



**CARDIAC SAFETY**  
RESEARCH CONSORTIUM

# **Detection, Assessment and Risk Mitigation of Cardiac Safety Signals in Oncology Drug Development**

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October 25 2017

# Disclosure

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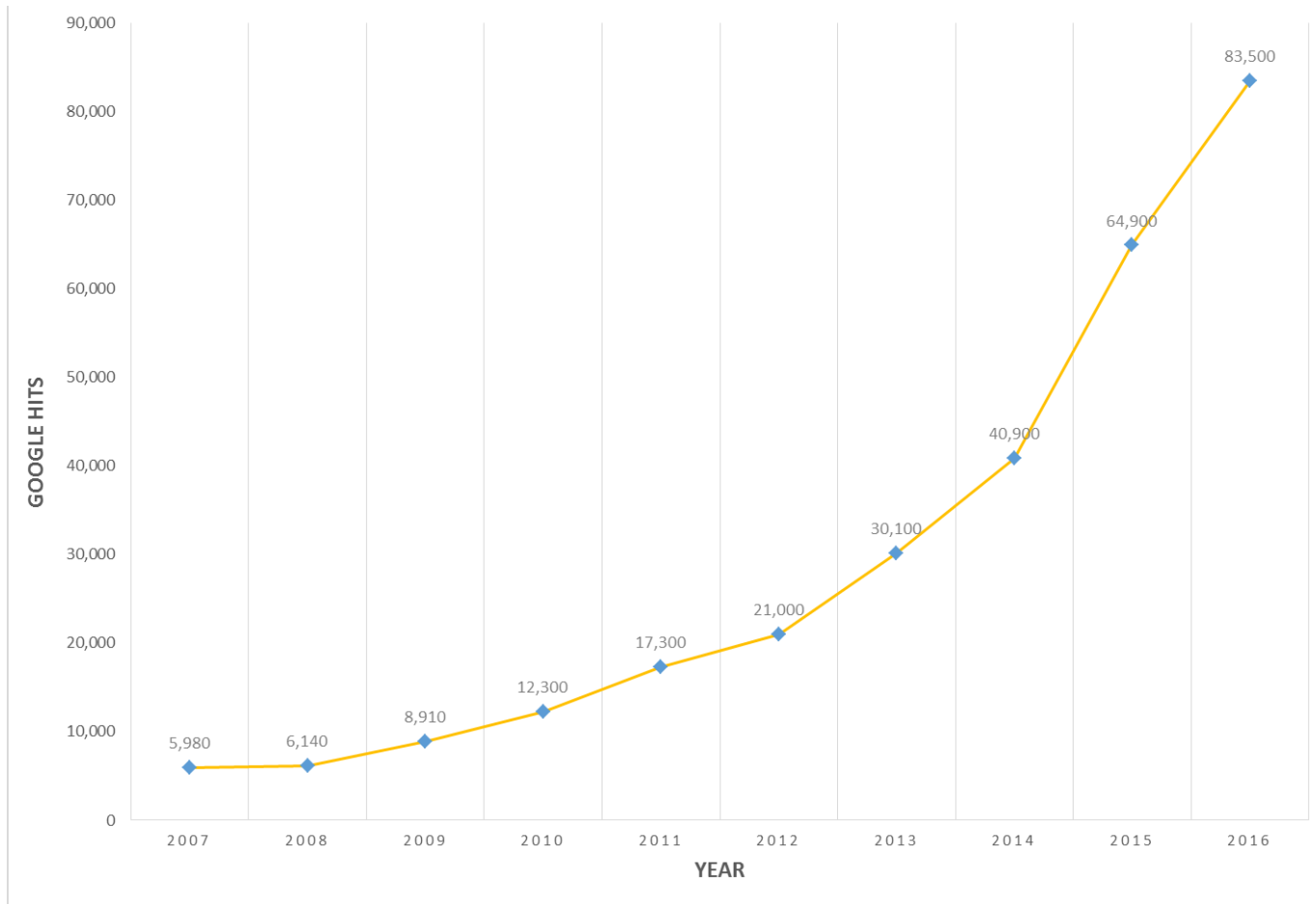
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ACI Clinical specializes in providing independent endpoint adjudication committees (EAC/CEC) and data monitoring committees (DMC) services.

Financial Disclosures related to ACI Clinical:

**<http://www.aciclinical.com/about-us/disclosure/>**

# Cardio Oncology Google Hits Per Year



# CO $\alpha$ GH

- QT
- CHF
- Hypertension/Heart Rate
- Arrhythmia

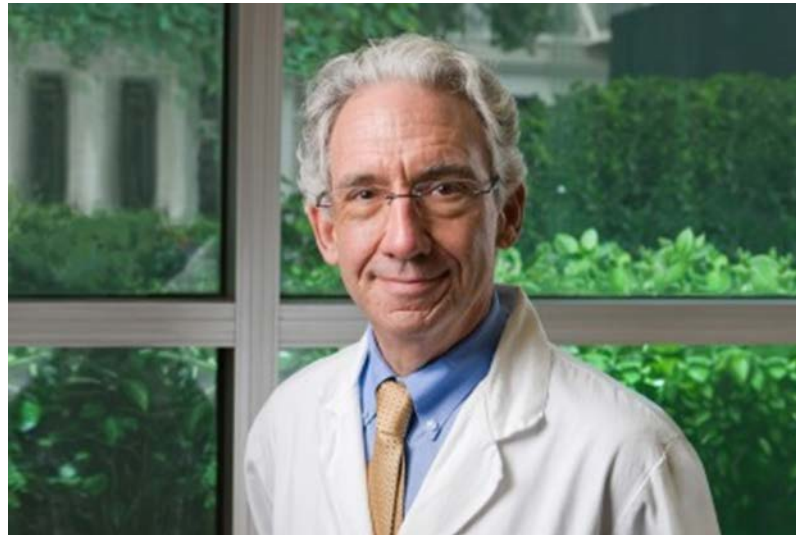




# 2017 MSK Cardio-Oncology Symposium

Cardiovascular Health and Disease  
During and After Cancer Therapy

Friday-Saturday, May 12-13, 2017



# Cardiac Safety in Oncology Drug Development

- What can we do to prevent untoward CV events?
- How do we evaluate potential CV events?

Chemotherapy Agents	Left Ventricular Dysfunction	Ischemia	Hypertension	Venous Thromboembolism	Bradycardia	QT Prolongation
Alkylating Agents	Yes	No	No	Yes	No	No
Angiogenesis Inhibitors	No	No	No	Yes	Yes	No
Anthracyclines	Yes	No	No	No	No	No
Antimetabolites	Yes	Yes	No	No	No	No
Antimicrotubule Agents	Yes	Yes	No	No	Yes	No
Histone Deacetylase Inhibitor	No	No	No	Yes	No	Yes
Miscellaneous	No	No	No	No	No	Yes
Monoclonal Antibody-Based TKI	Yes	Yes	Yes	No	No	No
Proteasome Inhibitor	Yes	No	No	No	No	No
Small Molecule TKI	Yes	Yes	Yes	Yes	No	Yes

# Thank You: Members of the Planning Committee

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**Anupam Agarwal**

**Corina Dota**

**Gary Gintant**

**Manish Gupta**

**Gretchen Kimmick**

**Bob Kleiman**

**Luana Pesco Koplowitz**

**Chiari Melloni**

**Boaz Mendzelevski**

**Eric Michelson**

**Melissa Nelson**

**Dakshesh Patel**

**Curtis Rambaran**

**Matthew Roe**

**Philip Sager**

**Jonathan Seltzer**

**Richard Steingart**

**Colette Strnadova**

**Shari Targum**

**Rick Turner**

**Polina Voloshkko**

**Tetsuro Wakatsuki**

**Baichun Yang**

# Agenda

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Session I: Translational medicine and non-clinical signals of potential cardiac toxicity

Session II- Specific CV issues in Oncology Development

Session III: Assessment of CV Signals

Session IV: Balancing CV risk vs benefit in Oncology Drug Development



# Meeting Goal: Recommend Best Practices

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- **Detection:**

- Robust and consistent monitoring system to distinguish between treatment induced CV events treatment-independent CV events

- **Assessment:**

- Event causality based on pre-clinical and patient risk
- Should there be Standard definitions for CV events
  - FDA standard definitions vs CTCAE terminology
  - Adjudication when indicated

- **Mitigation:**

- What are appropriate trial designs
- What are appropriate controls

# Meeting Overview

## ■ Short provocative presentations

- Presenters have promised to stay within their allotted time limit 😊
- End of Session Discussant will summarize major points
- Moderated Discussion to follow

## ■ Robust discussion time

- Discussion is key– AUDIENCE PARTICIPATION IS CRUCIAL
- Multiple viewpoints
- Taken in the order self-identified
  - Speakers: Please flip name cards
  - Audience: Please approach microphone

## ■ Goal

- Discussion to air various and conflicting viewpoints
- Areas of Consensus will be summarized
- Publication committee will author document for AHJ

# Housekeeping

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- **Breaks: mid-morning, lunch, mid-afternoon**
  - Breaks are in the lobby
- **Wi-Fi is available**
- **Please silence phones**

# Thank You

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Session #1: Translational medicine and non-clinical signals of potential cardiac toxicity

***Luana Pesco Koplowitz, MD, PhD***