ISCTM
THE INTERNATIONAL SOCIETY FOR CNS CLINICAL TRIALS AND METHODOLOGY

The Clinical Dilemma:

How to prevent and address the inevitable while addressing important clinical and public health questions.

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Outline

Looking ahead to avoid regret…

- Where to start
  - Document development
  - Trial set up and planning
- Trail conduct
- Ongoing activities

Where to start – Document development

- Protocol generation
  - Minimize participant burden
  - Allow flexibility – visit schedules and visit types
  - Differentiate between stopping study medication and stopping participation in the study
  - Define expectations for participant follow up when study medication is discontinued
  - Define what information will be collected for participants off study medication
  - Include the use of locator agencies as a means of follow up
  - Remove language which encourages discontinuation

Where to start – Document development

- Informed Consent generation
  - Clear expectations for follow up, even after discontinuation of study medication or withdrawal of consent
  - Ensure provisions for contacting other parties for follow up
  - Define alternative contact methods for follow up
  - Include information on the use of locator agencies
  - Provide explanation of what will happen in the event the site closure

Where to start – Trial set up and planning

- CRF design
  - Build in alerts and flags for the study team to receive
  - Consider the addition of intent-to-attend questions
- Training on the importance of missing data
  - All team members

Where to start – Trial set up and planning

- Site feasibility and selection
  - Recent history of enrollment and retention
  - Experience with locator services and utilization of public record data
  - Patient satisfaction scores
- Contracting
  - Site
    - Ensure provision for retention follow up, “Pay-for-performance”
  - Locator agency
  - Retention Committee

Where to start – Trial set up and planning

- Site start up
  - Expectations – if a participant is randomized, they are expected to complete
  - Stress the importance of the informed consent process
  - Training
  - Shift in focus from recruitment to recruitment *and* retention
    - Retention planning from the start

Trial Conduct – What creates missing data?

- Incomplete follow up
  - Adverse event profile
  - Efficacy – positive or negative
  - Rescue medication
  - Participant time constraints
  - Site issues

Trial Conduct – What creates missing data?

- Participants full withdrawal of consent
- Participants becoming lost to follow up

Trial Conduct – How to impact missing data

- Establishment of a good relationship between participant and site
- Make participation convenient
  - Completion of questionnaires via phone, snail mail or email
  - Be sensitive to wait times
  - Schedule visits times which are convenient – early morning, evenings and weekends
- Ensure multiple contacts for participants
  - Family, friends, other health care providers

Trial Conduct – How to impact missing data

- Maintain contact
  - Send reminders – text, email, mail and messages
  - Encourage good treatment compliance
- Minimize disruptions due to staff turnover
  - Need agreements for a minimum notice before staff leaving
  - Train new personnel prior to old personnel leaving
- Effective trial management
  - Support for sites is critical
  - Create dedicated retention team

Trial Conduct – How to impact missing data

- Incomplete follow up
  - Care and support for adverse events and efficacy impact
  - Participant appreciation
  - Ensure completion of trial related activities prior to participants leaving the office
    - Utilize check lists
  - Ensure site obligations

Trial Conduct – How to impact missing data

- Withdrawal of consent
  - Full withdrawal of consent is rare in well conducted trials
  - Site training necessary to ensure an understanding of levels of withdrawal of participation
  - Ensure provisions for withdrawing from study interventions while remaining in the study
  - Utilize a withdrawal of consent checklist

Trial Conduct – How to impact missing data

- Lost to follow up
  - Ensure multiple contacts
    - Check at each visit contacts are current
  - Utilize all other contact mechanisms – alternative contacts, family, employers, hospital or electronic records
  - Utilize publicly available resources
  - Utilize locator agencies

Ongoing activities

Training…..

Tracking…

Intervening

Ongoing activities

- Training on the importance of missing data
  - Everyone on the team needs trained
    - Site personnel
    - Site monitors and other site support
    - Central monitors
    - Data management
    - Medical monitors
  - Frequent, interesting and up to date

Ongoing activities

- Tracking
  - Real time tracking of participants with special attention to any who may be lost to follow up or withdraw consent
    - Utilize alerts
  - Utilize missing visit reports
  - Create algorithm which utilizes site metrics to determine site risk
  - Know where the ‘hot spots’ are
  - Utilize dedicated retention team

Ongoing activities

- Intervening
  - If you track it, be willing to intervene
  - Set algorithm up front so you know what actions will be taken and follow through
  - Interventions will often require additional training

Ongoing activities

Training...

Tracking…

Intervening

Avoiding regret…