Hong Kong College of Cardiology

Cardio-Oncology 2020: Opportunities and Challenges

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Immediate Past President American College of Cardiology
Q.E. and Sally Russell Professor of Cardiology
Indiana University School of Medicine

Indiana University Health

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Disclosures

- Cadent: DSMB
- Cook Medical: Clinical Events Committee
- Eli Lilly: Consultant
- ERT: Consultant
- Prilenia: Consultant

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How the road looked in 2018:

- Long
- Many Intersections
- Potholes and bumps

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Cardio Oncology 2020

Opportunities

- Established as a discipline with forum for exchange of ideas.
- Cross-cutting scientific interest
- Large unmet clinical need

Challenges

- Number of new therapies
- Shift from "reactive" to "pro-active" assessment of safety for new therapy
- Disparate data standards
- Working in the Covid era

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Introducing

JACC CardioOncology

Online, Open Access
Launching September 2019

Bonnie Ky, MD, FACC
Editor-in-Chief

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Submissions: JACCSubmit-CardioOncology.org

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LEADERSHIP PAGE

Cardio-Oncology

Stronger Together

Richard J. Kovacs, MD, FACC, *President, American College of Cardiology*
Howard A. Burris III, MD, FASCO, *President, American Society of Clinical Oncology*

Cardiology and Oncology are specialties at an intersection. Both specialties have made enormous strides in the past 50 years in helping patients live longer and fuller lives. Mortality rates for cardiac disease have declined dramatically over that period (1). There are now 15 million cancer survivors in the United States alone, and that number is projected to exceed 20 million by 2026 (2). Diseases

Our patients need us. Patients with cardiac disease who develop cancer, cancer patients with cardiovascular complications, and the caregivers for these patients all face major challenges. Any illness is accompanied by questions, worry about the future, and need for trusted clinicians to help navigate the patient and family through the maze that is modern medicine. Illness that requires multiple specialty cli-

Longitudinal Care Driven By Evidence-Based Pathways

Prior to Cancer Therapy
Identify high CV risk patients; Mitigate CTX risk; Inform cancer treatment

During Cancer Therapy
Monitoring to identify CTX; Avoid dose interruptions; Prevent CV events

After Cancer Therapy
Survivorship; Decrease risk of late CV events; Improve long-term health

Need to improve upon CV screening methods and develop strategies to identify high risk patients

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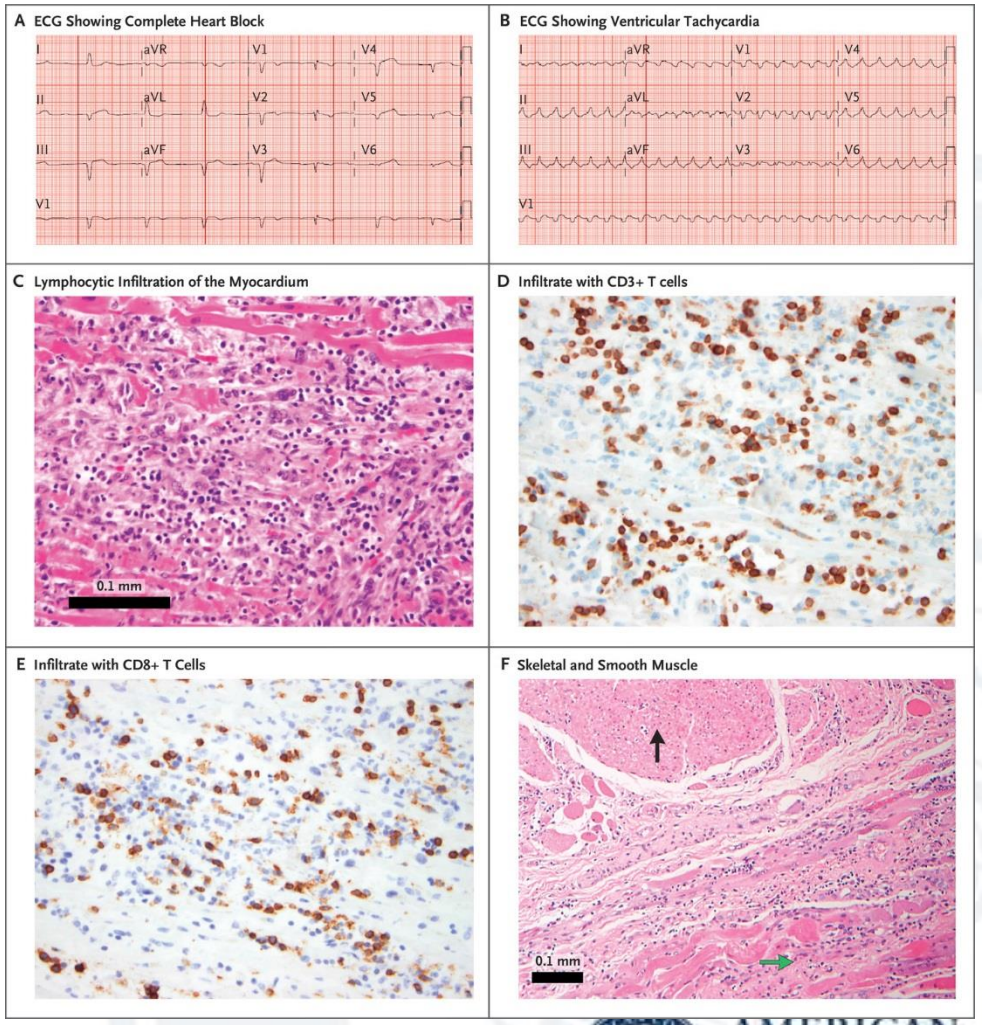
The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Fulminant Myocarditis with Combination Immune Checkpoint Blockade

Douglas B. Johnson, M.D., Justin M. Balko, Pharm.D., Ph.D., Margaret L. Compton, M.D., Spyridon Chalkias, M.D., Joshua Gorham, B.A., Yaomin Xu, Ph.D., Mellissa Hicks, Ph.D., Igor Puzanov, M.D., Matthew R. Alexander, M.D., Ph.D., Tyler L. Bloomer, M.D., Jason R. Becker, M.D., David A. Slosky, M.D., Elizabeth J. Phillips, M.D., Mark A. Pilkinton, M.D., Ph.D., Laura Craig-Owens, M.D., Nina Kola, M.D., Gregory Plautz, M.D., Daniel S. Reshef, M.D., M.P.H., Ph.D., Jonathan S. Deutsch, M.D., Raquel P. Deering, Ph.D., Benjamin A. Olenchock, M.D., Ph.D., Andrew H. Lichtman, M.D., Dan M. Roden, M.D., Christine E. Seidman, M.D., Igor J. Koralnik, M.D., Jonathan G. Seidman, Ph.D., Robert D. Hoffman, M.D., Ph.D., Janis M. Taube, M.D., Luis A. Diaz, Jr., M.D., Robert A. Anders, M.D., Jeffrey A. Sosman, M.D., and Javid J. Moslehi, M.D.



Johnson DB et al. N Engl J Med 2016;375:1749-1755.

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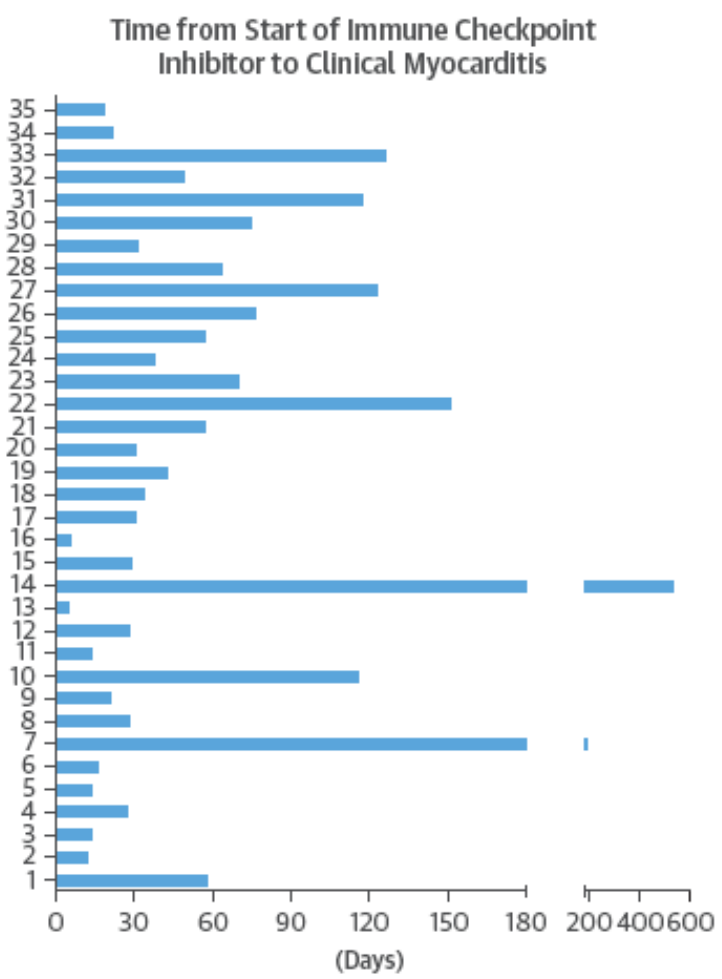
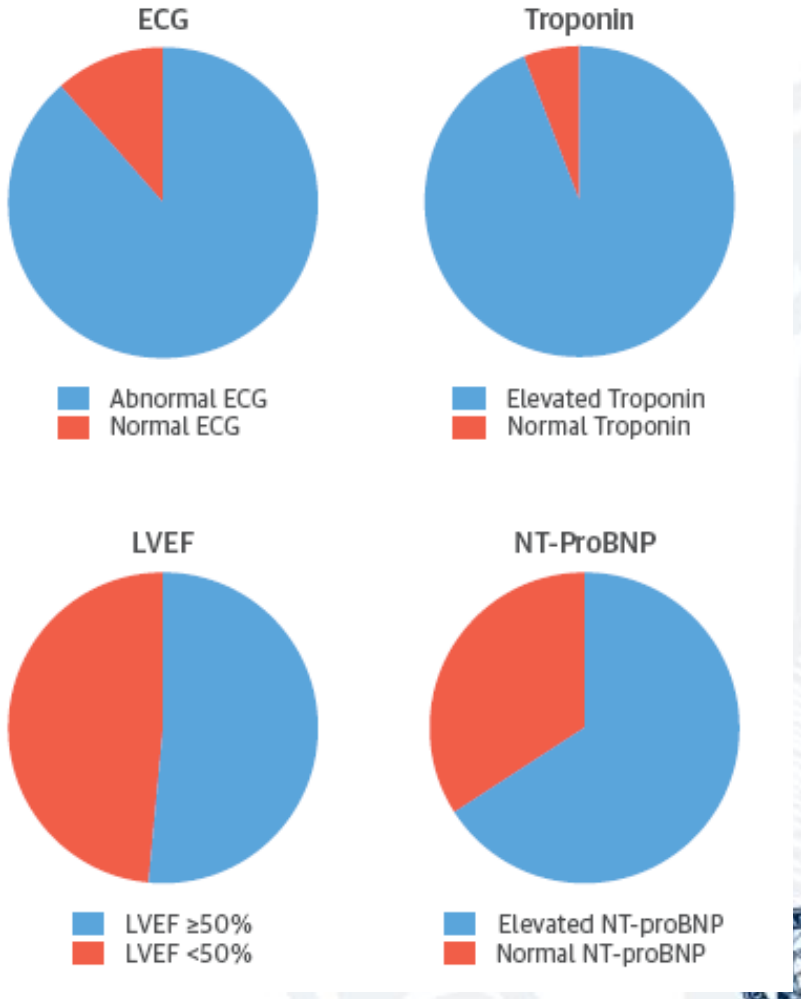
Typical Presentation of Immunotherapy Myocarditis





Mahmood, et al. JACC. 2018.

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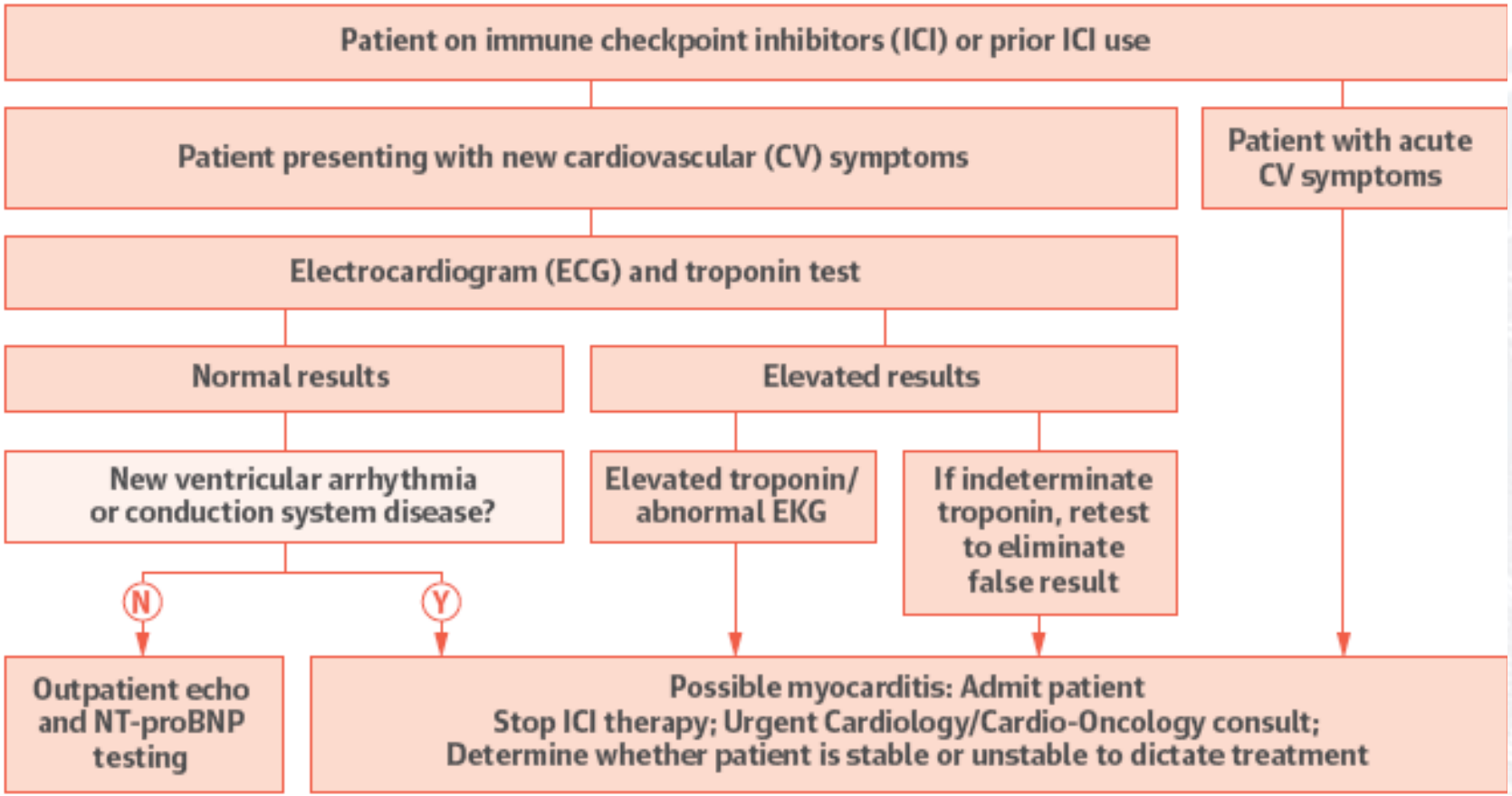
Diagnostic Algorithm: 2018



Mahmood, et al. JACC. 2018.

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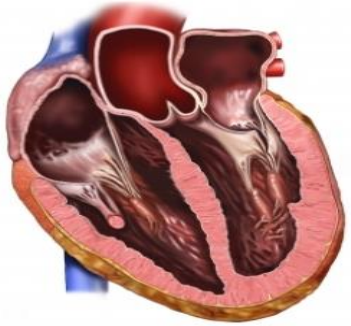
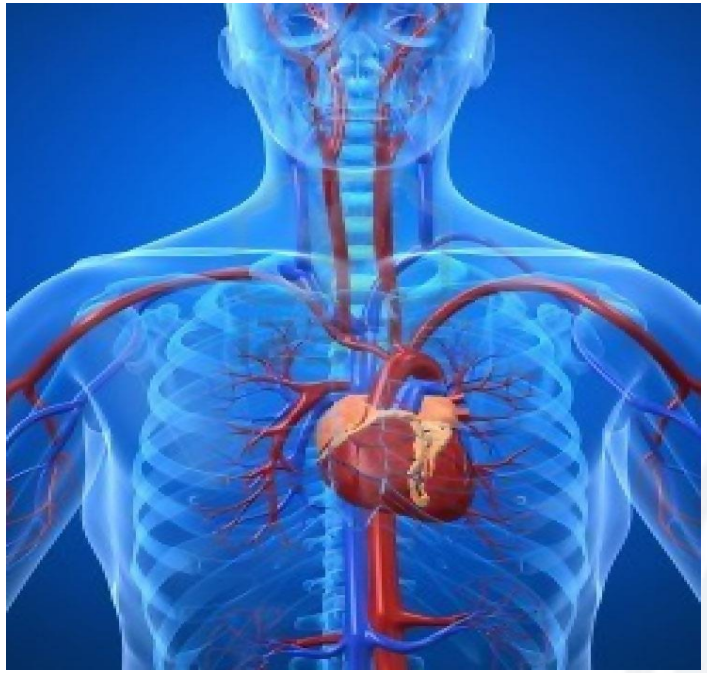
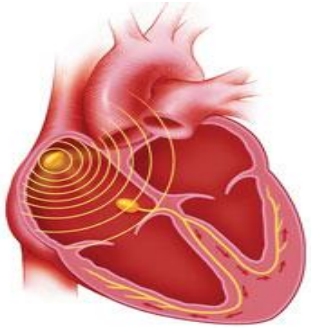
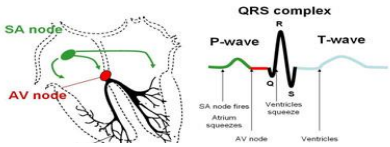
There are Multiple Ways Cancer Therapies Affect the CV System



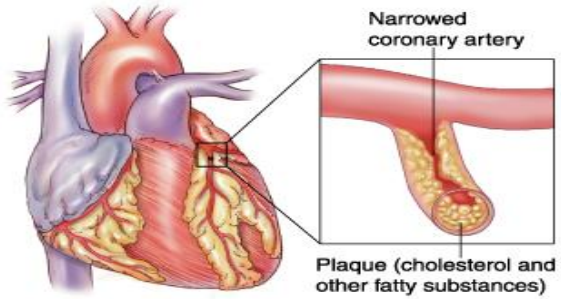
Heart Failure with reduced or preserved ejection fraction, Valvular disease, Pulmonary hypertension, Pericardial disease



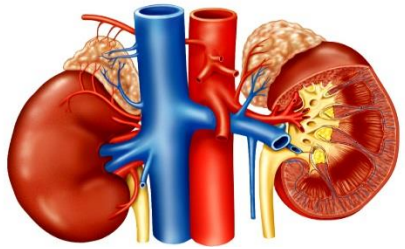




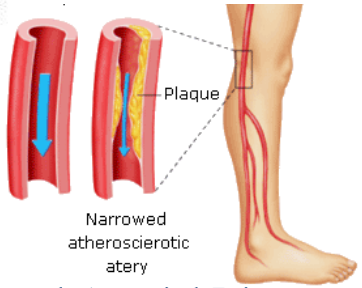
Arrhythmia
Long QT



Atherosclerosis, Coronary Vasospasm, Dyslipidemia



Hypertension



Peripheral Arterial Disease

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Circulation

AHA SCIENTIFIC STATEMENT

Cardiovascular Disease and Breast Cancer: Where These Entities Intersect

A Scientific Statement From the American Heart Association

ABSTRACT: Cardiovascular disease (CVD) remains the leading cause of mortality in women, yet many people perceive breast cancer to be the number one threat to women's health. CVD and breast cancer have several overlapping risk factors, such as obesity and smoking. Additionally, current breast cancer treatments can have a negative impact on cardiovascular health (eg, left ventricular dysfunction, accelerated CVD), and for women with pre-existing CVD, this might influence cancer treatment decisions by both the patient and the provider. Improvements in early detection and treatment of breast cancer have led to an increasing number of breast cancer survivors who are at risk of long-term cardiac complications from cancer treatments. For older women, CVD poses a greater mortality threat than breast cancer itself. This is the first scientific statement from the American Heart Association on CVD and breast cancer. This document will provide a comprehensive overview of the prevalence of these diseases, shared risk factors, the cardiotoxic effects of therapy, and the prevention and treatment of CVD in breast cancer patients.

Laxmi S. Mehta, MD, FAHA, Chair
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Vera Bittner, MD, MSPH, FAHA
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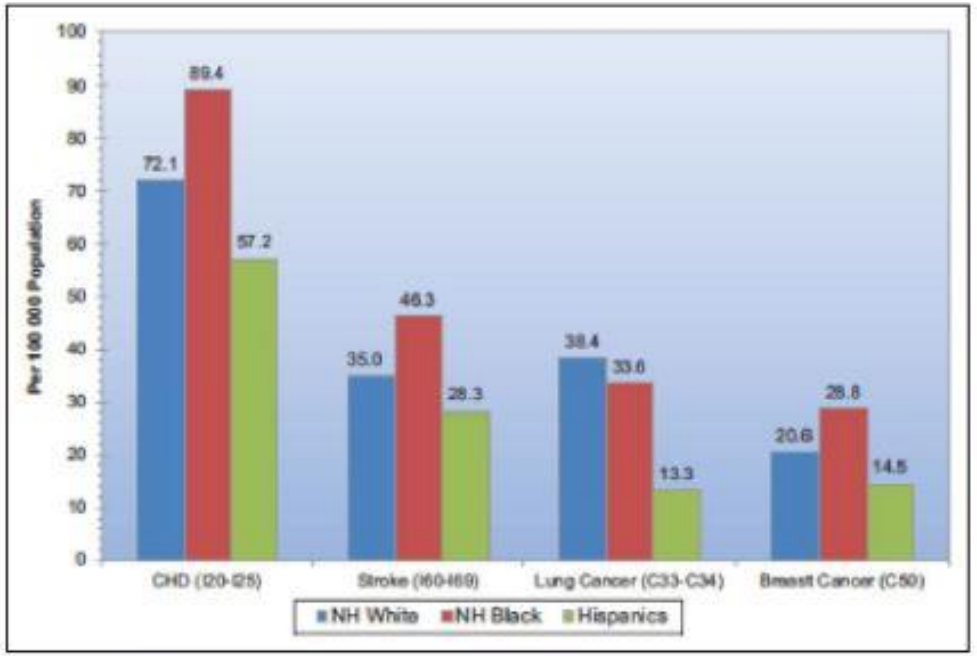
Tochukwu Okwuosa, DO
Ileana L. Piña, MD, MPH, FAHA
Annabelle Santos Volgman, MD, FAHA



Circulation

Mehta LS et al. Circulation, Feb 1, 2018 e-pub

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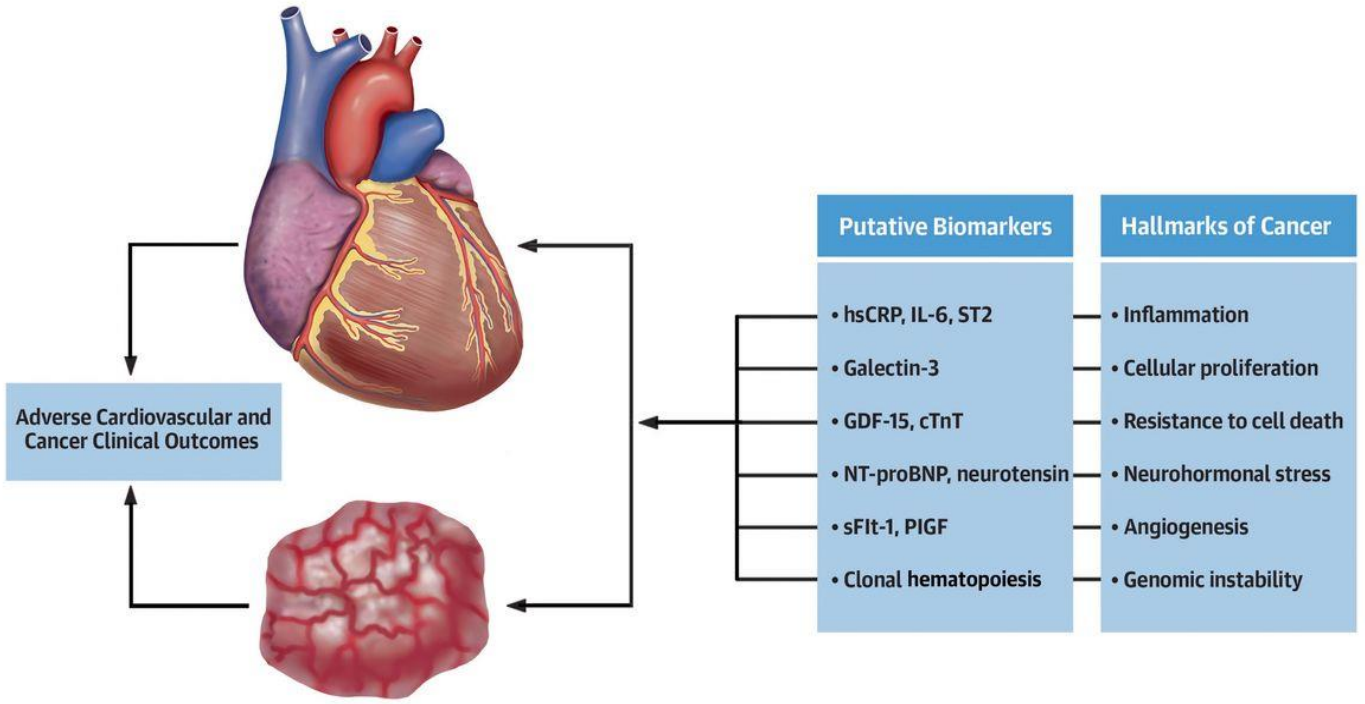
Mechanistic Similarities Between Cardiovascular Disease and Cancer

CENTRAL ILLUSTRATION: Shared Pathophysiological Mechanisms Between Cardiovascular Disease and Cancer



Narayan, V. et al. J Am Coll Cardiol. 2020;75(21):2726-37.

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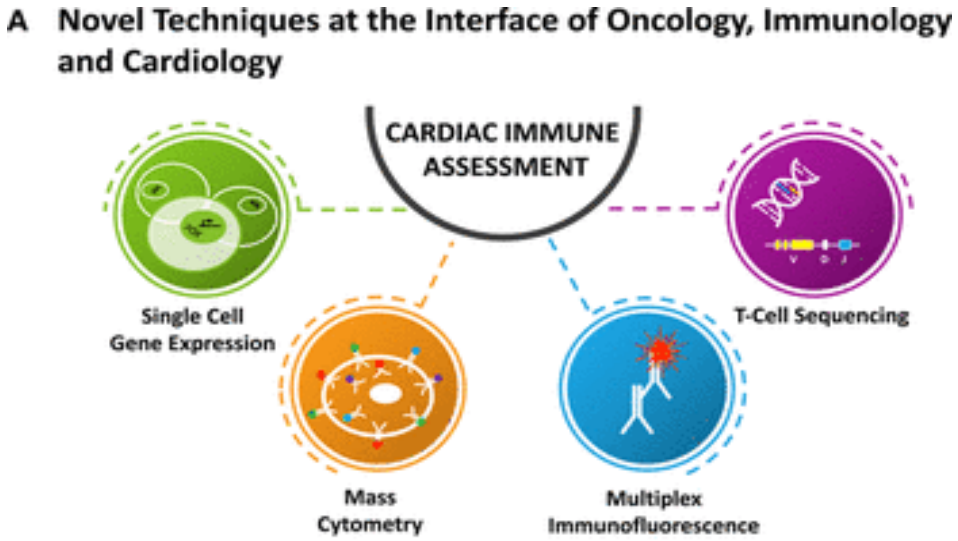
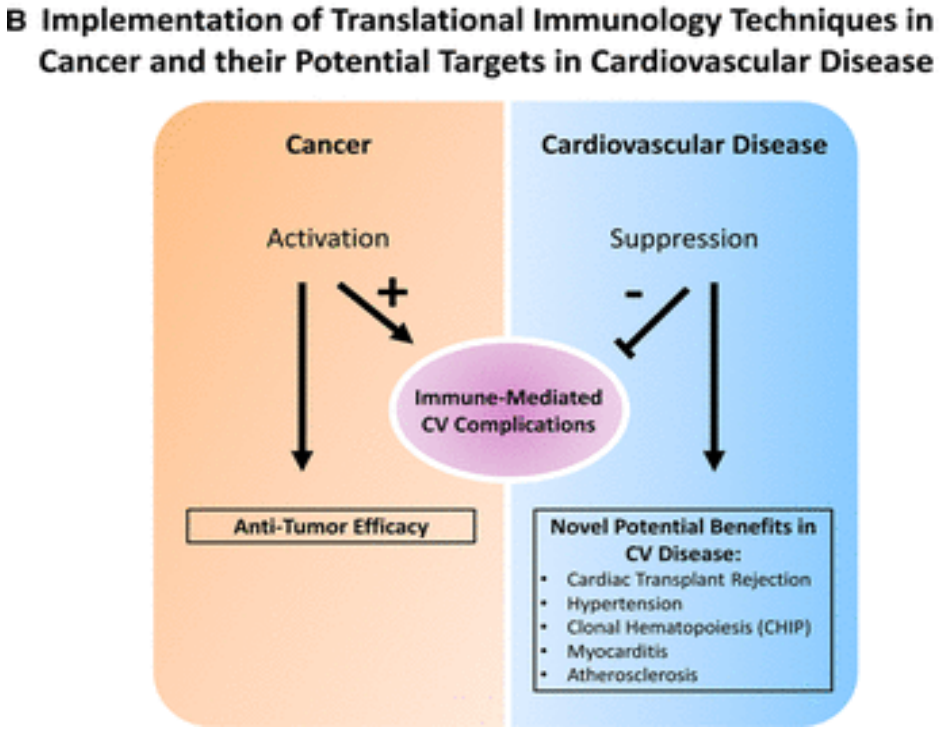
Opportunity for Cross-cutting Translational Science





Vlad G. Zaha. Circulation. Cardio-Immuno-Oncology, Volume: 141, Issue: 2, Pages: 87-89, DOI: (10.1161/CIRCULATIONAHA.119.042276)

Celebrate Progress

- World-wide expansion of clinical programs.
- Exponential increase in publication on the subject.
- Recognition of need for collaboration.

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Four Challenges to Consider "On the Road"

- Large volume of therapies in the pipeline.
- Shift from reactive to proactive safety assessment.
- Disparate data standards.
- Working in the Covid era.

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Cancer immunotherapy-based combination studies underway in 2016

A dramatic and unprecedented increase in clinical cancer immunotherapy combination studies (across Phase I, II and III trials) has occurred in recent years. The studies in this figure represent many of the current studies that include a PD-L1/PD-1 pathway inhibitor in combination with other immune modulators, targeted therapy, chemotherapy and/or radiation therapy. These studies are designed to characterize the efficacy, safety and biology related to combinability, synergy or antagonism associated with these combinations. Adapted from Vanessa Lucey of the Cancer Research Institute.

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Cardiac Safety Research Consortium

AHJ August 2019

Assessing cardiac safety in oncology drug development

Jonathan H Seltzer, MD, MBA, MA,[a] Gary Gintant, PhD,[b] Laleh Amiri-Kordestani, MD,[c] Jack Singer, MD,[d] Luana Pesco Koplowitz, MD, PhD,[e] Javid J Moslehi, MD,[f] Ana Barac, MD, PhD,[g] and Anthony F. Yu, MD[h]

The Cardiac Safety Research Consortium (CSRC; www.cardiac-safety.org) held a Think Tank on "Detection, Assessment, and Risk Mitigation of Cardiac Safety Signals in Oncology Drug Development" on October 24-25,

such as hypertension, venous and arterial thromboembolic events, peripheral artery disease, pulmonary hypertension, vasospasm, proteinuria, accelerated atherosclerosis, and metabolic derangements. There are also cardiac toxic effects

ESC European Society of Cardiology

European Heart Journal (2020) **0**, 1–12
doi:10.1093/eurheartj/ehaa006

CLINICAL RESEARCH
Heart failure/cardiomyopathy

Classification, prevalence, and outcomes of anticancer therapy-induced cardiotoxicity: the CARDIOTOX registry

José López-Sendón[1]*, Carlos Álvarez-Ortega[1], Pilar Zamora Auñon[1], Antonio Buño Soto[1], Alexander R. Lyon[2], Dimitrios Farmakis[3,4], Daniela Cardinale[5], Miguel Canales Albendea[1], Jaime Feliu Batlle[1], Isabel Rodríguez Rodríguez[1], Olaia Rodríguez Fraga[1], Ainara Albaladejo[1], Guiomar Mediavilla[1], Jose Ramón González-Juanatey[6], Amparo Martínez Monzonis[6], Pilar Gómez Prieto[1], José González-Costello[7], José María Serrano Antolín[8], Rosalía Cadenas Chamorro[9], and Teresa López Fernández[1]*; on behalf of the CARDIOTOX Registry Investigators

[1]University Hospital La Paz, UAM, IdiPaz, CiberCV, CiberONC, Paseo de la Castellana 261, Madrid 28046, Spain; [2]Royal Brompton Hospital and Imperial College, Cardiology, London, United Kingdom of Great Britain and Northern Ireland; [3]University of Cyprus Medical School, Nicosia, Cyprus; [4]Heart Failure Unit, Department of Cardiology, Athens University Hospital Attikon, National and Kapodistrian University of Athens, Athens, Greece; [5]Cardioncology Unit, European Institute of Oncology, I.R.C.C.S, Milan, Italy; [6]University Hospital of Santiago de Compostela, Cardiology, CiberCV, Santiago De Compostela, Spain; [7]University Hospital of Bellvitge, Cardiology, Barcelona, Spain; [8]University Hospital of Fuenlabrada, Cardiology, Fuenlabrada, Spain; and [9]University Hospital Infanta Sofia, Cardiology, San Sebastián de los Reyes-Madrid, Spain

Received 4 June 2019; revised 18 September 2019; editorial decision 9 January 2020; accepted 13 January 2020

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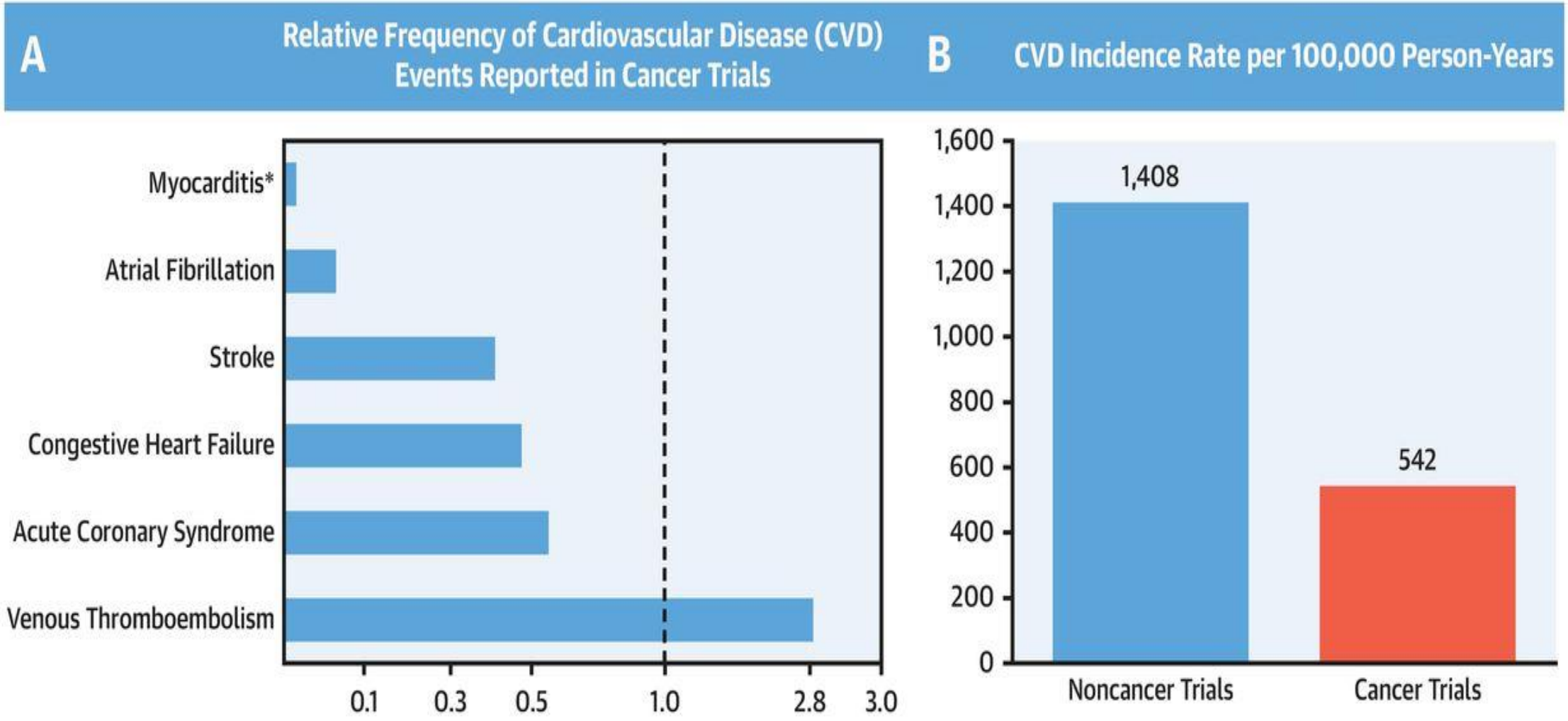
CENTRAL ILLUSTRATION: Cardiovascular Events in Pivotal Cancer Trials



Bonsu, J.M. et al. J Am Coll Cardiol. 2020;75(6):620-8.

Consistent Evaluation of New Therapies

- Model on ICH E14 process put in place to assess the pro-arrhythmia effects of non-anti arrhythmia drugs

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CSRC Meeting & CSRC Think Tank: Detection, Assessment and Risk Mitigation of Cardiac Safety Signals in Oncology Drug Development

Posted on November 29, 2017

Integrated Cardiac Monitoring

Serial Cardiac Serum Biomarkers:

- Troponin I
- Brain Natriuretic Peptide (BNP)
- C-reactive Protein
- Cystatin C

Structure/Function:

- Chamber dimensions (atrial and ventricle dilatation/hypertrophy)
- Valvular function (mitral, aortic, tricuspid, pulmonic)

Electrophysiology:

- Rhythm
- QRS
- QR
- PR
- RR
- QTc

Hemodynamics:

- Blood Pressure
- Left Ventricular Ejection Fraction
- Right Ventricular (RV) Systolic Pressure

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Comprehensive Cardiac Safety Assessment for Cancer Treatments

Cardiovasc Toxicol
DOI 10.1007/s12012-014-9297-4

Cardiac Safety of TGF-β Receptor I Kinase Inhibitor LY2157299 Monohydrate in Cancer Patients in a First-in-Human Dose Study

Richard J. Kovacs · Giuliana Maldonado · Analia Azaro · Maria S. Fernández · Federico L. Romero · Juan M. Sepulveda-Sánchez · Mary Corretti · Michael Carducci · Melda Dolan · Ivelina Gueorguieva · Ann L. Cleverly · N. Sokalingum Pillay · Jose Baselga · Michael M. Lahn

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Examination	Pre-study (days)		Cycle 1 (days)			Cycle 2 - onward (days)		
	14	7	1	12±2	26±2	1	12±2	26±2
Vital Signs (Blood Pressure and Heart Rate)	X		X	X		X	X	
Echocardiography/Doppler (after Cycle 2: every 2 cycles)	X				X			X
CT Scan of the Aorta (after Cycles 3: every 2 cycles)	X				X			X
ECG	X		X	X	X			X
Troponin I + BNP		X			X			X
hs-CRP		X			X			X
Cystatin C		X		X	X		X	X

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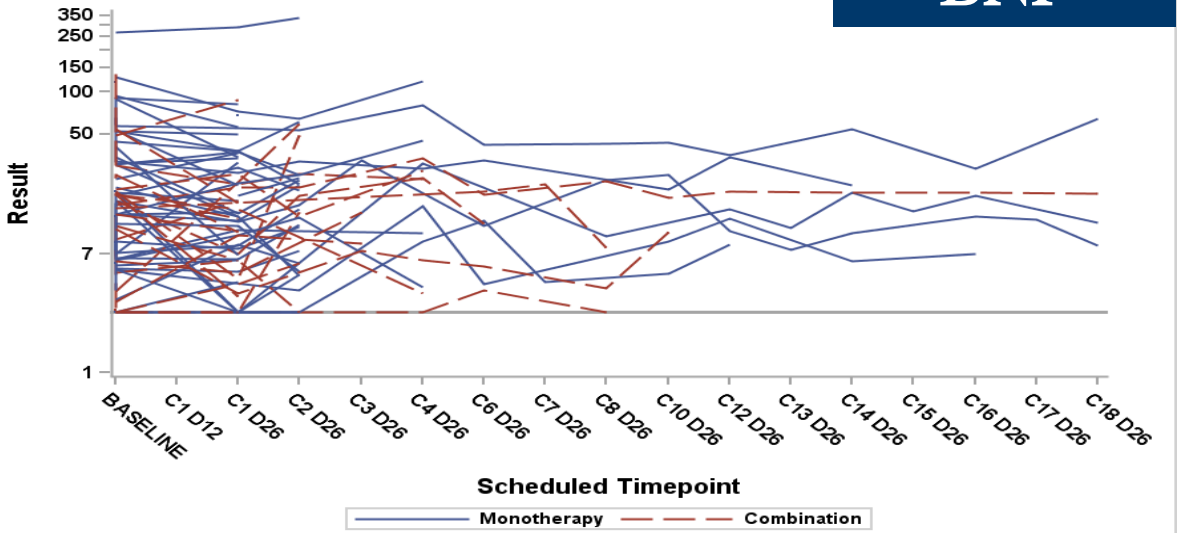
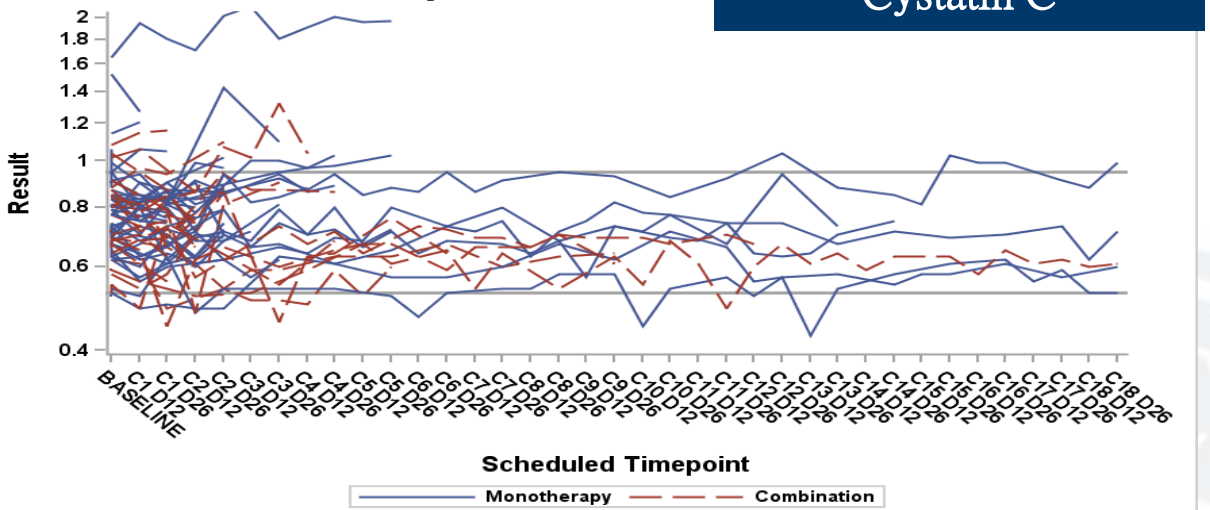
BNP



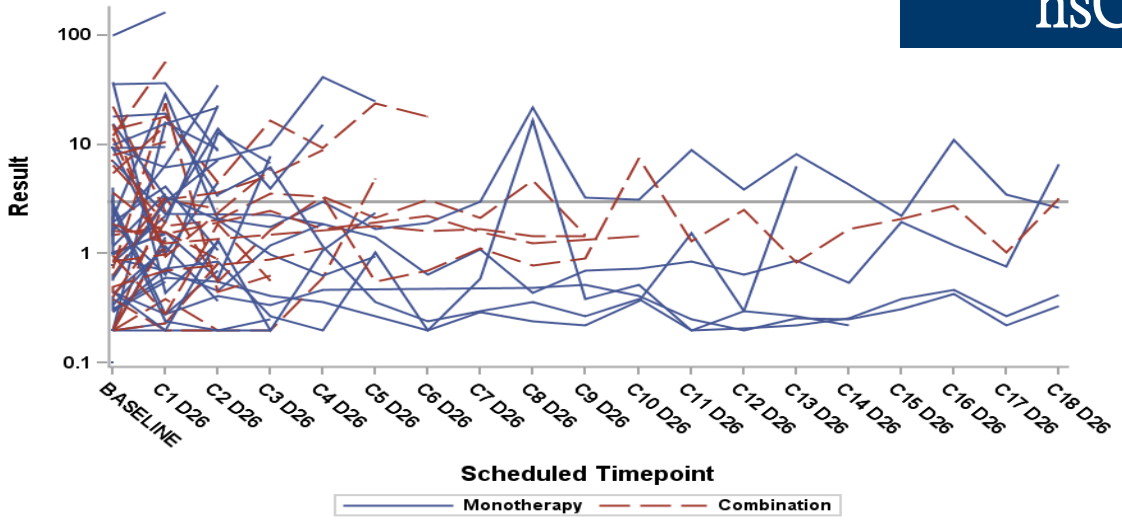
Note: The horizontal line on the plot represents the lower normal limit.

Cystatin C



Note: Subect 4011 result of 0.05 at Cycle 4, Day 12 has been omitted from this figure.
Note: The horizontal lines on the plot represents the upper and lower normal limit.

hsCRP



Note: The horizontal line on the plot represents the upper normal limit.

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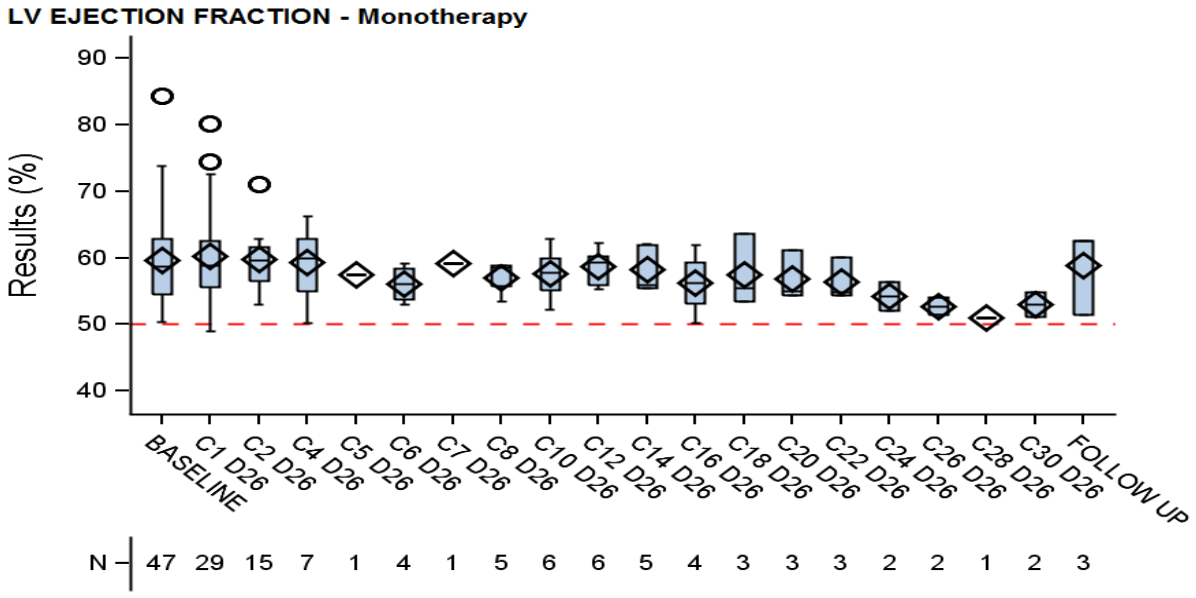

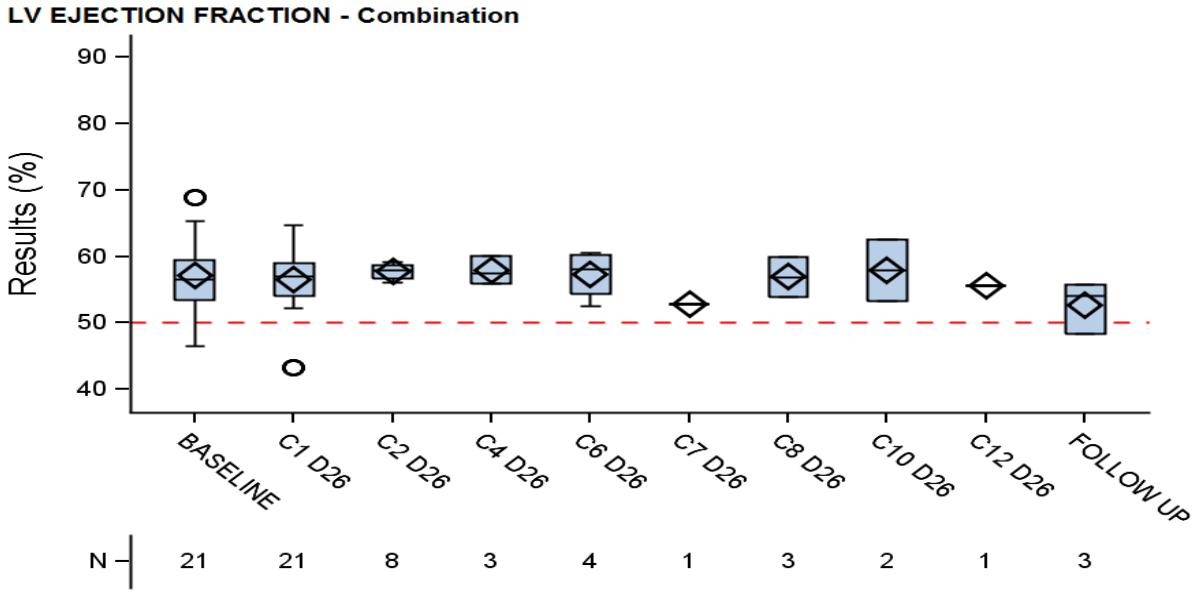

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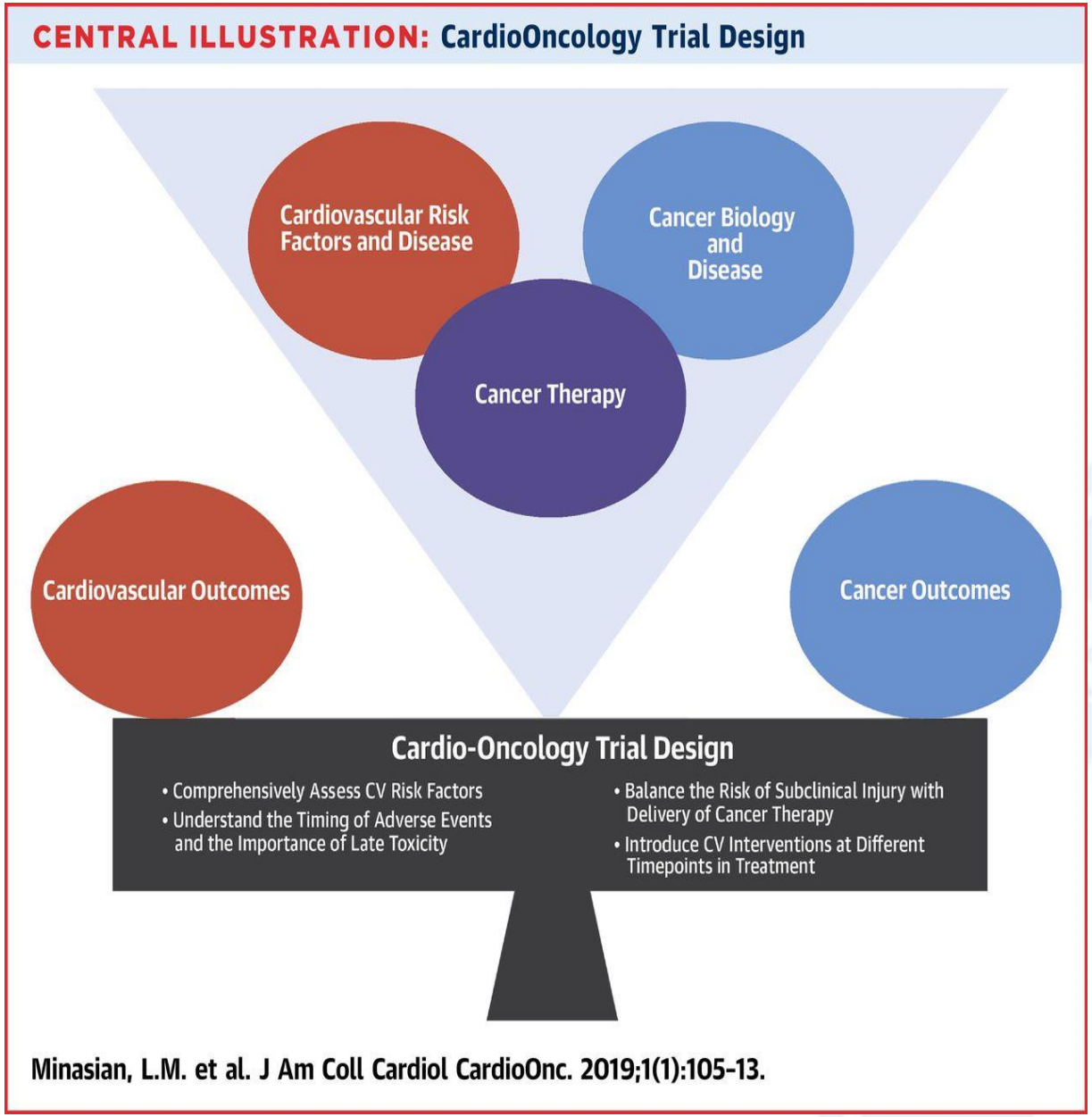

Lori M. Minasian et al. J Am Coll Cardiol CardioOnc 2019;1:105-113

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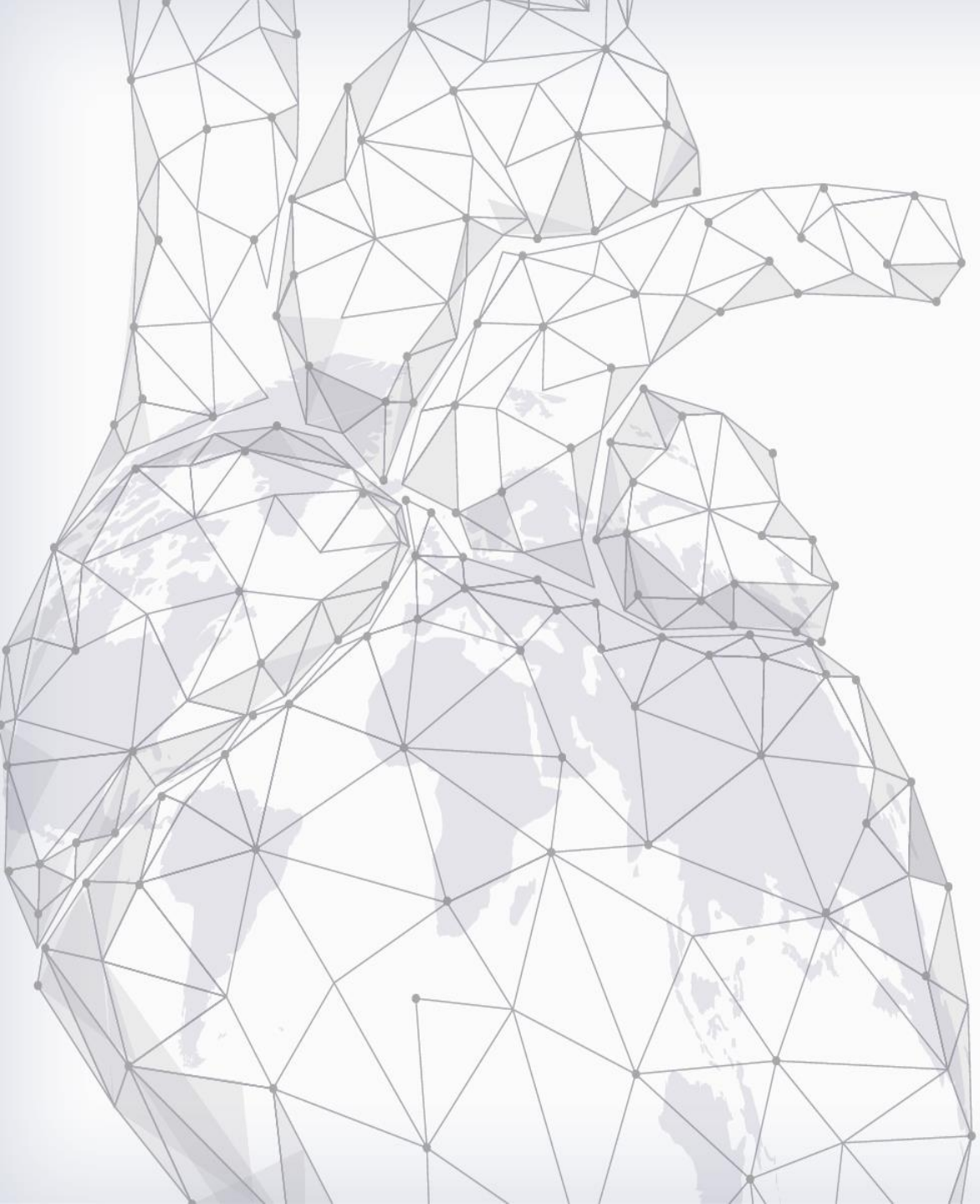

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The ACC Vision

A world where **innovation** and **knowledge** optimize cardiovascular care and outcomes.

Digital Transformation and ACC

Digital Cardio-Oncology

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ACC Digital Transformation

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ACC Digital Vision Statement

*Create and cultivate a **digital-first ecosystem** to provide **trusted**, **timely**, and **tailored** **knowledge** and **tools accessible** across all touchpoints of CV care delivery*

Digital Transformation

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Application of Digital Technology

- Pattern Recognition
- Digital Biomarkers
- Computational Phenotyping

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SaMD: Software as a Medical Device

"A SaMD best described as software that utilizes an algorithm (logic, set of rules, or model) that operates on data input (digitized content) to produce an output that is intended for medical purposes…"

https://www.fda.gov/media/100714/download

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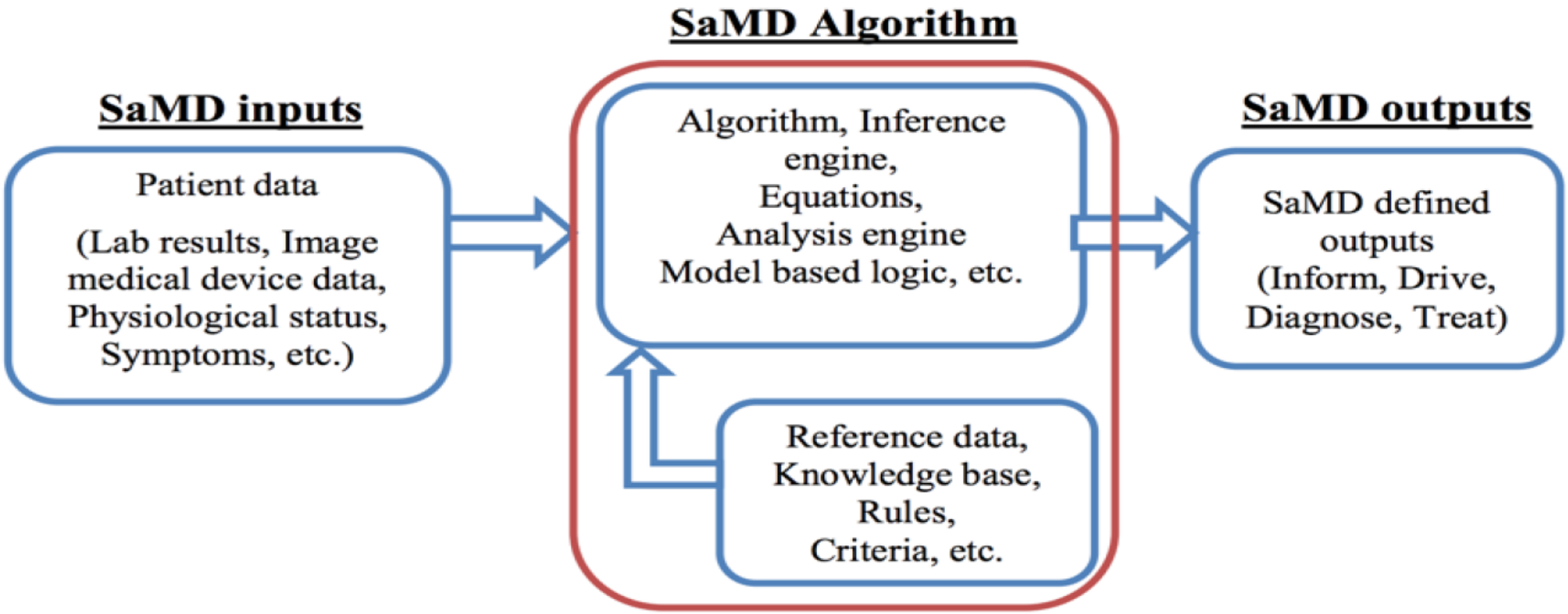
The Opportunity



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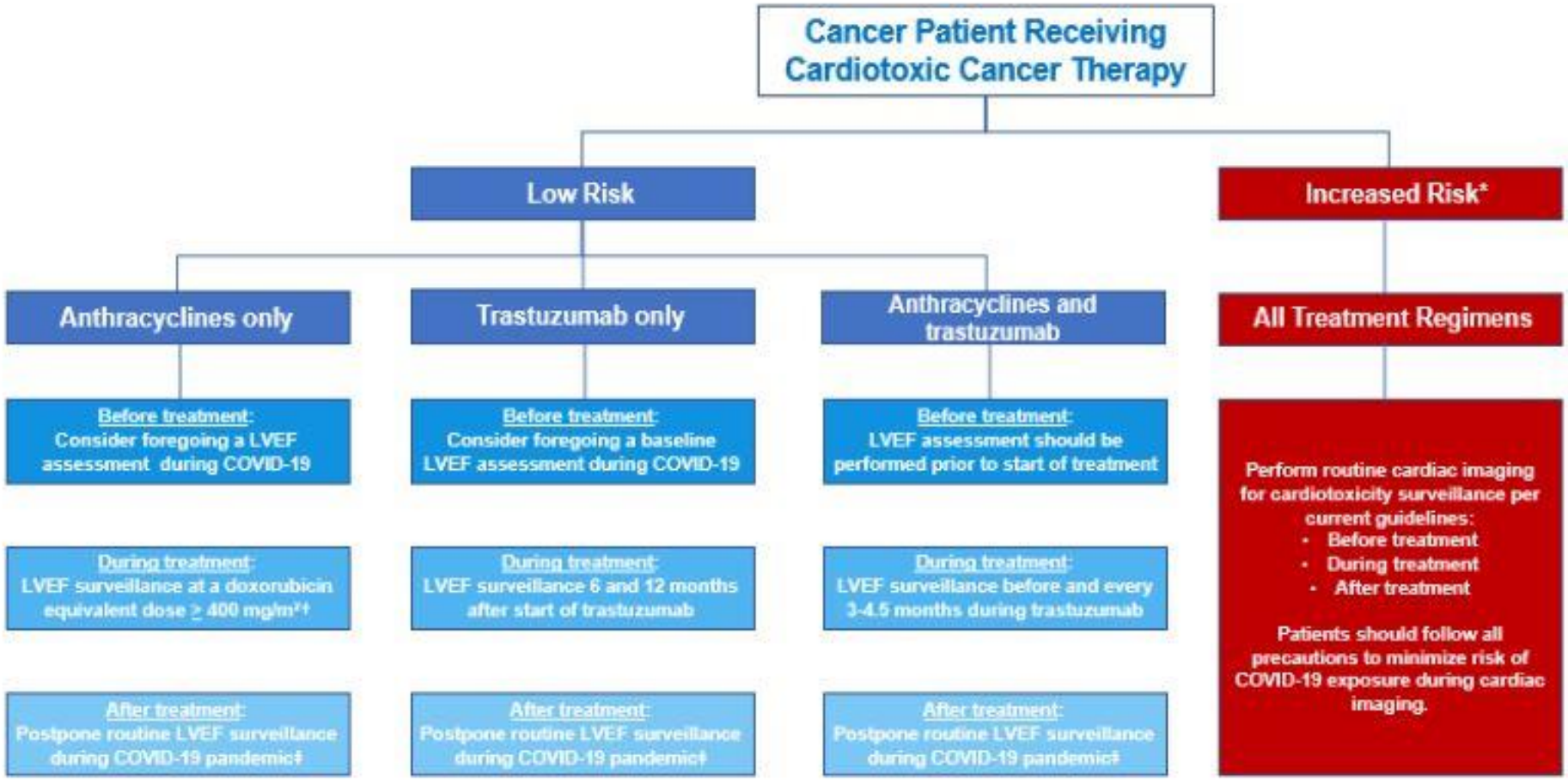
Delivery of Cardio-Oncology Care During the COVID-19 Pandemic

Jun 22, 2020 | Anthony F. Yu, MD, FACC; Michelle N. Johnson, MD, MPH, FACC; Richard M. Steingart, MD, FACC; Jennifer E. Liu, MD, FACC

Delivery of Cardio-Oncology Care During the COVID-19 Pandemic

Jun 22, 2020 | Anthony F. Yu, MD, FACC; Michelle N. Johnson, MD, MPH, FACC; Richard M. Steingart, MD, FACC; Jennifer E. Liu, MD, FACC

Figure 1: A Proposed Algorithm for Modified Cardiotoxicity Surveillance of Patients With Breast Cancer During the COVID-19 Pandemic



Cardio Oncology 2020

- Much has been done.
- The pace of change is rapid.
- Opportunity to become the first digitally transformed subspecialty.

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