DISCHARGE

# „Monitoring strategy“

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# Agenda

- Why monitoring?
- Objectives of the monitoring?
- Monitoring strategy

# ICH-GCP

**Good Clinical Practice (GCP)**

is an international set of ethical and scientific standards for the

- conduct, design, performance, monitoring, auditing, recording, analysis and reporting of CTs
- defines the roles and responsibilities of clinical trial sponsors, clinical research investigators and monitors.

# ICH-GCP

**Objectives of ICH-GCP**

- Protection of rights, safety and well-being of trial subjects
- Credibility of clinical trial data

- Quality management is an essentiell part of GCP
- Compliance with GCP is mandatory
- Traceability and reliability of all data and documents ➔ verifiable statement on study hypothesis

# Monitoring

ICH-GCP 5.18.1

*Purpose*

The purposes of trial monitoring are to verify that:

a ) The rights and well-being of human subjects are protected.

b) The reported trial data are accurate, complete and verifiable from source documents.

c ) The conduct of the trial is in compliance with the currently approved protocol / amendment(s), with GCP and with the applicable regulatory requirement(s)

# Monitoring

ICH-GCP 5.18.3

*Extent and Nature of Monitoring*

The sponsor

- should ensure that the trials are adequately monitored
- should determine the appropriate extent and nature of monitoring

based on considerations such as the objective, purpose, design, complexity, blinding, size and endpoints of the trial

# Monitoring

ICH-GCP 5.18.5

*Monitoring Procedures*

The monitor(s) should follow the sponsor's

- established written SOPs as well as those
- procedures that are specified by the sponsor for monitoring a specific trial.

→ **Monitoring Manual**

# Monitoring strategy

Extent and nature of the monitoring in the will be based on a DISCHARGE specific risk assessment:

- Identification of potential risks
  - for the patients
  - for the data
  - for the study

→ Risk based monitoring strategy

# Risk-based approach

- Depending on research questions and protocol design
- Assessment of the potential risk associated with intervention (compared to standard procedures / intervention)
- Trial specific risk analysis
  - Patient related indicators: vulnerable population, inclusion/ exclusion criteria, informed consent process
  - Indicators of robustness: Study design and primary endpoint
- Site related indicators (e.g. site performance)

$\rightarrow$ Classification with respect to the need of on-site monitoring

# Monitoring strategy

Monitoring in the DISCHARGE trial will be a combination of

- on site visits
- centralized monitoring

# Centralized monitoring

- Review for
  - Enrolment
  - Documentation status

  } Total / per site
- Data plausibility (SecuTrial)
- Missing data
- Site effects (e.g. cumulation of SAEs or no SAEs, late documentation, …)
- Communication with the sites

# Purpose of on-site monitoring

Focus on critical aspects of the study (risk to patient safety or rights or validity of the results)

- which can be influenced by on-site monitoring and
- which can be not controlled or only by increased costs and/or by other means

→ **Defining data / issues which should be verified by on-site monitoring**

# Key data/ issues

- Source Data Verification
  - Informed consent → **subject's rights**
  - (Serious) Adverse Events
  - Primary endpoint
  - Inclusion / Exclusion criteria

  } **Data quality**

- Further issues to be monitored
  - Investigator's Site File → **study documentation**
  - Subject status
  - Changes in staff (changes in responsibilities)
  - Problems and questions

  } **Projekt overview**



13

# Monitoring Manual

- Procedures for monitoring
- Definition of
    - key data for on-site monitoring
    - Data for central monitoring
    - amount and frequency of on-site monitoring
- Definition of critical protocol violations
- Communication lines
- Indicators for site performance (good, non-compliance, number of protocol violations, …)
- Escalation strategy in case of problems and non-compliance

# Open questions

- Study design: how is the information flow / contact (patient → investigator) during the follow up phase guaranteed?
- Controlling of follow up activities of the investigator (on-site)?
- Documentation
  - Who documents (investigator, family, physician, patient) where and what?
  - Language
  - Paper or / and electronically