Trial Description

Title

Personalised Prognostic Tools for Early Psychosis Management

Trial Acronym

PRONIA

URL of the trial

http://NA

Brief Summary in Lay Language

PRONIA aims at developing prognostic services for persons at risk of psychosis-related clinical, social and occupational outcomes. These services will be based on predictive models that work at the single-subject level and combine different data modalities (imaging, neurocognition, clinical data, genetic and metabolic information) in order to generate highly accurate and reliable prognostic information for (i) persons at-risk of pychosis, (ii) patients in a recent-onset state of psychosis, and (iii) patients in a recent-onset state of depression who do not fulfil psychosis-related risk criteria.

To build these prognostic services a multi-centre prospective naturalistic study will be performed across 6 different clinical centres, including the Ludwig-Maximilian-University Munich, the University of Basel, the University of Cologne, the University of Birmingham and the University of Udine. Across these centres, PRONIA will recruit 420 patients with a recent-onset stage of psychosis, 420 patients with a recent-onset stage of depression, 420 persons in a high-risk state for psychosis as defined by established high-risk criteria and 420 healthy volunteers. Study participants will be regularly followed over 18 months to determine and quantify clinical, social and occupational outcome variables. Neurobiological and clinical data will be collected at baseline and after 9 months.

From these data a machine learning system will be generated that will extract predictive multi-modal signatures capable of optimising the diagnostic workflow for an individual help-seeking person who has not been used for training the system. This will allow to minimise diagnostic workload for given person while maximising prognostic accuracy. Based on this information, the PRONIA prognostic service will contribute to improve preventive therapeutic interventions in the early and prodromal stages of severe mental illness

Brief Summary in Scientific Language

Affective and non-affective psychoses have a major negative impact on human society. They account for 6.3% of the global burden of disease and cost €207 billion per year in Europe alone, making them the most expensive brain-related disorders and even more expensive than cardiovascular diseases. This socioeconomic burden is largely caused by two core disease features: onset in adolescence and early adulthood and long-term disabling disease courses. Both factors lead to enduring social and vocational exclusion and contribute to 8-20

**times higher suicide rates in affected patients.
Reliable and accessible prognostic tools will alleviate this burden by enabling individualised risk prediction, thus facilitating the targeted prevention of psychoses. Thus, we will first use routine brain imaging and complementary data to optimise our candidate biomarkers for the prediction and staging of psychoses and generate a prognostic system that generalises well across mental health services. Secondly, we will implement new multi-modal risk quantification tools to predict mental health-related disability in young help-seekers. The fusion of these tools with clinical knowledge will produce cybernetic prognostic services that accurately identify help-seekers at the highest risk of psychosis, poor functioning and suicide-related mortality.
During this project we will secure our intellectual property rights and transform into a European company to commercially exploit these prognostic services through internet-based telemedicine applications. This will provide psychosis risk profiling tools to diverse target groups in the healthcare markets, including care-givers, the pharmaceutical industry and research institutions. By disseminating objective risk quantification, these products will provide firm diagnostic grounds for preventive therapy, improving outcomes and reducing costs. Thus, they will offer a unique selling proposition to the mental health sectors in Europe and beyond.**

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

[---]*

Description IPD sharing plan

[---]*

Organizational Data

- DRKS-ID: **DRKS00005042**
- Date of Registration in DRKS: **2013/10/07**
- 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.: **351/13 , Ethik-Kommission der Medizinischen Fakultät der Ludwig-Maximilians-Universität München**

Secondary IDs

Health condition or Problem studied

- ICD10: **F20 - Schizophrenia**
- ICD10: **F22 - Persistent delusional disorders**

- ICD10: **F23 - Acute and transient psychotic disorders**
- ICD10: **F25 - Schizoaffective disorders**
- ICD10: **F28 - Other nonorganic psychotic disorders**
- ICD10: **F29 - Unspecified nonorganic psychosis**
- ICD10: **F31.2 - Bipolar affective disorder, current episode manic with psychotic symptoms**
- ICD10: **F32.3 - Severe depressive episode with psychotic symptoms**
- ICD10: **F32 - Depressive episode**
- Free text: **Individuals in a clinically defined at-risk mental state for psychosis**
- Free text: **healthy volunteers**

Interventions/Observational Groups

- Arm 1: **Observation group (naturalistic design) including ROP patients, ROD patients, individuals in an at-risk mental state for psychosis and healthy volunteers**

  Examinations:
  In all subjects:
  - Blood analysis, cMRI and neuropsychological testing at baseline and at month 9

  In addition:
  In observation group:
  - Survey of clinical scales at baseline and every 3 months until month 18

  In the control group:
  - Survey of clinical scales at baseline, at month 9 and month 18

Characteristics

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

Primary Outcome

Sensitivity and Specificity of prognostic system

Secondary Outcome

Individuals diagnostic load / cost effectiveness of prognostic system

Countries of recruitment

- DE **Germany**
- CH **Switzerland**
- FI **Finland**
- IT **Italy**
- UK **United Kingdom**

Locations of Recruitment

- University Medical Center **Klinik und Polinklinik für Psychiatrie und Psychotherapie, München**
- University Medical Center **Universitäre Psychiatrische Kliniken (UPK), Basel**
- University Medical Center **University hospital of Turku, Turku**
- University Medical Center **Department of Psychiatry, Udine**
- other **Programma2000 - Hochrisiko-Zentrum, Mailand**
- University Medical Center **Department of Psychiatry, Birmingham**
- University Medical Center **Klinik für Psychiatrie und Psychotherapie, Köln**

Recruitment

- Planned/Actual: **Planned**
- (Anticipated or Actual) Date of First Enrollment: **2013/11/01**
- Target Sample Size: **1680**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **15 Years**

Gender: **Both, male and female**

Minimum Age: **15 Years**

■ Maximum Age: **40 Years**

Additional Inclusion Criteria

Recent-onset psychosis (ROP):
- **EITHER (i) transition criteria as defined by Yung et al. (1998)**
- **OR (ii) ICD-10: F20.x, F22.x, F23.x, F25.x, F28, F29, F31.2, F32.3**

Recent-onset depression (ROD):
- **ICD-10: F32.x**

At-risk mental states for psychosis (ARMS):
- **EITHER (i) CAARMS criteria**
- **OR (ii) SPI-A criteria**
- **OR (iii) GAF reduction ≥ 30% and positive family history of psychoses**
- **OR (iv) GAF reduction ≥ 30% and criteria for schizotypia (ICD-10: F21)**

Controllgroup:
• healthy volunteers without a personal history of affective or non-affective psychoses or other psychiatric conditions and no family history of psychoses (1° relatives)

Exclusion criteria

General exclusion:
- **Age < 15 OR > 40**
- **IQ < 70**
- **Current or past head trauma**
- **Current or past neurological illness**
- **Current or past serious medical or surgical illness affecting CNS function**
- **ICD-10: Dependence syndrome (F1x.24 / F1x.25)**

ROP:
- **Duration of psychoses > 12 months**
- **Duration of antipsychotic medication > 3 months**

ROD:
- **Inclusion criteria for ROP and ARMS**
- **Duration of depressive episode > 12 months**

ARMS:
Inclusion criteria for recent-onset psychoses

HC:
- **Personal history of affective or non-affective psychoses or other psychiatric conditions**
- **Family history of psychoses (1° relatives)**

Addresses

- **Primary Sponsor**

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Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

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Status

- Recruitment Status: **Recruiting planned**
- 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.*