# Overview
# **G**enetics of **I**schaemic **S**troke Functional **Out**come Study

# GISCOME

Arne Lindgren on behalf of
the GISCOME investigators

# Background

- Ischemic stroke patients often have considerable functional deficit after stroke

  43% mRS 3-6 at discharge

  Béjot. Neuroepidemiology 2013;41:169–173

- Some patients recover, some do not recover

# Background

- Different mechanisms for recovery
  - ”Stunned brain” recovering
  - Repair
  - Plasticity

- Recovery mechanisms may vary by time
  - Early recovery during first days-weeks
  - Later recovery weeks-months-years

# Background
# Risk for confusion in terminology

Functional outcome: status after ischemic stroke

- E.g. mRS

Recovery: Functional outcome in relation to initial stroke severity

- E.g. mRS in relation to baseline NIHSS

# Hypothesis

- Genetic mechanisms influence recovery after cerebral infarct
- An agnostic approach can detect these genetic mechanisms
- These mechanisms can be further studied to better understand recovery after stroke
- This better understanding will lead to treatments enhancing recovery

Primary purpose

# Test the hypothesis

genetic variation influences functional recovery after

the acute phase of ischemic stroke

# Other purposes

1. Describe functional outcome and recovery in very large cohort of ischemic stroke patients

2. Recovery in different subgroups
   - Age
   - CCS/TOAST
   - Severity strata

3. Examine genetic influene in the acute phase of ischemic stroke

# Methods

- Retrospective study
- Multi-center GWAS
- Primary outcome

  Good vs bad Outcome after 3 months

  - mRS 0-2 vs 3-6
  - adjustment for age, gender, onset NIHSS

# Methods

Secondary outcomes:

1. mRS at 3 months as ordinal scale
2. outcome in stroke subtypes CCS/TOAST
3. 1-year outcome mRS dichotomous
4. mRS evolvement by time

# Methods

- Additional Spanish samples n=800
  - Jordi Jimenez Condi

- Meta-analysis/replication with Spanish samples

# Retrospective study: compromises necessary

- Baseline time for enrolment

- mRS 3 months
  - Closest to 90 days (60 to 190 days accepted)

# Methods

- GISCoME data centrally collected in Cambridge, UK

  Steve Bevan

  – Phenotypic data

  – Genotype data

- Monthly teleconferences
- Abstracts for conferences
- Description paper
- Phenotypic paper?
- Main paper

# Current status Data

- Phenotype data from 14 studies now in Cambridge

- mRS at ”90 days” available, n=9412

| | | |
|---|---|---|
| Cincinnati | Woo | 642 |
| Edinburgh | Sudlow/ Rannikmae | 625 |
| Helsinki | Tatlisumak/Strbian | 469 |
| Hospital del Mar | Jimenes Conde | 930 |
| Leuven | Lemmens/Thijs | 491 |
| Lund | Lindgren | 1161 |
| MGH | Rost/Rosand | 1073 |
| Newcastle | Maguire | 665 |
| Oxford | Rothwell | 553 |
| SAHLISS | Jern | 1117 |
| Val de Hebron 1 | Fernandez Cadenas | 743 |
| Val de Hebron 2 | Fernandez Cadenas | 610 |
| WASH-U | Lee | 256 |
| VISP | Worrall | 2100 |
| **Total** | | **11453** |

# Baseline characteristics

| | |
|---|---|
| n in database | 11453 |
| Mean (median) age (years) | 68.1 (69) |
| Female (%) | 42.2 |
| Hypertension % | 67.2 |
| Diabetes % | 23.8 |
| Current Smoker | 23.8 |
| Atrial fibrillation % | 19.6 |

# TOAST / CCS

| | |
|---|---|
| TOAST | 8420 |
| CE | 2692 |
| LAA | 1499 |
| SVD | 1448 |
| Other | 508 |
| UND | 2273 |
| CCS | 5361 |
| CE | 1742 |
| LAA | 861 |
| SVD | 620 |
| Other | 270 |
| UND | 1868 |

# Baseline NIHSS Outrome mRS

| | median | n |
|---|---|---|
| Earliest NIHSS, within 1 week | 3 | 10863 |
| time for earliest NIHSS (days) | 1 | 6716 |
| mRS at “90 days” | 2 | 9312 |
| | | |

# Limitations

- Cohorts enrolled at different time points after stroke onset
- Patients evaluated at different time points after stroke onset
- Mixture of CCS and TOAST
- mRS not available as ordinal scale variable for all sites

# Current status Conferences

**GISCOME abstract European Stroke Conference,**
**Nice, May 2014. Accepted for e-poster presentation**

**Stroke Genetics Symposium at European Stroke Conference Nice, May 2014.** http://www.eurostroke.eu/ni_minisym6.html

**GISCOME abstract Stroke Society of Australasia meeting July/August 2014 submitted**

**Proposal of Stroke Genetics Symposium, International Stroke Conference, Nashville, Feb 2015 submitted**

# Current status funding

- Grants received
  - Jern
  - Lindgren

- New applications submitted/planned

# Further plans for 2014

- Collect genotype data in Cambridge database
- Write description paper
  - Jane Maguire and writing group
- Analyse early outcome
  - Jin-Moo Lee
- Perform outcome analyses

# Thank you

| | |
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SiGN

Riksstroke

Steve Bevan