

**PROTOCOL SUMMARY**

<b>Name of Sponsor Company:</b> Takeda Pharma GmbH  <b>Collaborators:</b> -	<b>Drug Under Study:</b> Pioglitazone 15 mg, 30 mg Ramipril 2.5 mg, 5 mg
<b>Brief Title of Protocol:</b> Effect of Pioglitazone compared to a combination therapy with Ramipril and to a Ramipril monotherapy on low grade inflammation and vascular function in patients with increased cardiovascular risk and an activated inflammation  A randomized double-blinded phase II study	
<b>Protocol Number:</b> D-Pio-110 (ATS K023)	<b>Phase:</b> II
<b>Interventions:</b> Study drug, active control  <b>Intervention Type:</b> Drug  <b>Intervention Name:</b> Pioglitazone 15 mg (titration), 30 mg, vs. Ramipril 2.5 mg (titration), 5 mg vs. Pioglitazone (15 mg resp. 30 mg) + Ramipril (2.5 mg resp. 5 mg)	
<b>Study Description:</b> The purpose of this study is to evaluate effects on low grade inflammation and vascular function of Pioglitazone in non-diabetic, hypertensive patients with pre treatment with ACE inhibitors (that will be replaced by the study medication at time of randomisation). Primary efficacy variable is the change of the hs-CRP value after 12 weeks of treatment. It is assumed that Pioglitazone has anti-inflammatory and endothelium protective effects and probably additive effects in the combination with Ramipril  Primary endpoint: Change of the hs-CRP value after 12 weeks  Secondary efficacy objective will be to investigate the effect of pioglitazone compared to a combination therapy with ramipril and to a ramipril monotherapy on various laboratory parameters	
<b>Study Type:</b> Prospective, comparative, randomized and parallel. Three arms: 1. Pioglitazone + Placebo 2. Ramipril + Placebo 3. Pioglitazone + Ramipril Titration phase (2 weeks): Pioglitazone 15 mg + Placebo once daily Ramipril 2.5 mg + Placebo once daily Pioglitazone 15 mg + Ramipril 2.5 mg once daily  Treatment phase (12 weeks): Pioglitazone 30 mg + Placebo once daily Ramipril 5 mg + Placebo once daily Pioglitazone 30 mg + Ramipril 5 mg once daily	
<b>Study Status:</b> recruiting	
<b>Study Purpose:</b> To evaluate the effect of Pioglitazone compared to combination therapy with Ramipril and Ramipril alone on low grade inflammation and vascular function	
<b>Condition or Disease:</b> T2D, insulin resistance, patients with elective PTCA	
<b>Key Criteria for Inclusion:</b> Anamnestic hypertension; 30-75 years; stable treatment with ACE inhibitor at least for 12 weeks, hs CRP $\geq$ 1.0 mg/l < 10 mg/l	

**Key Criteria for Exclusion:**

Manifest or newly detected diabetes mellitus type 2 according to WHO criteria

Type 1 diabetes

Chronic inflammatory diseases which cause elevated CRP-values (e.g. rheumatic diseases, pyelonephritis, osteomyelitis)

Uncontrolled hypertension (repeated blood pressure > 180/100 mmHg for at least three times within two weeks); persistent hypotension (systolic < 90 mmHg) or haemodynamic instability

Treatment with any other investigational drug within 3 months before trial entry

A history of significant cardiovascular (NYHA stage I – IV, haemodynamic relevant aortic or mitral valve stenosis, hypertrophic obstructive cardiomyopathy), respiratory, gastrointestinal, hepatic (ALAT > 2.5 times the normal reference range), renal (creatinine > 2.0 mg/dL), or haematological disease, history of macular oedema

Treatment with thiazolidinediones within 3 months prior to screening

If statin therapy applicable: Change of medication within the last 12 weeks

History of angioneurotic oedema (hereditary or idiopathic as consequence of previous ACE inhibitor treatment)

Dialysis or hemofiltration

LDL apheresis with dextran sulphate