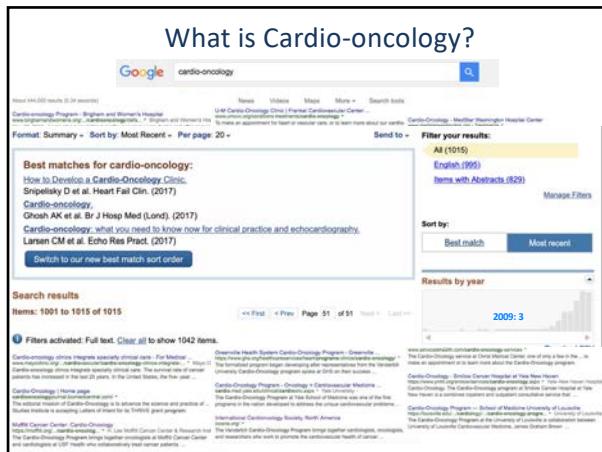
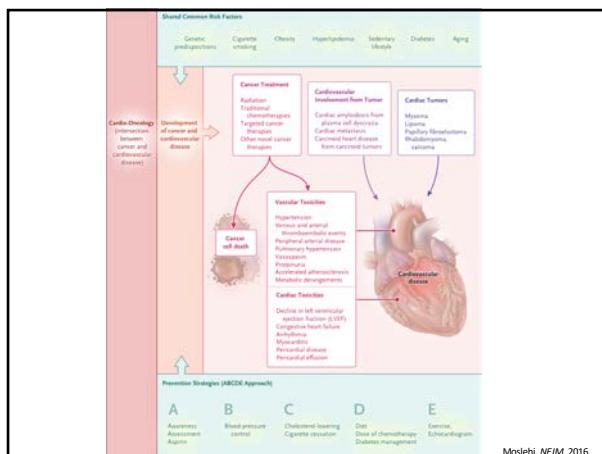


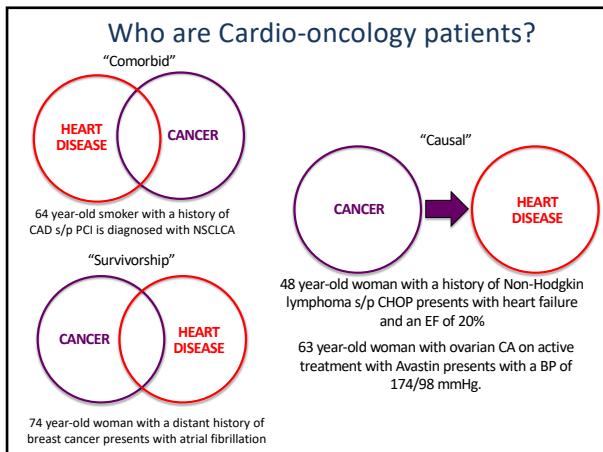
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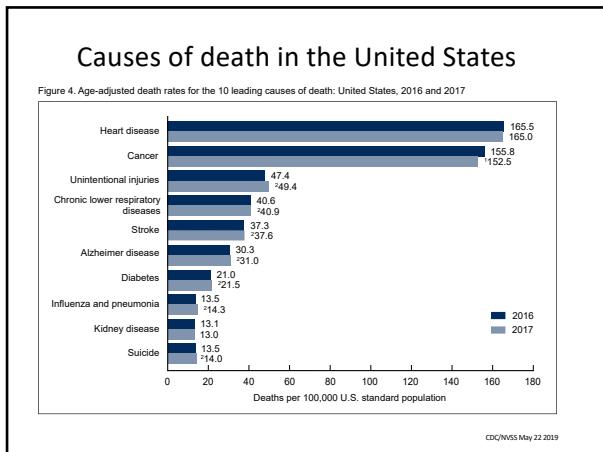
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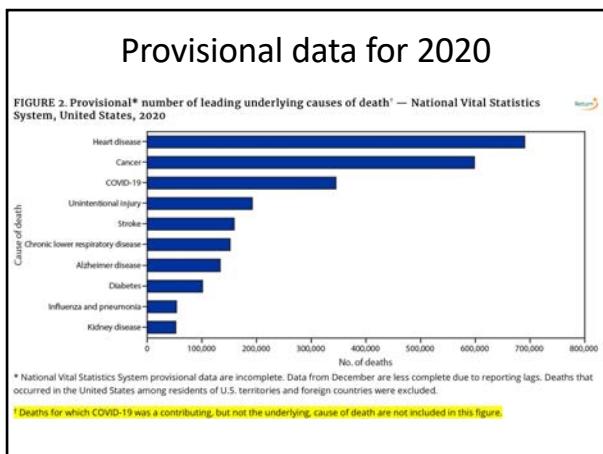
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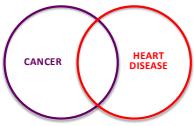


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Cancer increases risk for subsequent CV disease

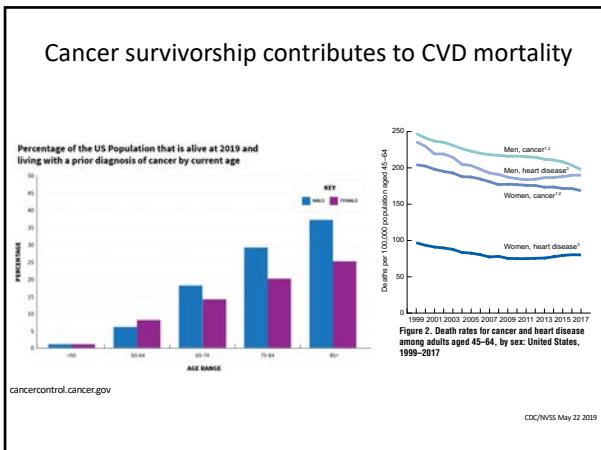


- Survivors have a 10 times higher risk for **coronary atherosclerosis**
- Survivors have a 15 times higher risk of **heart failure**
- Survivors have a 9.3 times the risk for **stroke**
- Risks are particularly high among survivors who had received **anthracycline drugs**, such as doxorubicin, or **high-dose radiation** therapy to the chest as part of their cancer treatment

Offinger et al, NEJM, 2006
Childrens Cancer Research Fund

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Cancer survivorship contributes to CVD mortality

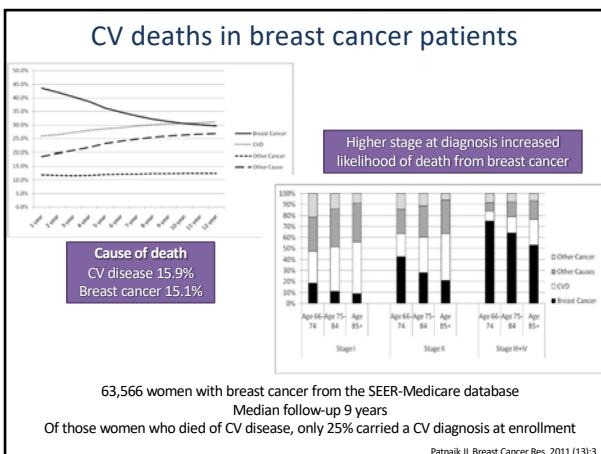


Percentage of the US Population that is alive at 2019 and living with a prior diagnosis of cancer by current age
cancercontrol.cancer.gov

Figure 2. Death rates for cancer and heart disease among adults aged 45-64, by sex: United States, 1999-2017
CDC/NCHS May 22 2019

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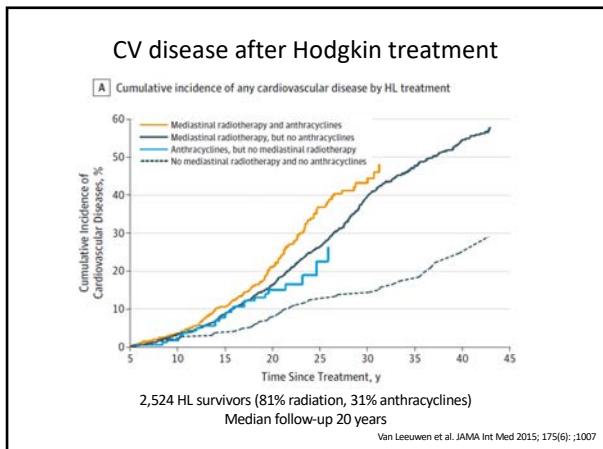
CV deaths in breast cancer patients



Cause of death
CV disease 15.9%
Breast cancer 15.1%

63,566 women with breast cancer from the SEER-Medicare database
Median follow-up 9 years
Of those women who died of CV disease, only 25% carried a CV diagnosis at enrollment
Pathriaik JL. Breast Cancer Res. 2011 (13):3

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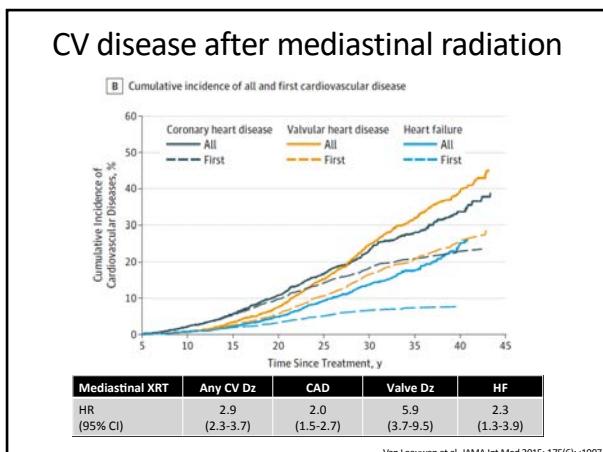
Risk factors for cardiotoxicity

Table 4 Baseline risk factors for cardiotoxicity

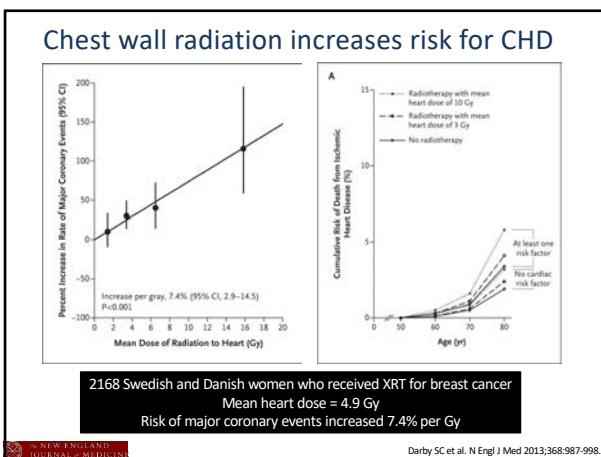
Current myocardial disease	Demographic and other CV risk factors
<ul style="list-style-type: none"> Heart failure (with either preserved or reduced ejection fraction) Ischaemic/haemodynamic LV dysfunction (LVEF <50% or high natriuretic peptide) Evidence of CAD (previous myocardial infarction, angina, PCI or CABG, myocardial haemorrhage, ischaemic and/or hyper-HD with LHF or LV impairment) Hypertensive heart disease with LV hypertrophy Cardiac amyloidopathy Dilated cardiomyopathy Restrictive cardiomyopathy Cardiac sarcoidosis with myocardial involvement Significant cardiac arrhythmias (e.g. AF, ventricular tachyarrhythmias) 	<ul style="list-style-type: none"> Age (pediatric population <18 years; >50 years for traditional >35 years for anthracyclines) Family history of premature CV disease (<50 years) Arterial hypertension Diabetes mellitus Hypercholesterolaemia
Previous cardiotoxic cancer treatment	Lifestyle risk factors
<ul style="list-style-type: none"> Prior anthracycline use Prior radiotherapy to chest or mediastinum 	<ul style="list-style-type: none"> Smoking High alcohol intake Obesity Sedentary habit

European Heart Journal 2016

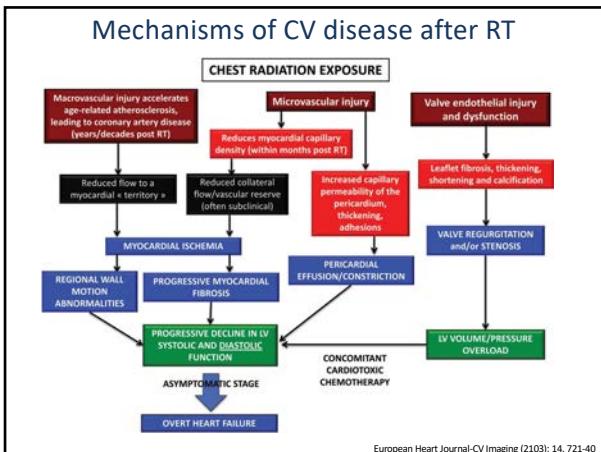
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Risk factors for radiation-related CV disease

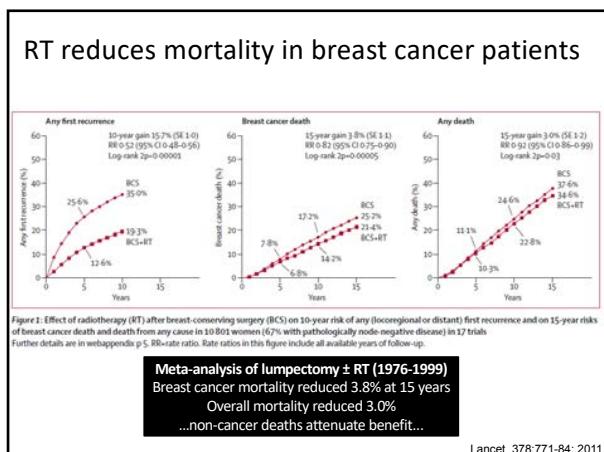
Table 2 Risk factors of radiation-induced heart disease

Anterior or left chest irradiation location
High cumulative dose of radiation (>30 Gy)
Younger patients (<50 years)
High dose of radiation fractions (>2 Gy/day)
Presence and extent of tumour in or next to the heart
Lack of shielding
Concomitant chemotherapy (the anthracyclines considerably increase the risk)
Cardiovascular risk factors (i.e. diabetes mellitus, smoking, overweight, ≥moderate hypertension, hypercholesterolaemia)
Pre-existing cardiovascular disease

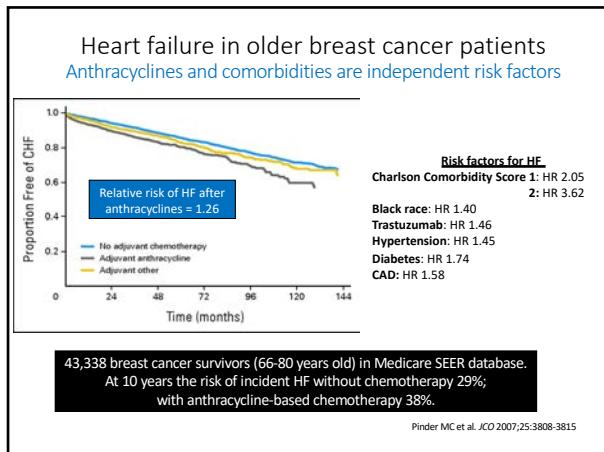
High-risk patients definition: anterior or left-side chest irradiation with ≥1 risk factors for RIHD.

Lancellotti et al. J Am Soc Echocardiogr 2013; 26:1013

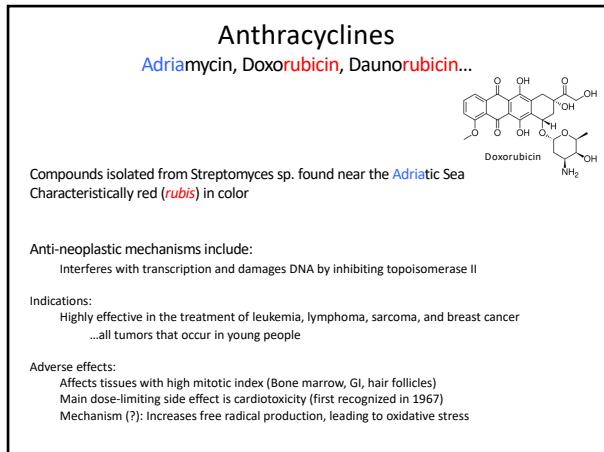
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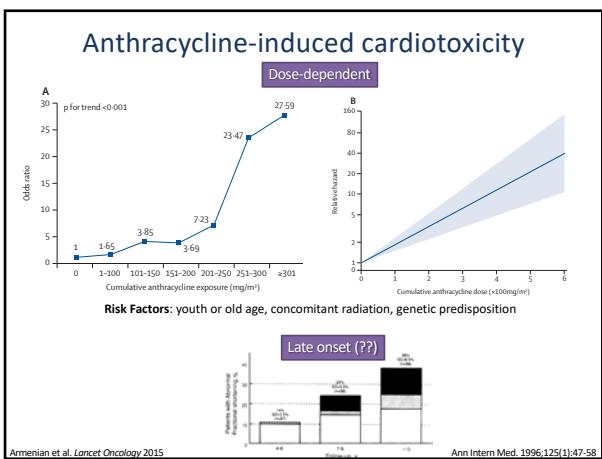
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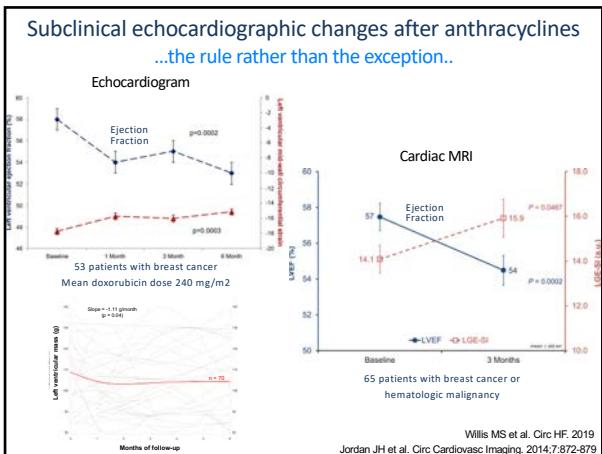
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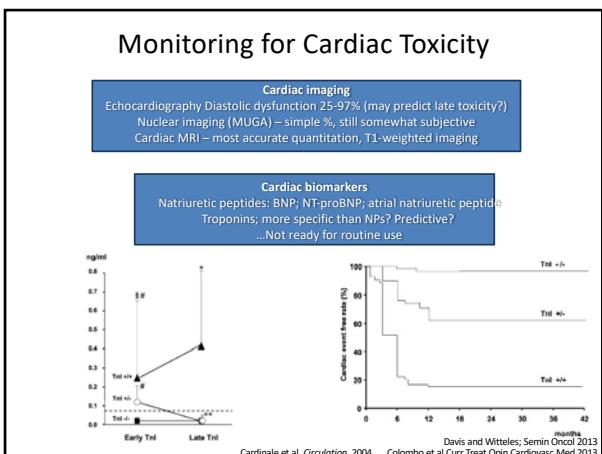
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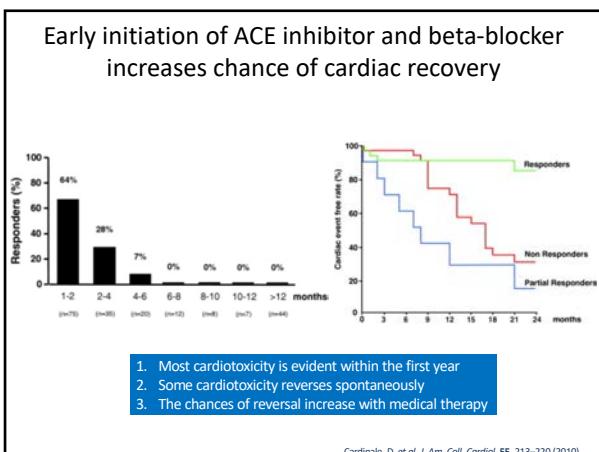
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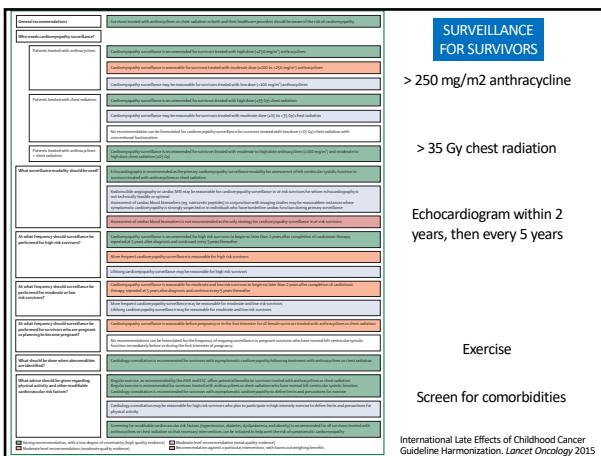
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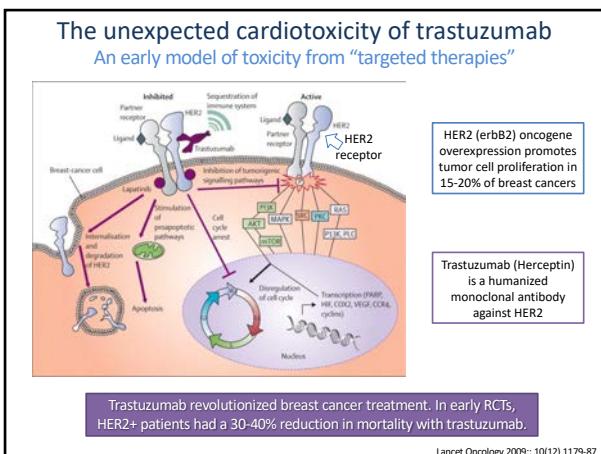
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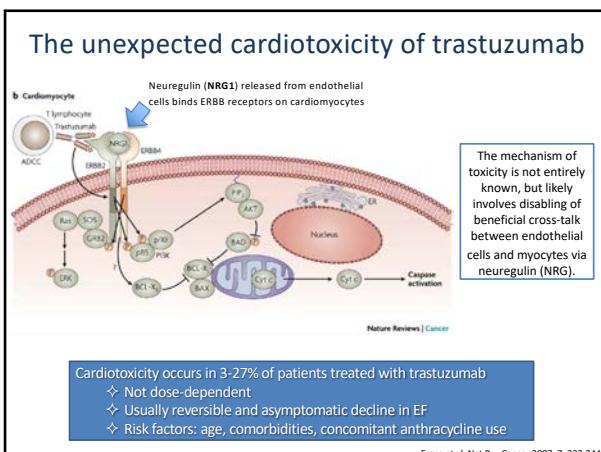
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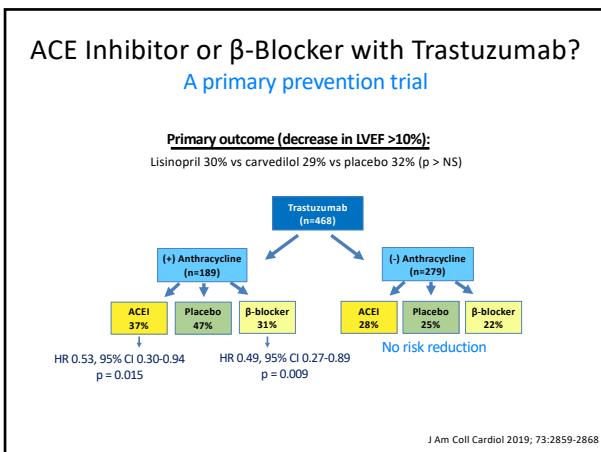
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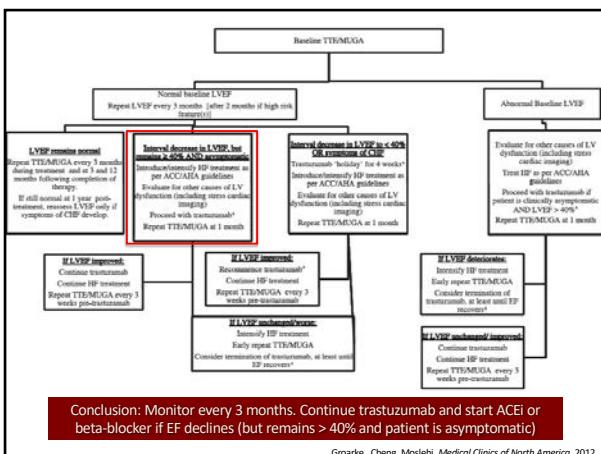
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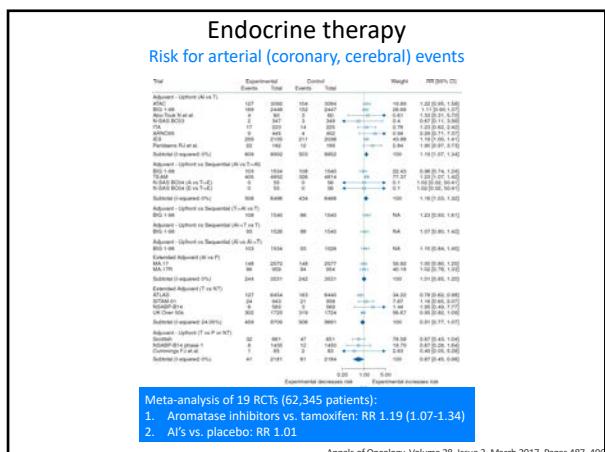
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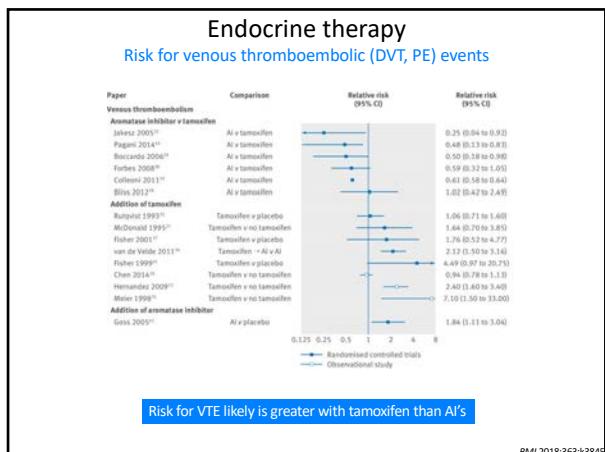
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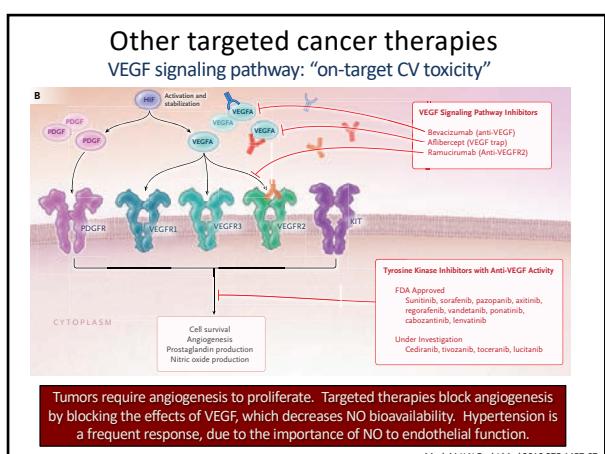
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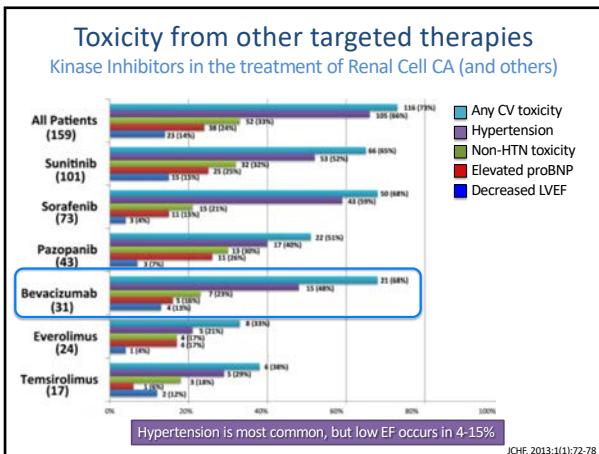
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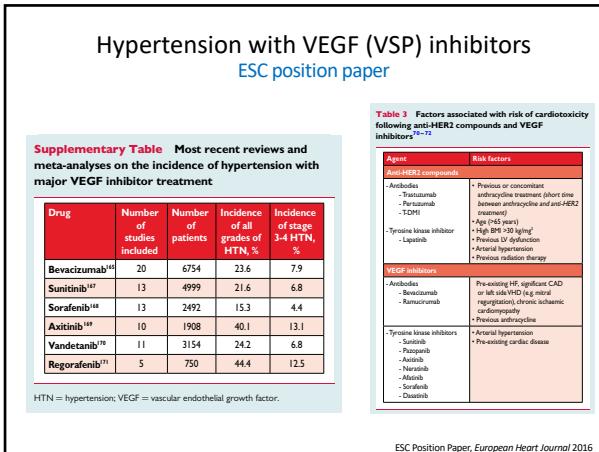
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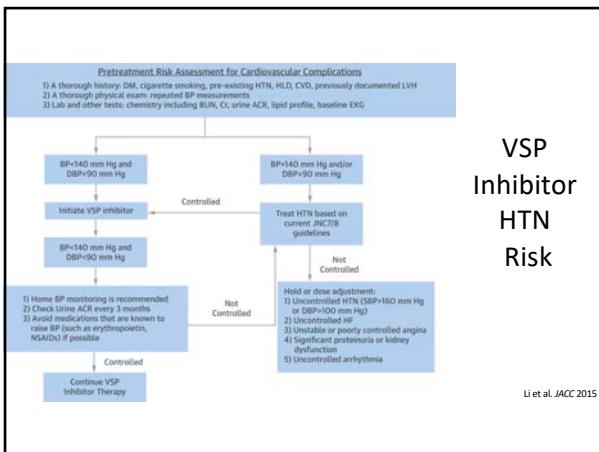
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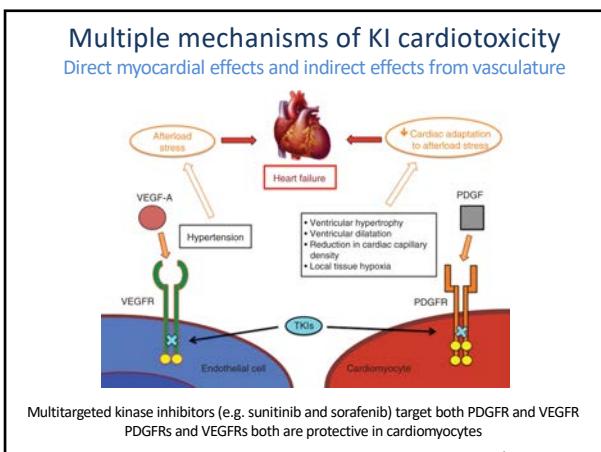
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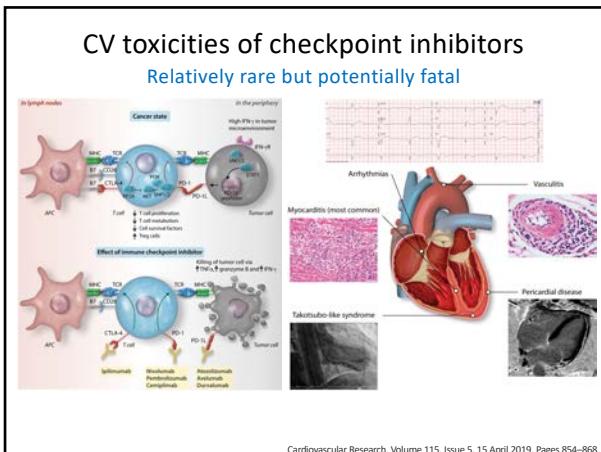
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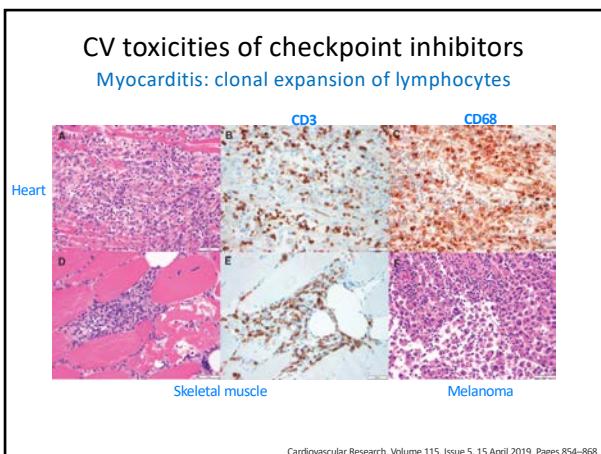
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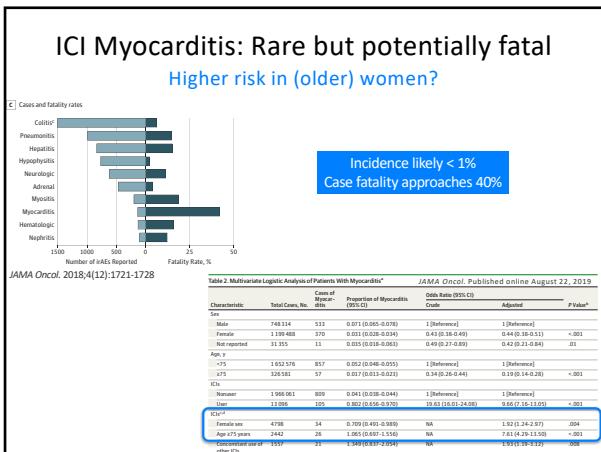
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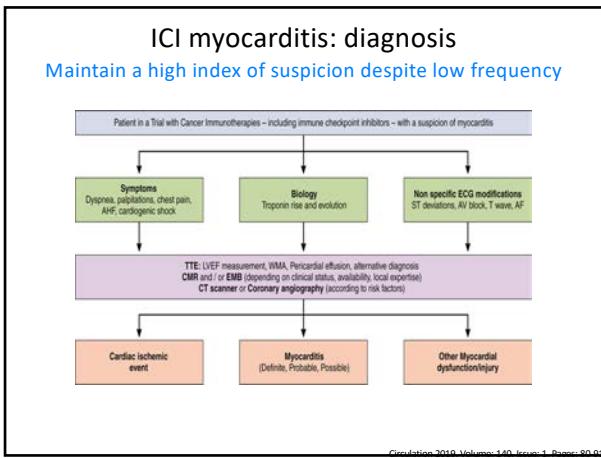
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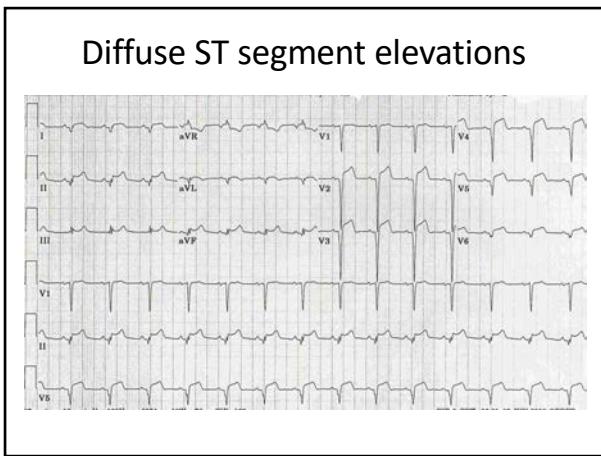
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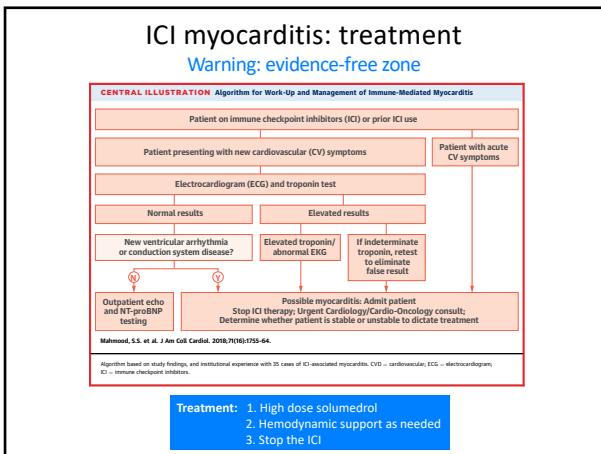
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How to Diagnose and Manage QT Prolongation in Cancer Patients

Peter Y. Kim, MD,¹ Jorge A. Irizarry-Caro, MD,² Tushar Ramesh, MD,³ Cezar Iliescu, MD,⁴ Juan C. Lopez-Mattei, MD^{4,5}

TABLE 1 Cancer and Non-Cancer Drugs Known to Cause Prolongation of the QTc

Therapy	Drug Type	Drug
Cancer therapeutics		
Antimetabolites		Capetabine
Anthracyclines		Epirubicin
Antimicrotubule agents		Paclitaxel
Tyrosine kinase inhibitors		Sorafenib, Dabrafenib, Lenvatinib, Nilotinib, Ponatinib, Vandetanib, Rasenitinib, Sorafenib/tarifitab
Histone deacetylase inhibitors		Panobinostat, Romidepsin
Proteasome inhibitors		Vorinostat
CDK 4/6 inhibitor		Bortezomib
B-Raf inhibitor		Ribociclib
Other		Vemurafenib
Non-cancer agents		
Antiarhythmic drugs		
Antiarrhythmic drugs		
Antibacterial and antifungal drugs		
Prokinetic and antiemetic drugs		
Antipsychotics		
Antidepressants		

The medications included in this table have been identified to cause elevation in the QTc. For a more complete list of these medications, please visit www.cancertherapeuticsinfo.org. *The FDA package insert provides guidance regarding electrocardiographic monitoring.

JACC: CARDIOONCOLOGY VOL. 3, NO. 1, 2021

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Trials and Tribulations of Corrected QT Interval Monitoring in Oncology: Rationale for a Practice-Changing Standardized Approach

Benjam Muluneh, PharmD¹; Daniel R. Richardson, MD, MA PhiL²; Charles Hicks, MD³; Brian C. Jensen, MD⁴; and Joshua F. Zeidner, MD⁵

ASCO Journal of Clinical Oncology[®]

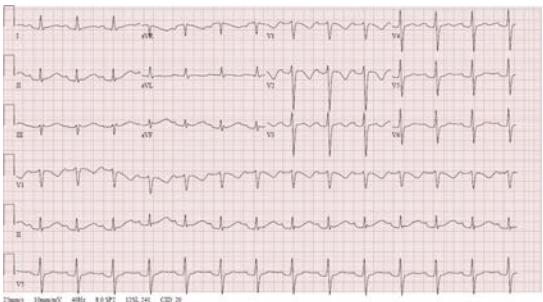
TABLE 1. Comparison of QTc Formulas

QTc Measurement	Formula	QT = 400 ms, HR = 75 beats/min		QT = 400 ms, HR = 95 beats/min		QTc Prolongation?		QTc Prolongation?	
		Normal Range, ms		QTc Prolongation?		QTc Prolongation?			
		Male	Female	Male	Female	Male	Female	Male	Female
Bazett	$\frac{40}{\sqrt{RR}}$	346-472	346-482	447	No	No	503	Yes	Yes
Framingham	$QT + 0.154 \times (1 - RR)$	350-449	351-467	431	No	No	457	Yes	No
Fridericia	$\frac{40}{\sqrt{RR}}$	349-448	349-468	431	No	No	466	Yes	No
Hodges	$QT + 1.75 \times (HR - 60)$	351-446	348-465	426	No	No	461	Yes	No

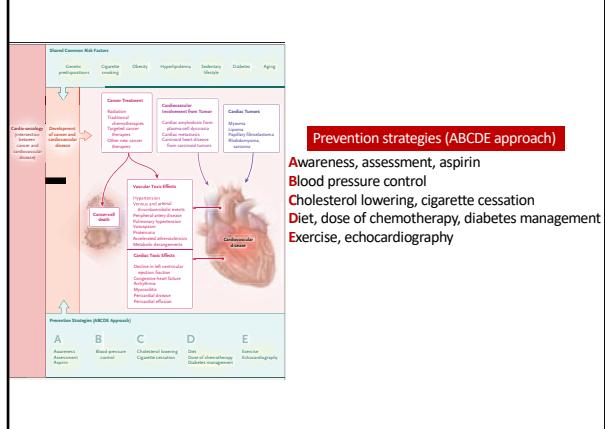
NOTE. From Raudaschl et al.¹
Abbreviations: HR, heart rate; QTc, corrected QT.

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QT prolongation



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Thank You

Questions?

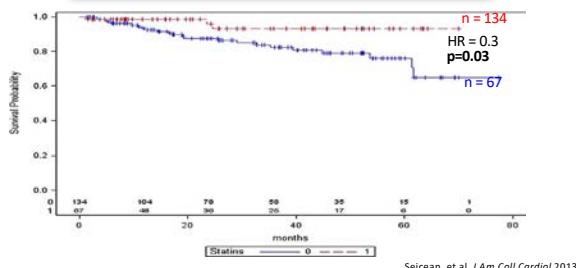
bcjensen@med.unc.edu

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Primary Prevention with Statins (?!?)

Effect of Statin Therapy on the Risk for Incident Heart Failure in Patients With Breast Cancer Receiving Anthracycline Chemotherapy

An Observational Clinical Cohort Study

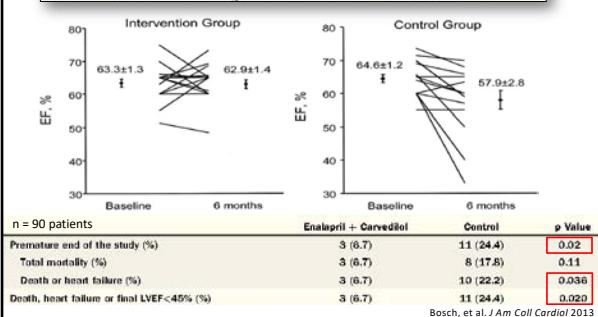
Suzana Seican, MD, MPH, PuD,* Andreia Seican, MPH,† Juan Carlos Plana, MD,*
C. Thomas Budd, MD,* Thomas H. Marwick, MD, PuD, MPH‡

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Primary prevention with ACEi and beta-blocker

Enalapril and Carvedilol for Preventing Chemotherapy-Induced Left Ventricular Systolic Dysfunction in Patients With Malignant Hemopathies

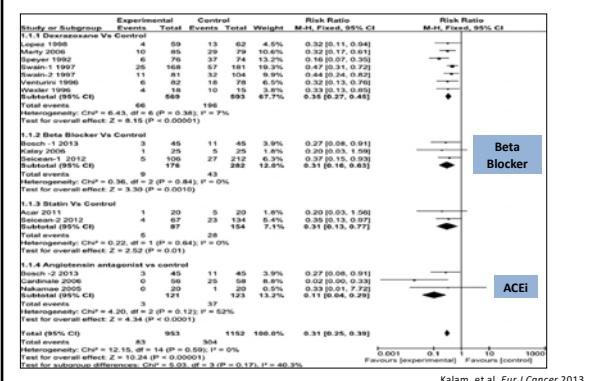
The OVERCOME Trial (prevention of left ventricular



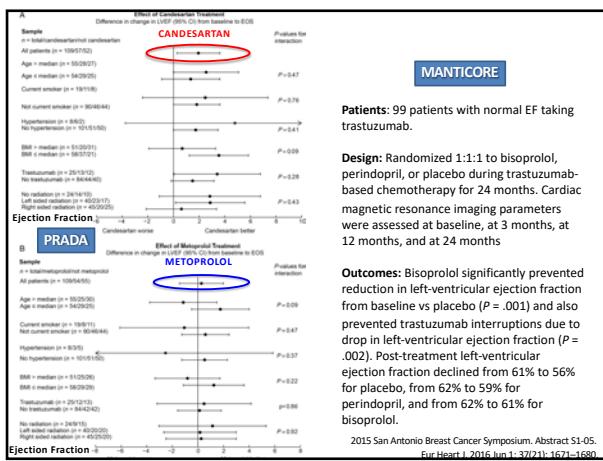
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Primary prevention with neurohormonal antagonists

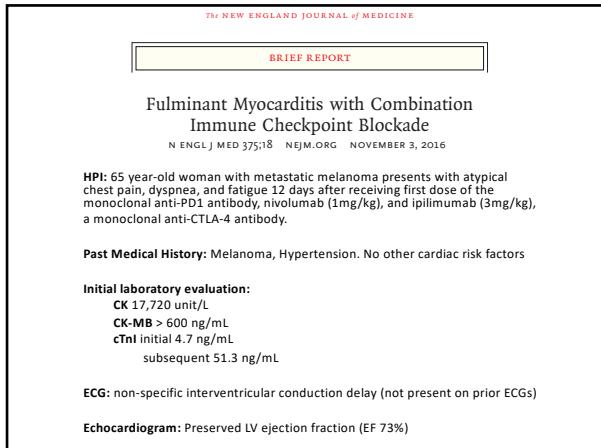
Insufficient data



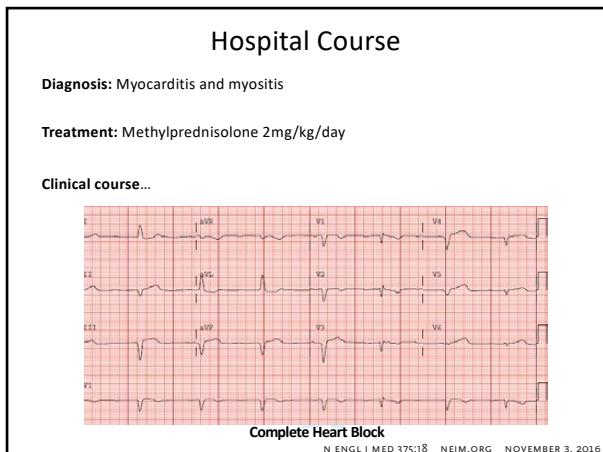
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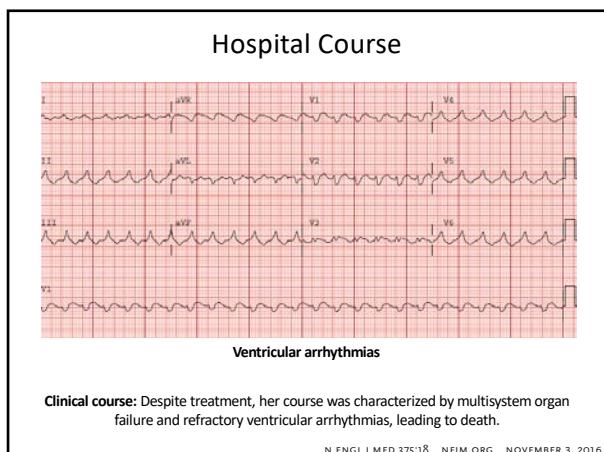
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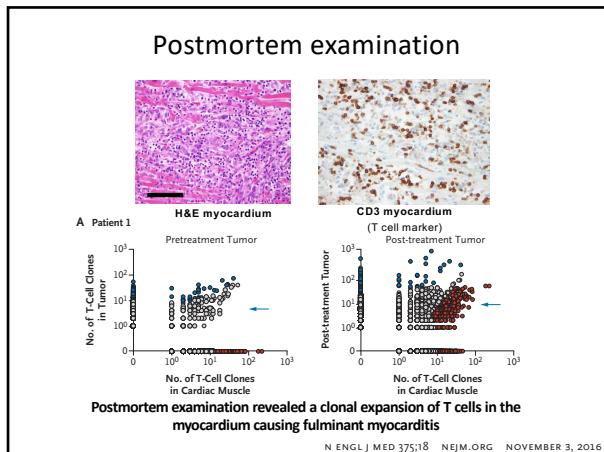
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Other potential CV complications of cancer therapy

Agent	Indication	Adverse reaction
Tamoxifen	Breast cancer	VTE
Aromatase inhibitors	Breast cancer	CAD
Ibrutinib	Lymphoma	Atrial fibrillation
Dasatanib	CML, ALL	Pulmonary hypertension
Carfilzomib	Multiple myeloma	CAD, thrombosis, HF
Trametinib	Melanoma	HF
Immune checkpoint inhibitors	Multiple	Myocarditis

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