

Design Issues of Clinical Trials for Chinese Herbal Medicine

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Chinese Herbal Medicine (CHM) is the practice of selecting combinations of herbs or natural items to reinstall the balance of a diseased body that is viewed as a microcosm interacting continuously and closely with the universe. Unlike the Western concept of medicine that is founded on structured concepts and principles, illnesses and symptoms are considered to be manifestations of imbalance in the flow of cosmic energy related to both internal and external environments. The philosophical frameworks are thus fundamentally different. In order to investigate the efficacy of CHM researchers should take into account of principles accepted by both herbalist and conventional medicine practitioners. The following design considerations for CHM trials will be discussed:

- 1) A pragmatic design on the “practice of CHM” and not just on the herbs or combination will be used, since CHM is not a practice of one drug for one disease.
- 2) Phase I and II studies for determination of safety and dosage may not be appropriate before conducting phase III trials in most circumstances since the knowledge of adverse effects on herbs has been past from one generation to the next and according to the first principle a fixed dosage is not warranted.
- 3) The basic principle of study design, data management monitoring and analysis (according to Good Clinical Practice Guidelines) for randomized phase III study must be closely followed to sustain the scientific merit of the study.
- 4) Randomized phase III study should be double-blind as much as possible to avoid assessment bias since CHM carries a mythical appeal to most patients. A strong element of hope may potentate the placebo effect.
- 5) The blinding process should be designed carefully with properly prepared placebo herbs or combination of herbs that have similar look, smell and taste.
- 6) In CHM, where all natural substances are potentially therapeutic, researcher may face the problem of defining placebo substance(s). The choice of appropriate placebo will be discussed
- 7) Endpoints must be clearly defined because the concept of "therapeutic effect" in CHM and conventional medicine are different.

We will use a phase III randomized, double-blind, placebo-controlled CHM trial carrying out by the Comprehensive Cancer Trials Unit of the CUHK to illustrate the above principles.