

**PROTOCOL SUMMARY**

<b>Name of Sponsor Company:</b> Takeda Pharma GmbH	<b>Drug Under Study:</b> Pioglitazone Atorvastatin
<b>Collaborators:</b>	
<b>Brief Title of Protocol:</b> Double Blinded Study of the Effects of Pioglitazone in Combination with Atorvastatin in Comparison to Atorvastatin Treatment Alone on Intima-Media Thickness in Patients at Risk for Vascular Complications	
<b>Protocol Number:</b> ATS K015	<b>Phase:</b> III
<b>Interventions:</b> Study drug Intervention Type: Drug <b>Intervention Name:</b> Pioglitazone, Atorvastatin	
<b>Study Description:</b> To generate data on the alteration of Intima-Media-Thickness in patients with a vascular risk profile and a risk for developing diabetes, characterized by proven cardiovascular disease with atherosclerotic vascular changes. This study should help to get cardiologists, and other specialties focused on vascular medicine interested in pioglitazone treatment. This is important for market preparation prior to launch of the PROactive Study. Because the PROactive Study involved severely ill patients with advanced atherosclerotic disease it will be crucial to provide also evidence for the benefit of pioglitazone treatment in earlier stages of the disease. The recruitment of non-diabetic patients should establish that the effects observed in this study are independent of glucose control and represent unique and direct effects of the drug, which is a precondition for the comparability with atorvastatin treatment. The primary comparison should be a superiority of PIO plus Statin versus the statin arm. Pioglitazone: oral 30 - 45 mg /day; dose titration from 30 to 45 mg after four weeks; uptake: 1-0-0, before breakfast (capsules containing 30 or 45 mg Pioglitazone) Atorvastatin: oral 20 - 40 mg/day; dose titration from 20 mg to 40 mg after four weeks; uptake: 1-0-0, before breakfast (tablets containing 20 or 40 mg Atorvastatin) Placebo: oral; uptake 1-0-0, before breakfast (matching placebo capsules to Pioglitazone)	
<b>Study Type:</b> Double blind, prospective, comparative, randomized and parallel	
<b>Study Status:</b> completed	
<b>Study Purpose:</b> Protective effects of pioglitazone in patients at high risk for developing vascular complications.	
<b>Condition or Disease:</b> vascular complications	
<b>Key Criteria for Inclusion:</b> - Carotid Intima Media Thickness $\geq$ 0,8 mm - BMI $\geq$ 25 kg/m <sup>2</sup> - age 30 – 70 years - no overt type-2-diabetes according to the WHO criteria	
<b>Key Criteria for Exclusion:</b> - overt type-2-diabetes according to the WHO criteria (FBG $\geq$ 7,0 mmol/l) - heart failure NYHA II-IV - ALT > 2,5 ULN - Statin therapy within the last 4 weeks	