An Industry View of FIH Studies: What do we get right and where can we improve?

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● Sarah Robertson is an employee of Vertex Pharmaceuticals Incorporated and may own stock or options in that company.

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Hindsight 20/20
WHAT DO GET RIGHT?
Safety comes first

✓ Risk-based approaches to FIH, not one-size-fits all

✓ Protocols with clear, well-defined dose escalation and stopping criteria on the basis of emerging PK and safety

✓ Strong safety record defining starting doses based on ICH M3(R2)

✓ Sentinel subject dosing, where appropriate
Strong partnership with CRO

✓ PI is well-informed of investigational agent and risks
  • Early review of the IB
  • PI and staff provide input on draft protocol
  • Frank and open communication of anticipated risks

✓ Protocol training, site initiation visits and a LOT of preplanning

✓ Clearly documented roles and responsibilities for decision-making

✓ Candid and frequent dialogue between Sponsor Medical Monitor and PI
Smart study design & conduct

✔ Multi-part studies allow for safe yet expedient development

✔ Innovation in data reporting/analysis + modern bioanalytical methods ensure safe and efficient dose escalation and study progression

✔ Maximize dose escalation in controlled Phase 1 setting to allow for safe dose-ranging in patients in Phase 2
WHAT CAN WE DO BETTER?
**Technology**

- More timely and interactive review of safety data for the Sponsor
- More efficient data collection, cleaning, and reporting

**Biomarkers**

- Identification of therapeutic target and dose escalation based on PD endpoints, not just PK

**Modeling**

- Better use of PBPK and other innovative modeling approaches for clinical PK predictions (moving beyond allometric scaling)
- Modeling approaches for dose escalation decisions, accounting for variability/outliers

**Subjects**

- Better integration of women in FIH
- Earlier exploration of safety, PK, and PD in limited patient cohorts as part of FIH
Foresight 20/20