

# Getting risk stratification right: the clinical perspective

Teresa López-Fernández, FESC  
La Paz University Hospital, IdiPAZ, Madrid  
20 January 2025



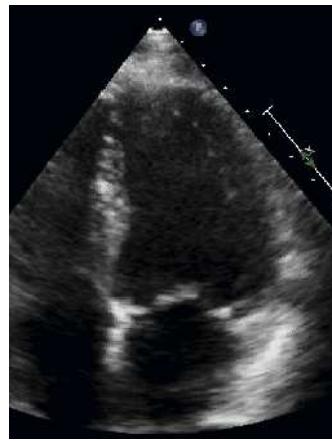
# • **Disclosures**

Speaker and advisory board fees: Philips, Myocardial Solutions, Johnson & Johnson, Astra Zeneca, Lilly, Pfizer, Accord, Nordicpharma not related with this presentation

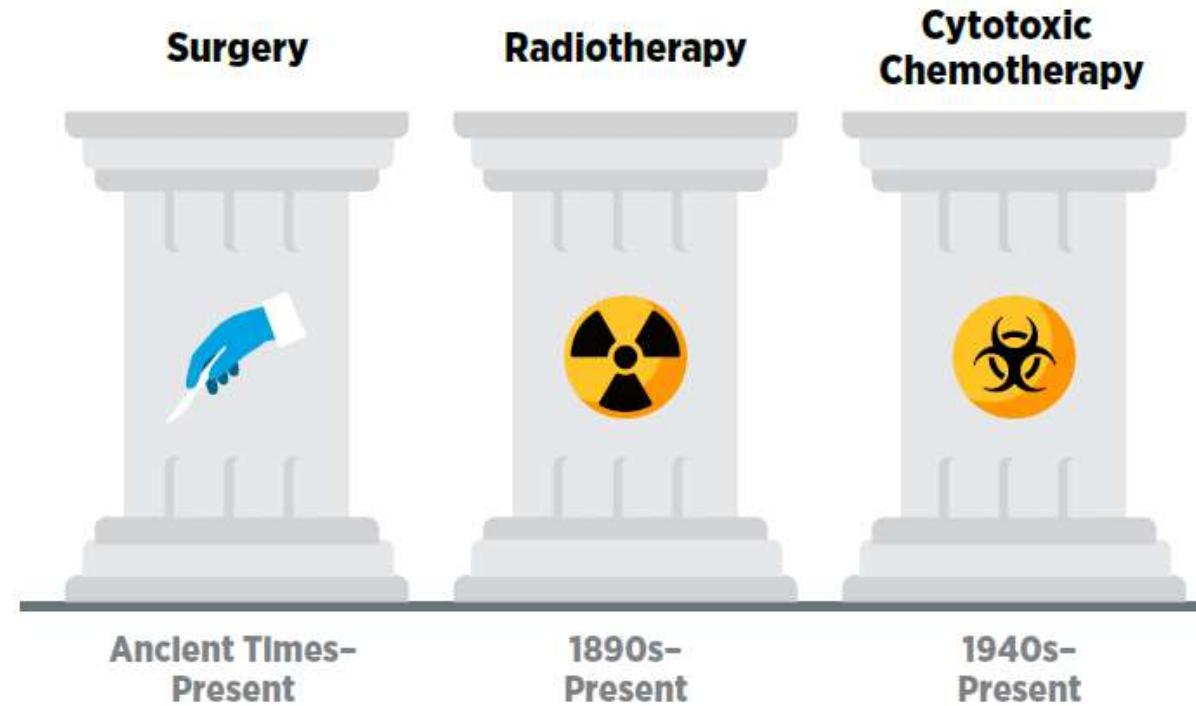
# • Legacy approach: LVEF-based stratification



>50%

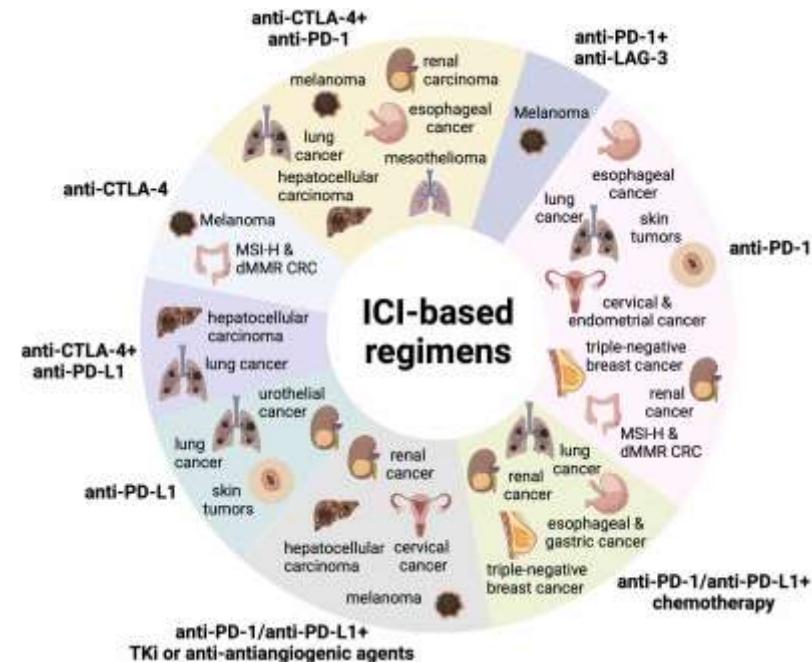


<50%

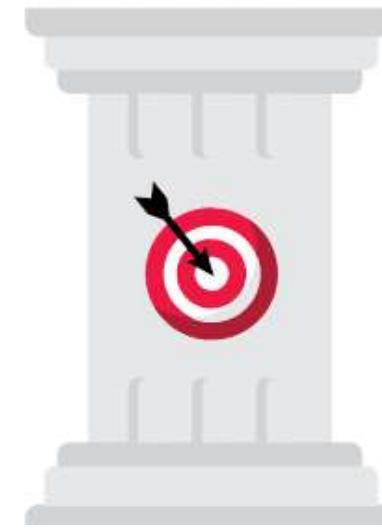


AACR Cancer Progress Report 2024

# The new era of cancer care



## Molecularly Targeted Therapy



Siegel et al., CA Cancer J Clin 2025 Jan-Feb;75(1):10-45; Tonorezos et al. Journal of the National Cancer Institute, 2024  
 Cerella C et al. Pharmacol Res. 2023 Oct;196:106914.

# The CTR-CVT landscape has changed



2022 ESC Guidelines on cardio-oncology. European Heart Journal (2022) 43, 4229–4361

# • What defines CTR-CVT risk?

## Clinical cases

#1

### 53-year-old man

- Bicuspid aortic valve (AVA 0.6cm<sup>2</sup>/m<sup>2</sup>)
- **2024 Locally advanced NSCLC (IIIB) EGFR +**
- **LVEF 65%**

#2

### 44-year-old women

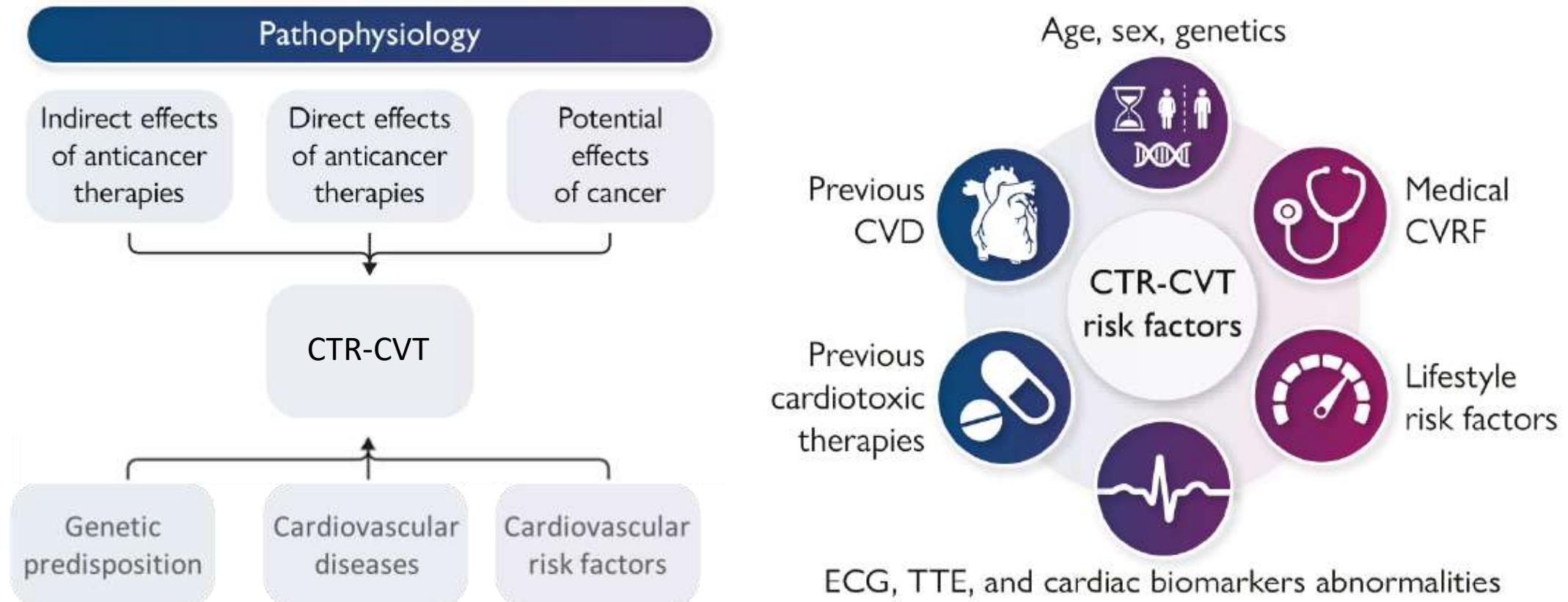
- Hodgkin lymphoma at age 17: ABVD + RT
- **2024 Triple-negative breast cancer**
- **LVEF 53%**

#3

### 62-year-old women

- 2004 CML Ph+
  - *Imatinib*
  - *Nilotinib*
  - *Dasatinib*
  - *Bosutinib*
  - 2024 Asciminib
- **LVEF 56%**

# What defines CTR-CVT risk?



Rakisheva A. et al Eur J Heart Fail. 2025 Nov;27(11):2084-2099.

# HFA-ICOS risk score

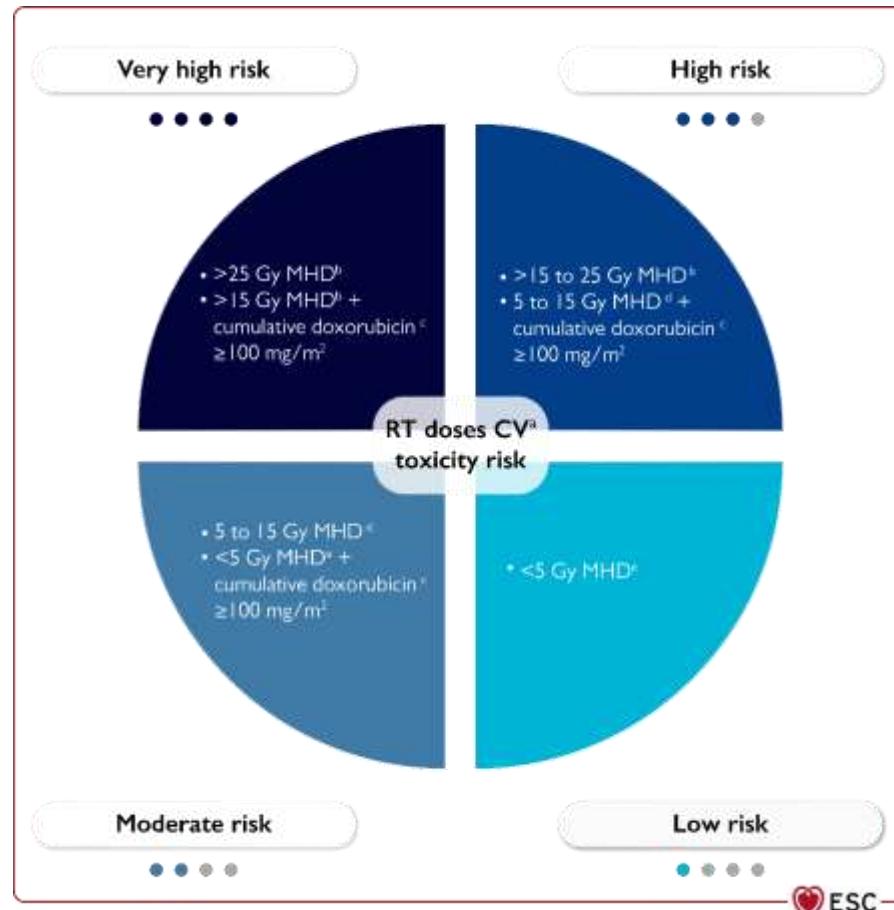
Risk factor	Score	Current cancer treatment regimen	
		Includes anthracycline before HER2-targeted therapy	Medium <sup>1f</sup>
<b>Previous CVD</b>			
HF or cardiomyopathy	Very high	Prior trastuzumab cardiotoxicity	Very high
MI or CABG	High	Prior (remote) anthracycline exposure <sup>g</sup>	Medium <sup>2</sup>
Stable angina	High	Prior RT to left chest or mediastinum	Medium <sup>2</sup>
Severe VHD	High		
Arrhythmia <sup>h</sup>	Medium <sup>2</sup>	<b>Lifestyle risk factors</b>	
<b>Cardiac imaging</b>		Current smoker or significant smoking history	Medium <sup>1</sup>
Baseline LVEF < 50%	High		
Borderline LVEF 50–54%	Medium <sup>2</sup>	Obesity (BMI > 30 kg/m <sup>2</sup> )	Medium <sup>1</sup>
<b>Cardiac biomarkers (where available)</b>			
Elevated baseline troponin <sup>b</sup>	Medium <sup>2</sup>		
Elevated baseline BNP or NT-proBNP <sup>h</sup>	Medium <sup>2</sup>		
<b>Demographic and CVRF</b>			
Age ≥ 80 years	High		
Age 65–79 years	Medium <sup>2</sup>		
Hypertension <sup>c</sup>	Medium <sup>1</sup>		
DM <sup>d</sup>	Medium <sup>1</sup>		
Chronic kidney disease <sup>e</sup>	Medium <sup>1</sup>		
<b>Current cancer treatment regimen</b>			
Includes anthracycline before HER2-targeted therapy	Medium <sup>1f</sup>		



	Score	CTR-CVT risk
Low risk	0-1	<2%
Med risk	2-4	2-9%
High risk	≥5 or any HR	10-19%
Very HR	any very HR	>20%

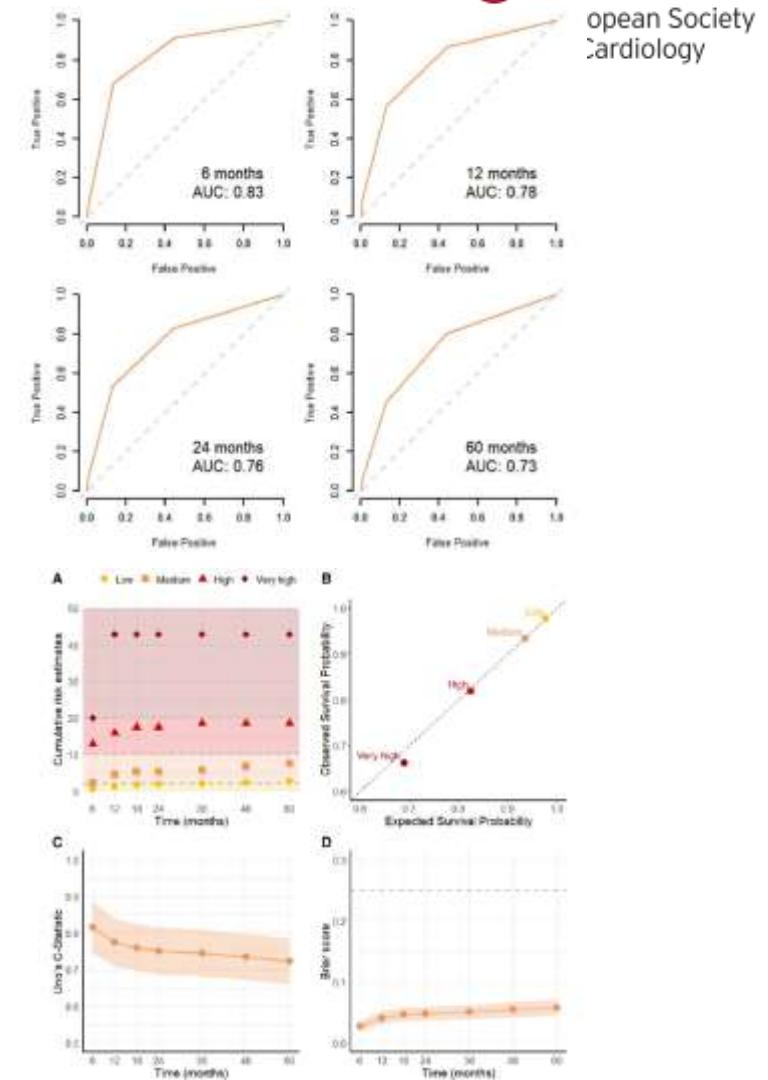
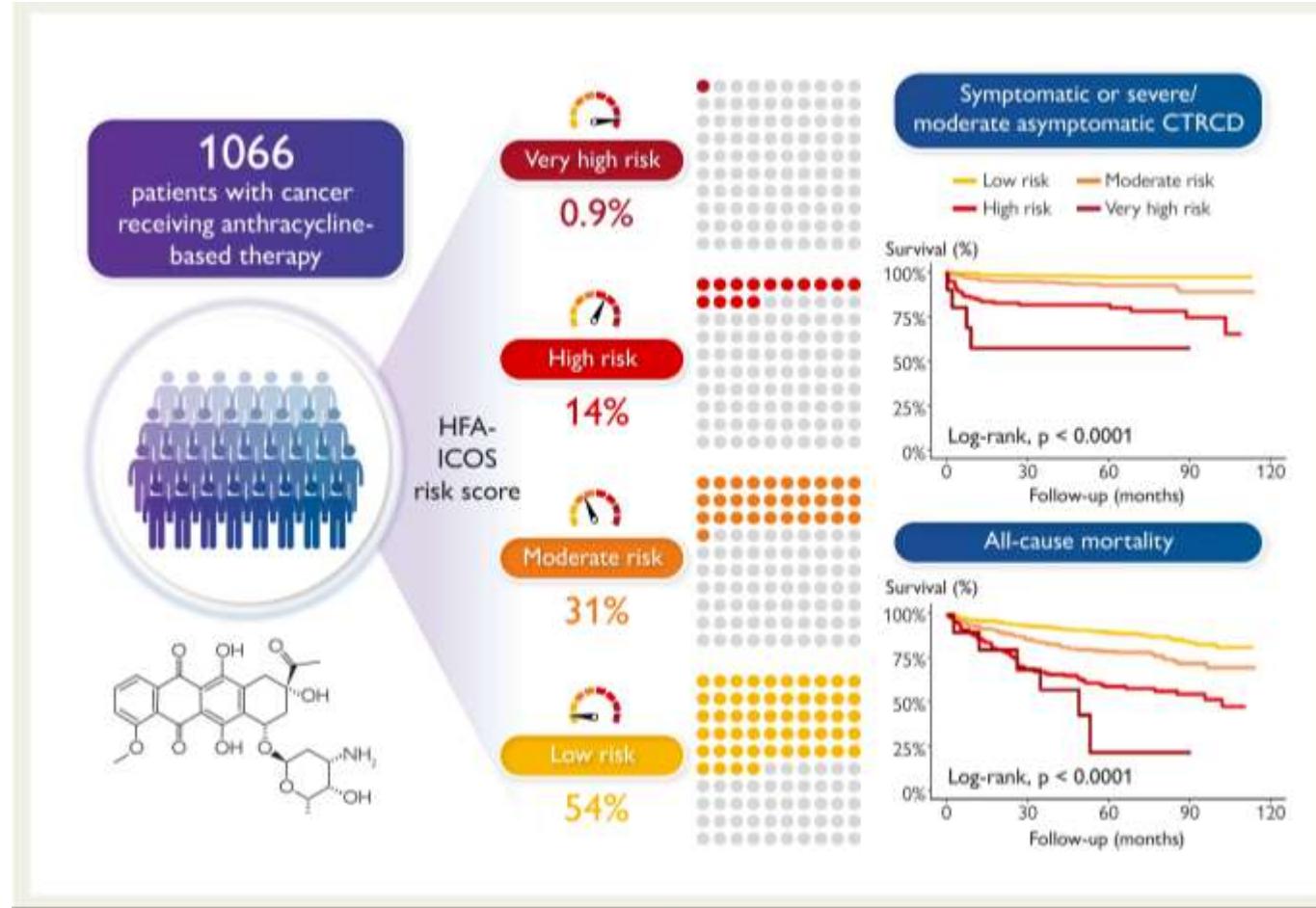
- Anthracycline
- HER2 targeted therapies
- VEGF inhibitors
- RAF/MEK inhibitors
- BCR-ABL inhibitors
- Multiple myeloma

# Thoracic radiotherapy



- **SCORE2/SCORE2-OP**
- **RT risk categorization based on MHD** is recommended over categorization based on prescribed dose, which may not accurately reflect cardiac radiation exposure.
- **Depending on dose distribution and exposure of specific cardiac substructures** (as well as clinical risk factors) the treatment team may judge the patient to belong to a **higher or lower risk category**.

# HFA-ICOS risk score



# HFA-ICOS risk score

## Representative studies validating HFA-ICOS tool

### Anthracyclines

Borja Rivero-Santana et al (2024; n = 1066): sens 49%, spec 87%, NPV of 95% for severe CTRCD and good HFA-ICOS score discriminatory ability across CTRCD risk groups

Published in the European Heart Journal

### HER2-targeted therapies

Di Lisis et al (2024; n = 109): good HFA-ICOS score discriminatory ability across CTRCD risk groups

Battisti et al (2021; n = 931) and Suntheralingam et al (2022; n = 629): good performance of HFA-ICOS score to predict high/very high risk CTRCD patients

Cronin et al (2023; n = 507): good HFA-ICOS score discriminatory ability across CTRCD risk groups

Fernando et al (2024; n = 229): Nilotinib in CML-HFA-ICOS tool was an efficient discriminator of CTRCD risk

### RAF + MEK

Glen et al (2023; n = 63): HFA-ICOS risk score performed well in medium and high-risk groups in melanoma patients on BRAF/MEK inhibitors.

## Who is at low-risk?

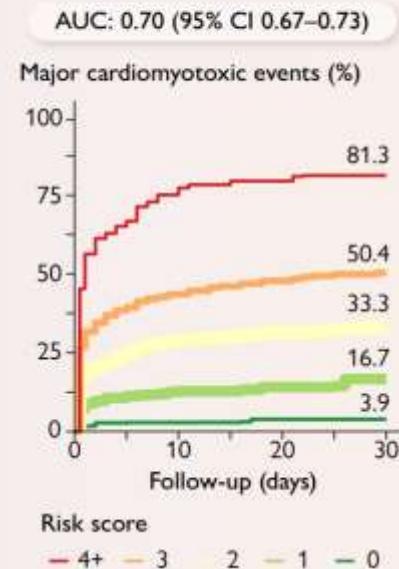
Lloyd E. Butel-Simoes, Doan T.M. Ngo, and Aaron L. Sverdlov et al *European Heart Journal* (2025) 46, 285–287

# Risk score for severe ICI-myotoxicity

## Derived risk score

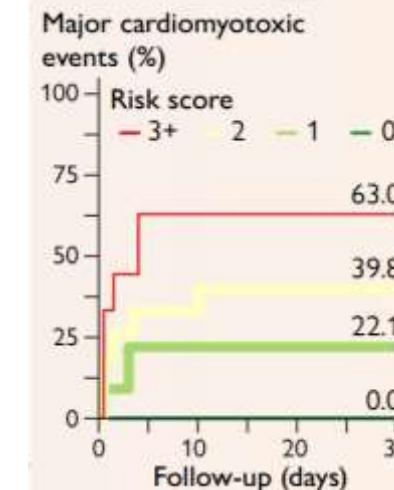
Risk score parameters	Points
Active thymoma	+2
Cardiomuscular symptoms	+1
ECG: Sokolow-Lyon voltage $\leq 0.5$ mV	+1
Left ventricular ejection fraction $< 50\%$	+1
Troponin (preferentially T, otherwise I)	
• $> 20$ to $200$ folds the ULN	+1
• $> 200$ to $2000$ folds the ULN	+2
• $> 2000$ folds the ULN	+3

Cumulative incidence  
of major cardiomyotoxic events  
according to risk score



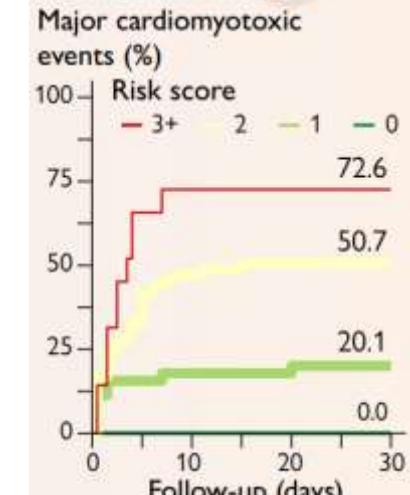
## Replication cohorts

Sorbonne University

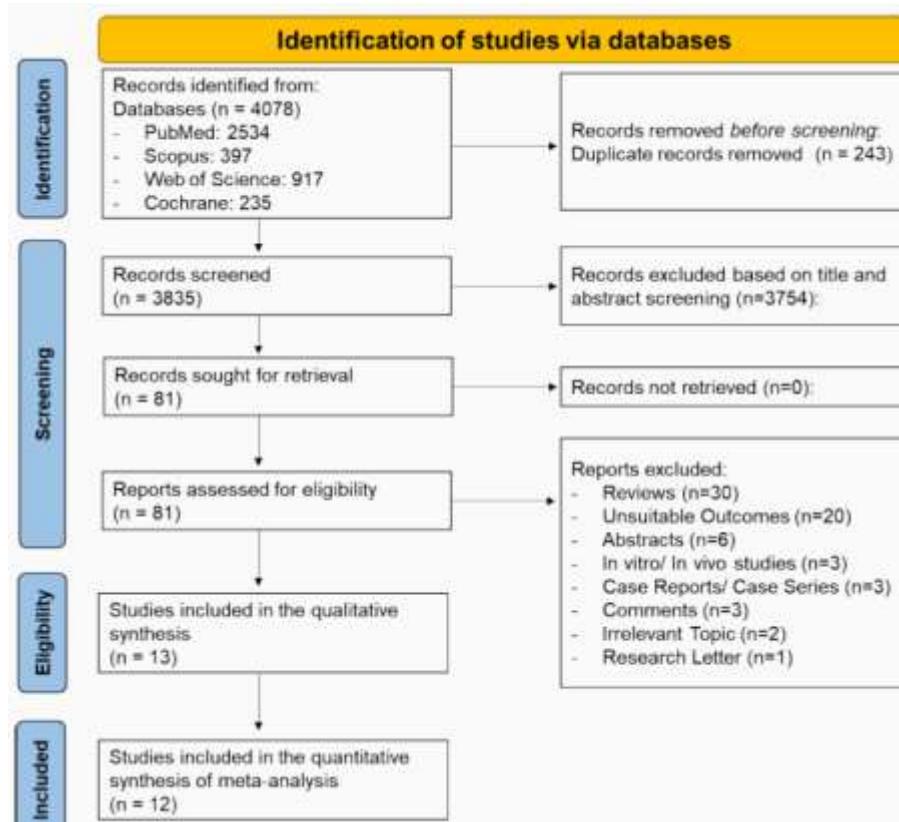


## Replication cohorts

Mass General Brigham



# CAR-T7 baseline risk score

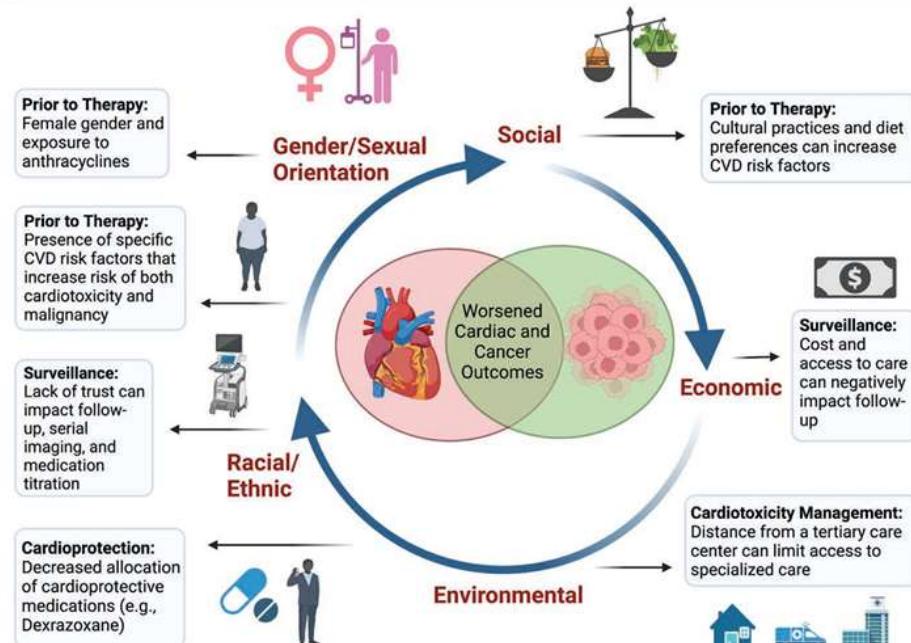


Risk factors	Points
<b>Heart Failure</b>	<b>10</b>
<b>Atrial Fibrillation</b>	<b>9</b>
<b>Coronary Artery Disease</b>	<b>8</b>
<b>Hyperlipidaemia</b>	<b>2</b>
<b>Diabetes</b>	<b>2</b>
<b>Hypertension</b>	<b>1</b>
<b>Smoking</b>	<b>1</b>

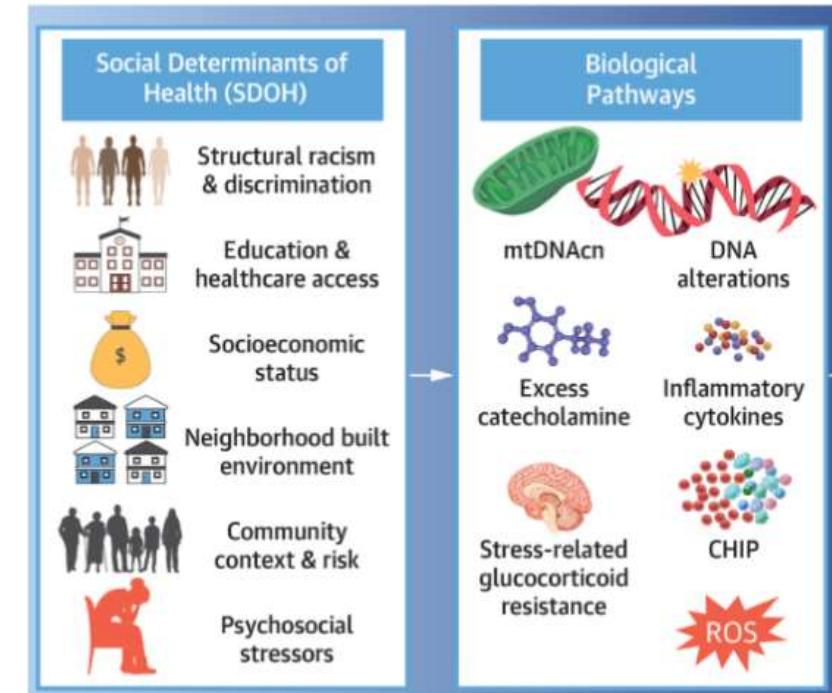
Total score	Risk level
0-8	Low
9-17	Moderate
18-25	High
26-33	Very high

# Uncovering Hidden Risks: SDOH

## Drivers of Inequity and Disparities in Cardio-Oncology

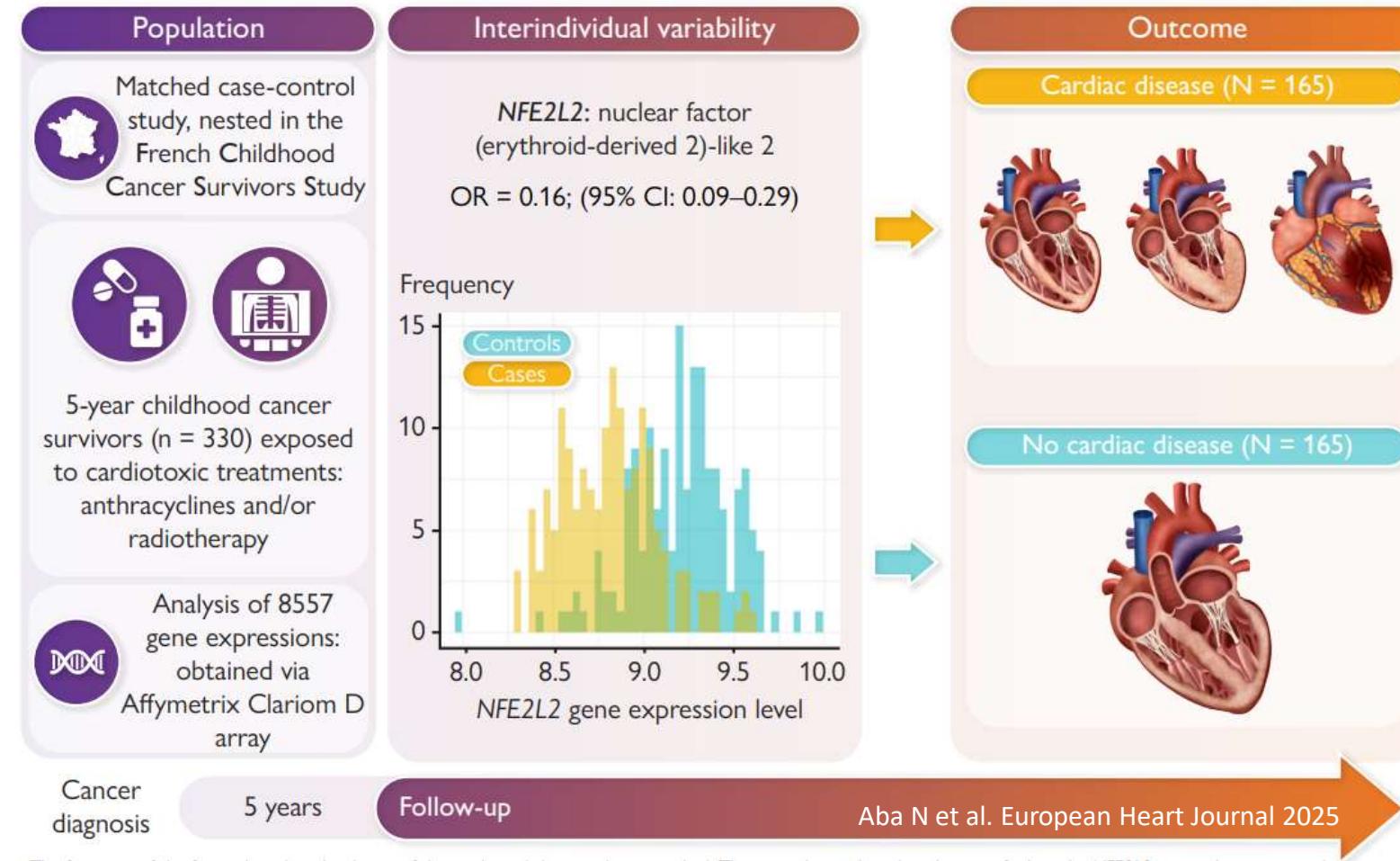


*Circulation.* 2023;148(3):297-308

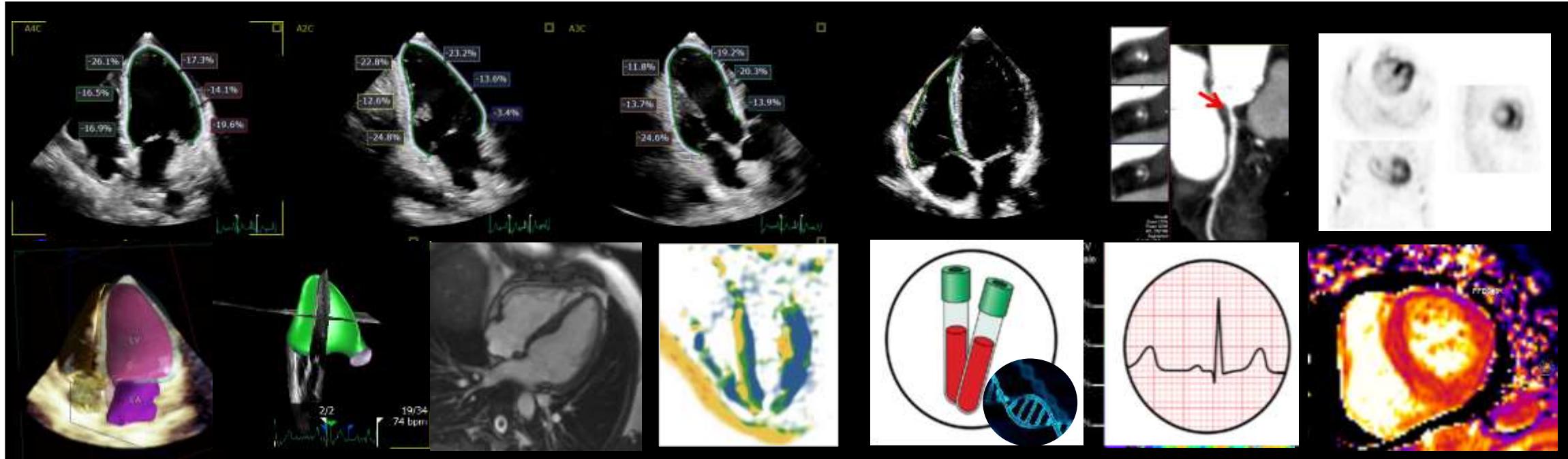


*J Am Coll Cardiol CardioOnc* 2024;6:331–346

# Uncovering Hidden Risks: Genetics



- From LVEF to comprehensive imaging, biomarkers, genes and



# New challenges

*The supporting  
evidence is  
continually  
developing*

Is there a possibility that we  
are detecting too much?

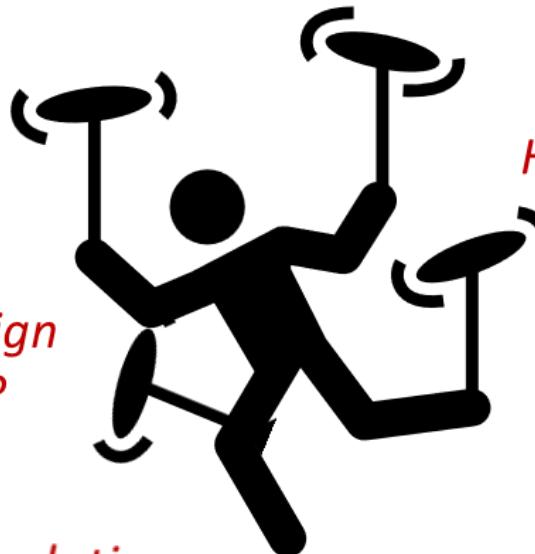
*What should guide  
our decisions?*

*Mild toxicity: warning sign  
or background noise?*

*Special populations...*

*Where is the threshold?  
How much is too much?*

*How much toxicity can  
we safely tolerate?*



*Timely access to  
new resources*

# ESC CARDIO ONCOLOGY 2026

The annual conference of the ESC Council of Cardio-Oncology

**19-20 JUNE**  
**VIENNA**  
**AUSTRIA**

Important deadlines  
 **29 January 2026**

Abstract submission

 **05 February 2026**  
Clinical Cases submission



#ESCardioOnco26

SAVE  
THE DATES



 **ESC**  
Council  
Cardio-Oncology

# CAS in Cardio-Oncology



A global programme designed to shape future leaders in Cardio-Oncology

Accredited by University of  
Zurich (UZH)

Diploma of attendance co-  
signed by ESC & ESMO & EHA  
for international recognition

Bologna compliant qualification  
ensuring academic rigor and  
wide recognition

**10 ECTS credits/300 hours**



**Universität  
Zürich**<sup>UZH</sup>



- **Risk stratification** is essential to structure cardio-oncology strategies in an era of **increasingly complex patients, novel therapies, and a growing cancer population.**

## Future needs for CV toxicity risk assessment

- **Standardising CTR-CVT criteria** (definitions and grading)
- A stronger stream of **basic and translational research**
- **Adopt a risk-adapted trial approach** to CV data collection and monitoring in onco-haematology trials and RWD

# Thank you!

*To champion excellence and innovation  
by fostering future leaders in cardiovascular medicine*

[www.EuropeanHeartAcademy.org](http://www.EuropeanHeartAcademy.org)

<https://www.escardio.org/events/councils-events/esc-cardio-oncology/>