Experience in Clinical Trials of Chinese Medicine

Seminar on Research and Development of Chinese Medicine 2014
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What kinds of TCM studies have been supported by CTC HKU?
How we conducted TCM clinical studies?
Elements Supporting Clinical Trials

Clinical Trials

Subject Protection
Science
Data Integrity
Methodology used

Conventional Clinical Trial Research Methodology

- Open label / Randomized Controlled
- Single agent / Add-on therapy
- Double / triple blinded
- Prospective
Objectives well set - clinically relevant, valid and reliable measure available

- Only one primary objective
- Secondary objective 1
- Secondary objective 2 or more
Primary Endpoint well set - clinically relevant, valid and reliable measure of the primary objective
Endpoints/Outcome Measures

Some examples on measuring efficacy:

- **Chronic knee Osteoarthritis**
  - Primary: Pain intensity measured by VAS
  - Secondary: Change in WOMAC total score

- ** Decompensated cirrhosis**
  - Primary: Model for End-Stage Liver Disease
  - Secondary: Child-Pugh’s score, CLDQ, EQ5D, SF36

- **Parkinson**
  - Primary: Unified Parkinson’s Disease Rating Scale
  - Secondary: Modified H &Y Scale, S & England Activities of Daily Living Scale, Total daily dose of levodopa prescribed, daily number of “off” hours
Endpoints/Outcome Measures

Safety Outcome Measure: 
*Adverse Events* – defined by ICH guideline E2A & E6

Incidence of adverse events by,
- Serious adverse event (SAE)
- Relationship to study intervention
- Expectedness of event
- Severity of event

A safety management plan:
- Safety specification
- Unblinding
- Monitoring
- Reporting
Safety Measures Used

- Common safety assessments:
  - e.g. physical examinations & vital signs, biochemistry, hematology, urinalysis, ECG / ECHO, pregnancy test

- Active detection of adverse events (solicited & non-solicited)

- Collect information of any concomitant treatments

- For add-on treatment, no co-administration of standard treatment
Data Safety Monitoring Committee reviewed safety data of high risk studies

Independent Members: Clinicians/Experts & Statistician

DSMC would recommend sponsor to continue/modify/terminate the study
Studies were conducted in accordance with the respective protocols, ICH GCP guidelines, standard operating procedures (SOPs) and applicable regulatory requirements.

- Protocol, GCP, SOPs compliance
- Investigational drug accountability
- Site staff training
- Source documentation & data capture
- Site monitoring including source data verification
- Data management
- etc......
What were the challenges during the studies?
Beating the Odds

- pCm placebo without herbal aroma

- pCm placebo absorbed slight aroma of the pCm when stored in a confined area
- Arranged subjects’ visits in different schedule and avoid chance of comparison of trial pCm among subjects

- pCm was accessible from the market. There was a possibility of self-purchase of the trial pCm.

- Named the trial pCm with code but not the product name
- Informed the trial subjects about the ingredients of the active pCm and manufacturing standards but not the brand name or name of the manufacturer/dealer
What are the limitations & challenges ahead?
Limitations & Challenges Ahead

The dose of trial pCm used may not be appropriate for showing the anticipated effects.

The bioactive compounds that account for the therapeutic effects remain unclear.

The conventional dose finding phase 1 study i.e. maximum tolerated dose / optimal biologic dose / pharmacokinetic / pharmacodynamic study.
Limitations & Challenges Ahead

Better understand the efficacy and pharmacological mechanisms

Integrating transcriptional profiling with network-based methodologies for revealing molecular mechanisms of traditional Chinese medicine
L Huang¹, L Jiang¹, Q Kuang¹, M Li¹, Z Wen¹,²*, L He²*

Material Basis of Chinese Herbal Formulas Explored by Combining Pharmacokinetics with Network Pharmacology
Lixia Pei¹,², Yuanwu Bao¹,², Sheng Liu¹, Jin Zheng¹, XiuPing Chen²*
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Limitations & Challenges Ahead

The current systematic conventional clinical trial approach may not be a good way to test TCM which works on ‘syndromes’ rather than ‘disease’

- Inclusion of trial subjects based on western diagnosis and also pattern (syndrome) differentiation in TCM i.e. hot, warm, cool and cold
- Involve TCM practitioner in selection of subjects
While we are focusing subject protection, science, data integrity in conducting TCM clinical trials, the pre-clinical development of TCM in identifying bioactive compound and mode of actions is the key.
Thank you!