# Trial Description

## Title

**Multicenter prospective analysis of hypertrophic olivary degeneration following infratentorial stroke: Evaluation of disease epidemiology, clinical presentation and MR-imaging aspects**

## Trial Acronym

**HOD-IS**

## URL of the trial

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## Brief Summary in Lay Language

**After a stroke in the brain stem or the cerebellum, some patients with a delay of weeks develop symptoms such as troubles coordinating the arms and hands, disturbances in ocluar movement and a rhythmic tremor of the soft palate. This is not due to a new stroke, but due to a complex neurodegenerative disease called hypetrophic olivary degeneration (HOD), which can be induced by strategical localized strokes. Often the HOD is not recognized or mistaken for another disease. In our tertiary care center, we encountered close to 50 patients with HOD already and had to realize, how little medical professionals know about this illness. Even the frequency of HOD is still completely unknown and we can not tell whether it is a very rare, or maybe even quite common finding. The intention of this study is to answer those questions and provide medical insights on HOD and its prevention.**

## Brief Summary in Scientific Language

**Background: Ischemic and hemorrhagic strokes in the brainstem and cerebellum can affect the dentato-rubro-olivary-pathway. Lesions in this functional loop, the so-called Guillain-Mollaret triangle, may result in secondary trans-synaptic neurodegeneration of the inferior olivary nucleus, a condition called hypertrophic olivary degeneration (HOD). The characteristic clinical syndrome of HOD occurs slowly over months and includes a rhythmic palatal tremor, primarily vertical pendular nystagmus and Holmes-tremor of the upper limbs – greatly reducing patients' life quality. Fiberoptic endoscopic examination of swallowing (FEES) is essential to detect swallowing difficulties and prevent aspiration pneumonia. The incidence of HOD occurrence following lesions in the Guillain-Mollaret triangle has not yet been determined and no prospective studies on HOD were conducted to date.**
**Purpose: The primary endpoint of this prospective clinical multicenter study is to determine the risk of HOD development in patients with ischemic or hemorrhagic lesions within the Guillain-Mollaret triangle. Further study targets include describing the time course and pattern of HOD development on advanced MR-imaging including quantitative imaging with diffusion tensor imaging and proton density-weighted imaging, the manifestation of the clinical syndrome as well as identification of lesion localizations more prone to HOD occurrence, in order to detect patients at high risk of developing HOD.**

**Methods: Patients with ischemic and hemorrhagic strokes in the brainstem and cerebellum with a topo-anatomical relation to the Guillain-Mollaret triangle will be recruited within 12 hospitals with certified stroke-units of the Interdisciplinary Neurovascular Network Rhine-Main. Patients who meet inclusion criteria will be followed up prospectively for 8 months and present at the Frankfurt Brain Imaging Center (BIC) at 3-4 months and at 7-8 months after the index event. During each of these visits, a clinical neurological examination, dysphagia screening (FEES) and an MRI scan of the brain with T2w-imaging, proton-density weighted imaging, FLAIR and Diffusion Tensor Imaging (DTI) will be acquired. Hereafter, analysis of clinical systematics and imaging patterns will be carried out.**
**Concluding remarks: This is the first prospective study in literature determining the incidence of HOD after ischemic and hemorrhagic strokes in the brainstem and cerebellum affecting the Guillain-Mollaret triangle. We intend to generate a deeper understanding of the entity and the course of disease, aiming for clinical consequences and facilitation of future studies on therapeutic options.**

**Do you plan to share individual participant data with other researchers?**

**No**

**Description IPD sharing plan**

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## Organizational Data

- DRKS-ID: **DRKS00020549**
- Date of Registration in DRKS: **2020/03/05**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **19-467 , Ethikkommission des Fachbereichs Humanmedizin der Johann-Wolfgang-Goethe-Universität Frankfurt am Main**

## Secondary IDs

## Health condition or Problem studied

- Free text: **Hypertrophic olivary Degeneration (HOD)**
- Free text: **Ischemic stroke**
  **Hemorrhagic stroke**
- ICD10: **I63 - Cerebral infarction**
- ICD10: **I61 - Intracerebral haemorrhage**
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ICD10: **I62 - Other nontraumatic intracranial haemorrhage**

- ICD10: **I69 - Sequelae of cerebrovascular disease**

## Interventions/Observational Groups

- Arm 1: **Single-arm study (Patients who meet inclusion criteria will be followed up prospectively for 8 months and present at the Frankfurt Brain Imaging Center (BIC) at 3-4 months and at 7-8 months after the index event. During each of these visits, a clinical neurological examination, dysphagia screening (FEES) and an MRI scan of the brain with T2w-imaging, proton-density weighted imaging, FLAIR and Diffusion Tensor Imaging (DTI) will be acquired.)**

## Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Observational study**
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Basic research/physiological study**
- Assignment: **Single (group)**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

### Primary Outcome

**The primary endpoint of the study is the presence of HOD on follow-up imaging at 7-8 months after the index event.**

### Secondary Outcome

**Secondary endpoint values are for one the imaging-recorded incidence rate of the HOD at the time point 3-4 months after the index event, analogous to the main target value recorded, as well as identification of lesion localizations at significantly higher risk of HOD occurrence. Other secondary targets include the presence of the clinical syndrome of HOD (rhythmic palatal tremor, Holmes tremor and pendular nystagmus) in 3-4 and in 7-8 months after the index event, respectively. These are clinically recorded by the study team and study centers. In addition, baseline medical data (age, gender), clinical parameters (blood pressure at admission, presence of oral anticoagulation) and clinical outcome parameters (modified Rankin Scale, National Institute of Health Stroke Scale) are correlated with the occurrence of HOD.**

## Countries of recruitment

- DE **Germany**

## Locations of Recruitment

- University Medical Center **Klinik für Neurologie, Frankfurt a.M.**

## Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2020/03/01**
- Target Sample Size: **100**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

### Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

### Additional Inclusion Criteria

**Inclusion criteria**

**Intracerebral hemorrhage or cerebral infarction involving the brainstem or the cerebellum**

**Topo-anatomical relation of the stroke lesion to the Guillain Mollaret triangle (a template will be used to define the regions of interest on MRI scans**

**Maximum diameter of the stroke lesion as defined by MRI of 3 cm**

**Maximum time from stroke symptom onset to study inclusion 7 days**

**Signed informed consent form**

### Exclusion criteria

**Exclusion criteria**
**Sopor and coma at planned study inclusion**
**Intensive care treatment at planned study inclusion**
**operative Injury to the Guillain Mollaret triangle during the acute presentation**
**Contraindications to MR imaging (such as pacemakers, ferromagnetic materials in the body, claustrophobia)**
**Age less than 18 at the time of the index event**
**Modified Rankin Scale (mRS) of > 4 points (patient transportation not feasible)**
**Lack of legal competence or ability to consent (e.g. in the case of legal support)**

## Addresses

■ **Primary Sponsor**

**Klinik für Neurologie Universitätsklinikum Frankfurt, Goethe-Universität**
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■ **Contact for Scientific Queries**

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## Sources of Monetary or Material Support

■ **Institutional budget, no external funding (budget of sponsor/PI)**

**Klinik für Neurologie**

**Institutional budget, no external funding (budget of sponsor/PI)**

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## Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

## Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*