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

Irving K. Hwang, PhD
ICG

The 2011 3rd Annual Meeting of DIA China
Beijing, China
May 16-18, 2011

Outline

- Independent Data Monitoring Committee (iDMC) 独立数据监测委员会
  - Names of A Few
  - Why Monitor Trial Data?
  - Clinical Trial Bodies
  - iDMC Components
- 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) 数据和安全监测委员会
- Ethical Review Committee (ERC)
- …

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

Canner (1981)

"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

- ICH E9 Guidance (1998)
- 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*
- Hwang, IK (1992) Peace ed. *Mercel Dekker*
- Hwang, IK (2005) Buncher & Tsay ed. *Chapman & Hall*
- Canner, PL (1981) *Cont Clin Trials*

谢 谢 各 位 !