Revacept, an inhibitor of platelet adhesion in symptomatic carotid stenosis: Results from a phase II study

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Revacept is a novel lesion-specific inhibitor for platelet adhesion and thrombus formation. The biological drug is based on the platelet GPVI receptor and prevents collagen-mediated platelet activation from the atherosclerotic plaque. The unique characteristic of Revacept is the specific inhibition of plaque-mediated thrombus formation without alteration of hemostasis.

To test this concept in patients with plaque-mediated thrombosis we investigated patients with symptomatic carotid artery stenosis (at least 50% cf. ECST) with a recent ischemic cerebral stroke or transient ischemic attack (TIA). 150 patients were evenly randomized in blinded fashion to receive placebo, 40mg or 120 mg Revacept by IV infusion. To investigate anti-thrombotic efficacy, we assessed microemboli in the middle cerebral artery by transcranial Doppler (MES) and micro-infarctions in the brain by diffusion-weighted nuclear magnetic resonance (DWI-NMR) imaging. Ischemic complications such as myocardial infarctions and ischemic stroke were clinically followed up to 3 and 12 months. Bleeding complications were thoroughly monitored according to the RE-LY study group criteria. All patients were on standard anti-platelet therapy and underwent guideline conform treatment with carotid endarterectomy (CEA), carotid artery stent implantation or intensified conservative treatment.

The study was conducted in 16 centers in Germany and the UK from May 2013 to September 2018. Due to lost to follow-up investigations the planned patient numbers were slightly exceeded to 158 patients, who were finally included in the study according to intention to treat. Currently data clearance and detailed analysis of unblinded data is going on. 7.6% of patients underwent carotid artery stenting, 11.4% were under intensified conservative treatment and 81.0% were surgically treated with CEA. The safety data of the overall 158 patients which was closely monitored by an independent data safety board are available. In the overall study population (before unblinding for treatment) ischemic strokes and myocardial infarctions were numerically lower compared to previous studies with symptomatic carotid stenosis patients undergoing CEA or stenting (meta analysis from the EVA-3S, SPACE and ICSS study). Despite comparable basal anti-thrombotic therapy addition of Revacept did
not increase bleeding complications in the overall study population.

The Revacept CS02 study has successfully achieved the aimed patient recruitment. Safety analysis shows a favorable profile. Bleeding complications in these high-risk patients with recent ischemic stroke were not increased compared to historic data from similar control patients. There is a trend for increased anti-thrombotic and anti-ischemic potency with regard to clinical events. Final data will be presented at the congress.