Abstract Submission for Global Cardio-Oncology Summit 2016

Title: Identifying research-practice gaps for mapping research priorities in response to clinical cardiotoxicity induced by targeted anticancer therapeutics

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Dysregulated kinase signaling molecules identified in cancers are thought to be attractive therapeutic targets for cancer therapy. Some have been developed as druggable targets for anticancer therapy (designated as "targeted therapy"). A primary goal of targeted therapy is to kill cancer cells more specifically, but this hope has been unreality manifested as many unanticipated toxicities on multiple organs/tissues, although these newer drugs have revolutionized the treatment of a group of cancers. Clinical cardiotoxicity remains the most serious complication, reflecting new challenges because the new clinical entity is clinically and mechanistically different from the cardiotoxicity resulting from traditional chemotherapeutic agents. Many mechanistic principles underpinning the cardiotoxicity remain to be elucidated. There are some common mechanisms that underlie the toxicity**:** on- and off-target effects, others (production of toxic metabolites, harmful immune responses, idiosyncratic). Identifying research**–**practice gaps is the first step of medical innovations, and research priorities are defined in line with this concept. Off-target and other toxic effects might be minimized or overcome by advanced pharmacological research**.** While on-target toxicity represents an intrinsically ingrained research**–**practice gap in relation to the problematic specificity of "cancer-specific signaling molecules" as drug targets. It is gaining realization that there are numerous overlapping signaling pathways of driving tumorigenesis but also essential for normal cardiac function - a main cause of on-target effects. Unfortunately, these molecular pathways are often targeted in the modern treatments of cancers (molecular targeted therapies). From a biological perspective, cardiotoxicity would be inevitable (theoretically) as long as a targeted kinase is functionally expressed in the heart. Kinase family is believed as the cornerstone of molecular targets for anticancer drug development (pharmacological innovations). Thus, it is crucial to identify research priorities to meet the growing challenges. This presentation will address some research priority areas in relation to the clinical and fundamental challenges in predicting and managing of targeted therapeutics-induced cardiotoxicity.