Monitoring Guidelines for Non-interventional Studies
NIS Considerations

- We all know that monitoring is key to ensure patient safety and data quality.
- However, non-interventional studies (NIS) are not randomised controlled clinical trials.
- Monitoring of NIS needs to be tailored to accommodate a range of NIS considerations including the study design, regulatory requirements, study duration, number of sites and patients and study outcomes.
NIS Considerations

- Why are NIS different?
  - Drug commercially available and used according to marketing authorisation
  - Not protocol driven
  - Retrospective and prospective designs
  - Country-specific requirements
  - Breach of data privacy is greatest study risk to patient, not IMP-related SARs
Monitoring Options

- When designing an NIS monitoring plan, need to consider:
  - Regulatory requirements
    - e.g., monitoring of NIS is a legal requirement in Spain
  - Study design and purpose/endpoints
  - Study size, duration and global footprint
  - Therapeutic area
  - Business policy - The degree of risk the business is willing to accept
    e.g., a 0% monitoring policy significantly increases the risk that any data generated will not be credible or submissable (e.g., RMP) or publishable
Monitoring Options

- On-site monitoring
- On-site & remote monitoring (Hybrid)
- Remote monitoring
  - Phone calls, emails, eCRF etc
- No monitoring
On-site Monitoring

- Classic gold standard
  - On-site monitoring every 4 to 8 weeks
  - 100% SDV of X% of CRFs

- NIS Opportunity
  - Can be used for short-term prospective NIS such as PASS where data credibility is paramount

- Challenge
  - Impractical for large, long-term prospective studies
  - High cost and resource implications
No Monitoring

- Not an option for interventional clinical trials
- NIS Opportunity
  - Effective for retrospective NIS based on patient information collected from managed core databases
- NIS Challenge
  - Not effective for prospective NIS as need to ensure/assure quality/credibility of data
Remote Monitoring

- **NIS Opportunity**
  - Allows for frequent contact with sites to provide support and reinforce appropriate performance
  - Reduced resource and cost requirements
  - Can be used to trigger on-site monitoring

- **NIS Challenge**
  - Needs to be conducted by an experienced CRA for it be effective
  - Doesn’t account for on-site auditing of data - credibility of data therefore unknown
Hybrid Monitoring

- NIS Opportunity
  - Allows for frequent contact with sites to provide support and reinforce appropriate performance
  - Reduced resource and cost requirements
  - Can be used to trigger on-site monitoring
  - Schedule periodic site visits to address site needs and assess data quality
Hybrid Monitoring

NIS Challenge

- Needs to be conducted by an experienced CRA for it to be effective
- Sponsor-site relationship is more effective when a single point of contact is maintained (may be impacted by staff turnover)
- Need to clearly define ‘triggers’ for on-site monitoring prior to study start e.g.,
  - Suspected fraud
  - Rate of enrollment
  - Missing CRFs
  - Number of data queries
Overview of NIS Monitoring Approaches

- **100% on-site monitoring**
- **100% remote monitoring**
- **Hybrid monitoring**
- **0% monitoring**
- **Short-term Prospective NIS PASS**
- **First choice for most NIS**
- **Retrospective data mining**

First choice for most NIS
References