PROTOCOL SUMMARY

Name of Sponsor Company: Takeda Pharma GmbH **Collaborators:** -	**Drug Under Study:** CANDESARTAN plus HCTZ

Brief Title of Protocol:
Double-blind, randomized trial to investigate the antihypertensive and metabolic effects of candesartan in insulin-resistant obese patients with a hypertension not adequately controlled by previous ß-blocker or calcium channel blocker

Protocol Number: D-CAN-545	**Phase:** IV

Interventions: Study drug, active control

Intervention Type: Drug

Drug: Candesartan **Intervention Name:** Candesartan 16mg plus HCTZ 12,5mg versus HCTZ 12,5mg

Study Description:

Abdominal obesity is a major risk factor for insulin resistance and the development of type 2 diabetes. It is associated with sodium retention, left ventricular hypertrophy and elevated markers of inflammation and is an important predictor of cardiovascular morbidity and mortality. Activation of the sympathetic nervous system and the RAAS are either involved in the development of hypertension in obese individuals. Hypertension in these individuals is complicated by dyslipidemia, hyperinsulinemia and impaired glucose tolerance. When compared to leaner patients obese individuals do not respond as well to antihypertensive medication. They need the full array of antihypertensive drugs. Candesartan is a blocker of the RAAS and reduces in a dose dependent manner hypertension and is possibly effective in improving the metabolic situation in patients with a pre-diabetic condition what may prevent or delay new-onset diabetes.

Primary endpoint: Efficacy of Candesartan 16 mg + Hydrochlorothiazide (HCT) 12,5 mg on blood pressure reduction in comparison to Placebo + HCT 12,5 mg both working on top of previously ineffective ß-blocker- or calcium channel blocker-therapy

Secondary endpoints: Efficacy of Candesartan 16 mg+ HCT 12,5 mg on glucose- and lipid-metabolism, inflammation (as assessed by human serum C-reactive protein (hs-CRP)) and coronary risk (as assessed by Prospective Cardiovascular Münster (PROCAM)-risk score).

Study Type: interventional, treatment, randomized, double blind, active controlled

Study Status: recruiting

Study Purpose: Efficacy of Candesartan in insulin-resistant hypertensive and obese patients

Condition or Disease: Hypertension, obesity, insulin-resistant

Key Criteria for Inclusion:

Outpatients, aged 35 to 70 years, abdominal obesity (waist circumference > 102 cm (men) and > 88 cm (women), BMI > 30 kg/m^2), hypertension not controlled (SDBP) > 95 mmHg and ≤ 110 mmHg) by monotherapy with either ß-blocker or calcium channel blocker, insulin resistance (acc. HOMA-IR)

Key Criteria for Exclusion:

Existing HCT therapy at start of the study, Diabetes type 1 or 2, chronic renal impairment, hyperkalaemia, familial hypercholestaerolemia, hepatic impairment, chronic heart failure, coronary heart disease, previous MI, previous stroke , ACE inhibitor or ARB therapy in the previous 4 weeks