

## **Enhancement of Stroke Rehabilitation with Levodopa (ESTREL): a randomized placebo-controlled trial**

Principal Investigator:	PD Dr. med. Georg Kägi
Status:	planned
Project Start:	2019
Project End:	2022
Trial Design /Class:	Multicenter, randomized (ratio 1:1), parallel-group, placebo-controlled superiority trial with blinded patients, care-providers, investigators, and outcome assessors, Class: C
Number of Patient:	610 participants
Centers:	stroke centers and units (12 acute centers anticipated), rehabilitation centers (7 centers anticipated)
Sponsor/Partner:	Chair Rehabilitation, Felix-Platter Spital Basel, Prof. Dr. med. Stefan Engelter
Funding:	Chair Rehabilitation, Felix-Platter Spital Basel, Swiss National Science Foundation

### **Summary:**

In stroke medicine, the large body of high-quality evidence proving benefits of acute revascularization therapies and secondary prevention is offset by a large gap of evidence on means to enhance stroke recovery. Levodopa is a promising candidate for the pharmacological enhancement of stroke recovery. Dopamine is a key player in processes of motor learning, reward, and brain plasticity. Preclinical research and studies with healthy individuals suggest that there is scope for benefit from applying levodopa in addition to standardized rehabilitation. Given the high prevalence and tremendous burden of stroke, a straightforward applicable measure to improve motor outcome is highly relevant. Given the promising but inconclusive clinical trial evidence on benefits, a well- designed randomized controlled trial studying the usefulness of levodopa in enhancing motor recovery after stroke is warranted.

### **Objectives:**

#### **Primary Objective**

To investigate whether Levodopa/Carbidopa compared to matching placebo given in addition to standardized rehabilitation based on the principles of motor learning is associated with a patient-relevant enhancement of functional recovery in acute ischemic stroke patients as measured by the between group difference of final scores in the Fugl-Meyer-Motor-Assessment (FMMA) 3 months after randomization.

#### **Secondary Objectives**

- 1) To study whether levodopa compared to placebo given in addition to standardized rehabilitative therapy in patients with acute ischemic stroke is associated with
  - a) improvements of physical function based on the patient's self-assessment
  - b) improvement in patient-self assessed general health aspects, pain, mood, anxiety, fatigue and social participation
  - c) long-term sustainability of a patient-relevant improvement of motor function
  - d) improvement of selective hand and wrist movement
  - e) a higher rate of patients walking independently of the help of another person.
  - f) less severe impairment
  - g) a higher level of activity of daily living
  - h) improvements of quality of life
  - i) better cognitive performance
  - j) no signals of harms (i.e. indications for increased all-cause mortality, recurrent stroke or serious adverse events).