



**CGCM 15th Annual Meeting – Taipei
Clinical Investigation I
Cancer, Liver Disease, and Inflammation
Tuesday, August 23, 2016
Time: 14:00 – 16:00 pm**



Chair: Edward Chu (UPCI, USA)
Co-Chair: Shuang-En Chuang (NHRI, Taiwan)

Panelists: Guo-Feng Pan (Capital Medical Univ. Beijing)
Vincent CH Chung (CUHK, Hong Kong)
Chung-Hua Hsu (Taipei City Hospital/National Yang Ming Univ, Taiwan)





Overview: Edward Chu

Talks: 10 oral presentations

(1) Chinese herbal medicine for improving quality of life in non-small cell lung cancer patients: overview of systematic reviews and network meta-analysis

(2) Effectiveness and safety of Chinese herbal medicine for cancer palliative care: overview of systematic reviews and network meta-analysis



(3) Radix astragali-based Chinese medicines and transarterial chemoembolization for intermediate or advanced hepatocellular carcinoma: meta-analysis of randomized controlled trials

(4) Literature review of Chinese medicine used with tamoxifen treatment

(5) Anadamide induced human hepatoma cells death through the DNA damage and apoptosis induction





- (6) Prescription pattern of Chinese herbal products and risk of breast cancer among females with type 2 diabetes in Taiwan: a population-based study**
- (7) Evaluation of *Antrodia cinnamomea* in liver protection effects on irradiation-induced acute hepatitis**
- (8) The traditional Chinese medicine “Kuan-Sin-Yan” improves meridian energy and cancer-related symptoms in advanced colon cancer patients**



- (9) Influence of weight loss on different TCM constitutional types of patients with head and neck cancer who underwent radiotherapy: an observational study**
- (10) Meta-analysis of oxaliplatin-based chemotherapy combined with traditional medicines for colorectal cancer: contributions of specific plants to tumor response**



Reasons and Expectations for TCM Usage

- Desire to improve **quality of life**
- Enhance the **immune** system
- **Relieve symptoms** related to cancer treatment
- Provide hope regarding **treatment outcome**
- Desire for greater control over the medical decision-making process

Challenges/Issues Relating to the Use of TCM and Botanicals

- **Quality control**
 - Multiple herbs are administered together in a given formulation making batch-to-batch standardization difficult
 - Contamination of herbal preparations
- Herbals are essentially black boxes, and their interactions with other prescribed or non-prescribed medications are not known.
- Characterizing **drug-herb interactions** difficult

Issues Relating to the Use of Herbal Therapies: Herb/Drug Interactions

- **St. John's Wort** - Widespread use for mild depression. Induces expression of CYP3A4 liver microsomal enzyme and MDR-1 P-170 expression
 - Reduced plasma levels of SN-38, active metabolite of irinotecan. Effects observed up to 3 weeks after last dose
 - Increased plasma clearance of HIV drugs, indinavir and nevirapine, resulting in lower drug levels
 - Lower levels of cyclosporine A in transplant patients
 - Alters warfarin metabolism
- **Ginkgo biloba, Ginseng, Garlic, and Kava** interfere with metabolism and/or efficacy of approved drugs

Challenges/Issues Relating to the Use of Herbal Therapies

- Herbal medicines **should not be assumed to be benign** products. Adverse effects are now well-described, including HSRs, liver toxicity (autoimmune hepatitis), and coagulopathy
- Complementary approaches may represent **confounding variables** that could affect the interpretation of clinical results of clinical trials.
- Significant financial cost to the use of herbals and CAM.

Challenges/Issues Relating to the Use of Herbal Therapies

- **Perception / skepticism of Western** physicians to potential role of herbal medicines in treatment of human diseases
- Main focus of Western medicine has been on **reductionist single molecule** approach to therapy as opposed to **polychemical** approach

PHY906 Clinical / Translational Research Project

- **NCI-PO1: Chinese Herbal Medicine as a Novel Paradigm for Cancer Chemotherapy**
- **Collaboration between Yale Cancer Center and UPCI**
- **Yung-chi Cheng, PhD (PI)**
- **Edward Chu, MD (Co-PI)**
- **Hongyu Zhao, PhD**

- **Represents bench to bedside to bench translation**



PHY906 Clinical / Translational Research Project

- P01: Three Research Projects
 - **Clinical Study of PHY906**, a Novel Chinese Herbal Medicine, as a Modulator of Irinotecan Chemotherapy (Edward Chu, MD)
 - Characterization of Predictive **Biomarkers** for the Clinical Efficacy of PHY906 (Yung-chi Cheng, PhD)
 - **Bioinformatic** Characterization/Analysis of Translational Biomarkers (Hongyu Zhao, PhD)



UPMC LIFE CHANGING MEDICINE

PHY906

- Traditional Chinese botanical formulation composed of four main herbs – Huang Qin Tang (HQT)
- Used in Asia for a variety of gastrointestinal ailments (**diarrhea, nausea/vomiting, and abdominal cramps**) since 300 AD



Scutellaria
baicalensis



Glycyrrhiza
uralensis



Paeonia
lactiflora



Ziziphus jujube

Lessons Learned Relating to the Use of PHY906: Pre-Clinical

- **Quality control and standardization** of Chinese herbal medicine are essential before proceeding to clinical trials.
- In vivo **pre-clinical studies** to establish efficacy, safety profile, and dosing schedule
(**知其然**: First, ID what TCMs 100% work for what diseases/conditions)
- **PK profiling** is critical as parent formulation and metabolized form may be different
- Investigate potential **mechanisms of action** using systems biology approach
(**知其所以然**: For further improvement)

Lessons Learned Relating to the Clinical Studies of PHY906

- Use of high quality **cGMP** herbal medicine
- Careful design of **clinical trials** with well-defined endpoints to determine effect of herbal medicine, including placebo-controlled arm
- Incorporation of **validated QOL** instrument tools
- Design clinical studies with translational **PD** biomarkers
- Comprehensive **bioinformatic** analysis critical to identifying clinically relevant PD biomarkers and potential bioactive component(s)
(**and/or by using connectivity map?**)

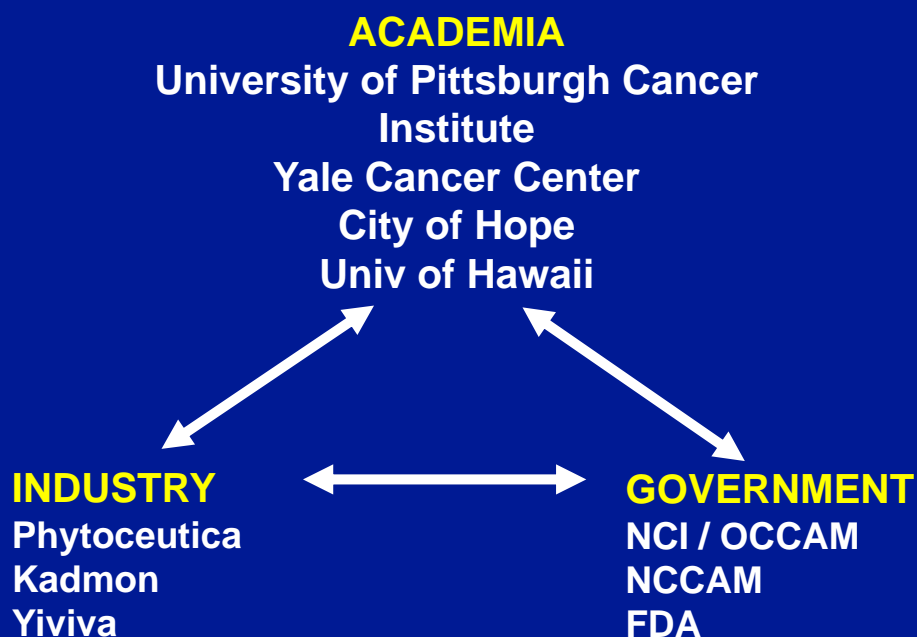
Lessons Learned Relating to the Clinical Development of PHY906: Practical Issues

- Need to carefully consider patient population
 - 1st-line mCRC
 - 2nd-line mCRC
- Clinical practice standards may change during course of study
- **Competing** clinical studies testing novel genome-driven targeted agents and immunotherapies
- **Regulatory issues** (IND, FDA, institution IRB)

Lessons Learned Relating to the Clinical Studies of PHY906

- Need to identify consistent source of cGMP material and ensure capabilities of manufacturer
- Coordination of multi-center clinical trials with oversight of data management, regulatory issues, and reporting to FDA
- Financial support of clinical trial (NCI, institution, pharma sponsor)

Lessons Learned: It Takes a Village



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Patients and their families/caregivers