurred. Both reported SAEs were considered to be not related to study medication or study interventions. Both SAEs were caused by complications of routine treatment of patients which were performed before inclusion in this clinical trial There were no relevant changes in clinical laboratory variables, vital signs, ECG parameters or in physical findings when comparing pre-study and post-study results. There were no safety concerns after dosing of the study medication.	
Conclusion	Ranolazine may have a beneficial effect in treatment of acute myocardial infarction with concomitant myocardial movement disorders.	
Date of Report	15 DEC 2015	