CITC Organ Toxicities Panel: Cardiac Toxicity

Shari L. Targum, M.D., M.P.H., F.A.C.C., F.A.C.P.

Associate Director for Biosimilars

Division of Dermatology and Dental Products/CDER/FDA

Impact of Drug-Associated Cardiac Toxicity

- Serious, life-threatening events
- Potential exposure of subjects/patients to unnecessary risk
- Withdrawal from market of several noncardiac drugs because of cardiac risk

Clinical Presentation	Associated Drug
Ventricular arrhythmia (Torsade de Pointes)	Terfenadine
Valvular heart disease	Dexfenfluramine
Myocardial infarction	Rofecoxib
Pulmonary hypertension	Dexfenfluramine, amphetamine
Cardiomyopathy	Anthracyclines, trastuzumab

Signal detection/risk management

- Helpful to understand mechanism
- Best if detected early in development
- Strategies include:
 - nonclinical screening, risk biomarkers (detection)
 - dose and/or population selection, use of other medications to reduce risk (management)
- Emergence of "cardio-oncology" field