Independent Data Monitoring Committee (iDMC) and Role of A Biostatistician

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Outline

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  - Clinical Trial Bodies
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- Role of A Biostatistician
  - As iDMC Chair
  - As iDMC Member
  - As independent Statistician

- Personal Experiences
Independent Data Monitoring Committee (iDMC)

独立数据监测委员会
Names of A Few

- Independent Data Monitoring Committee (iDMC)
- Data Monitoring Committee (DMC)
- Data & Safety Monitoring Board/Committee (DSMB/DSMC)
- Ethical Review Committee (ERC)
- ...
- ...
- Data and Safety Monitoring Committee (DSMC/DSMC)
Why Monitor Trial data?

NIH Policy; ICH E6, E9 Guidelines; FDA/EMA Guidance/Guideline:

• Monitoring trial conduct: progress, performance, and quality - a routine
• Monitoring trial ongoing outcome data
  ✓ Safety - a must!
  ✓ Efficacy
• Pending the size, phase, and potential risk of the intervention, an iDMC may be appointed *

* Often mandated by the FDA a/o NIH/NCI
Clinical Trial Bodies

- Sponsor/CRO
- Investigators
- Trial Coordinator (Lead PI)
- Steering Committee/Policy Board/Executive Committee (SC/PB/EC)
- Independent Data Monitoring Committee (iDMC)
- Data Analysis Center (DAC)
- Endpoint Adjudication Committee (EAC)
- Trial site IRBs
iDMC Components

- iDMC charter
- iDMC membership (expertise, independence, & conflict of interest)
- iDMC roles & responsibilities
- Data Analysis Center (DAC)/independent statistician
- Documents for iDMC (Charter; IB; protocol; tables, figures, MedWatch & CIOMS forms; IA reports)
- Data monitoring plan/guidelines; Statistical Analysis Plan (SAP)
- Meetings (open/closed; scheduled/ad hoc; F2F/TC), quorum, minutes, and recommendations (non-binding)
- Sponsor’s responsibilities
- Termination of iDMC
Role of A Biostatistician
Role of A Biostatistician

As:

- iDMC Chair
- iDMC Member
- Independent Statistician (non-voting)
As iDMC Chair

• Provides leadership to the iDMC. As the primary contact person between the iDMC and Sponsor. Also, to regulatory authorities, as necessary.
• Chairs the iDMC meetings (open, closed, and ad hoc)
• Provides statistical expertise to the iDMC
• Responsible for the closed meeting minutes. Maintains the minutes till the end of the trial.
• As spoke person for the iDMC and delivers iDMC recommendation to the Sponsor

One size fits all – almost!
As iDMC Member

• As the primary contact person between the iDMC and the independent statistician

• Provides statistical expertise to the iDMC. As the spoke person for the iDMC on statistical issues. Assists the iDMC Chair and other members in making sensible decision/recommendation.

• Reviews and comments on meeting minutes

• A key person to be present for maintaining the quorum of the iDMC meetings.
As Independent Statistician

- Independent of the Sponsor, investigators, and iDMC.
- As the bridge between the iDMC and the Sponsor
- Provides safety tables/figures and/or interim analysis reports to the iDMC
- May be present in the closed iDMC meeting for presentation, questioning, and clarification of data.
- Excused when iDMC is making the final vote
Personal Experiences

As:

- iDMC Chair
  - Ph IIb trial – Prophylaxis of VTE after knee replacement surgery
- iDMC Member
  - Ph III trial – Rx for Type II diabetes
  - Ph IIIb trial – Rx for recent onset of symptomatic AF
  - Ph II-III trial – Rx for flat warts
- Independent Statistician
  - Ph III trial – Rx for constipation relief in patients with use of chronic opioids
Remarks

• All trials need a data & safety monitoring plan
• Some may need (or mandate) an iDMC; now the number is ever-mounting
• Plan ahead with written Charter & SOP
• No single statistical rule to be used for decision-making
• Implications of iDMC
  ▪ Independence; confidentiality
  ▪ Trial safety; efficacy
  ▪ Trial quality; integrity; credibility
Decision-making in clinical trials is often complicated and often protracted. ... No single statistical decision rule or procedure can take place of well-reasoned consideration of all aspects of the data by a group of concerned, competent and experienced persons with a wide range of scientific backgrounds and point of view.”
What **Canner** talked about in the 1980’s

“a group of concerned, competent and experienced persons”

was exactly the **iDMC**!
Selected References

- FDA Draft Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees (2005)
- EMEA Guideline on Data Monitoring Committees (2005)
- Ellenberg SS et al. (2002) *Wiley*
- Canner, PL (1981) *Cont Clin Trials*
谢谢各位！