Toxicité cardiaque des chimiothérapies

Amicale des Cardiologues de la cote d'Azur

06 Novembre 2018

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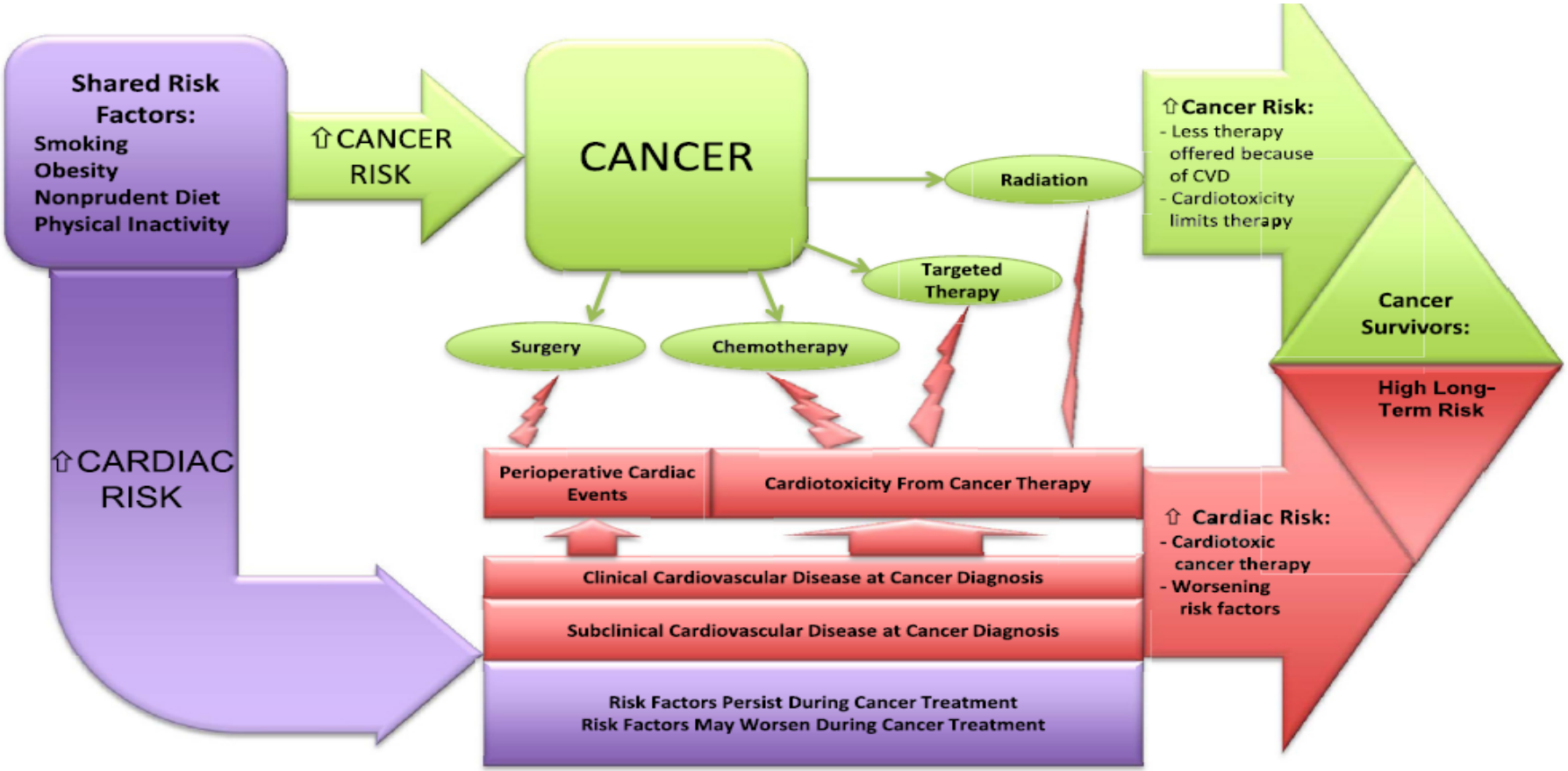
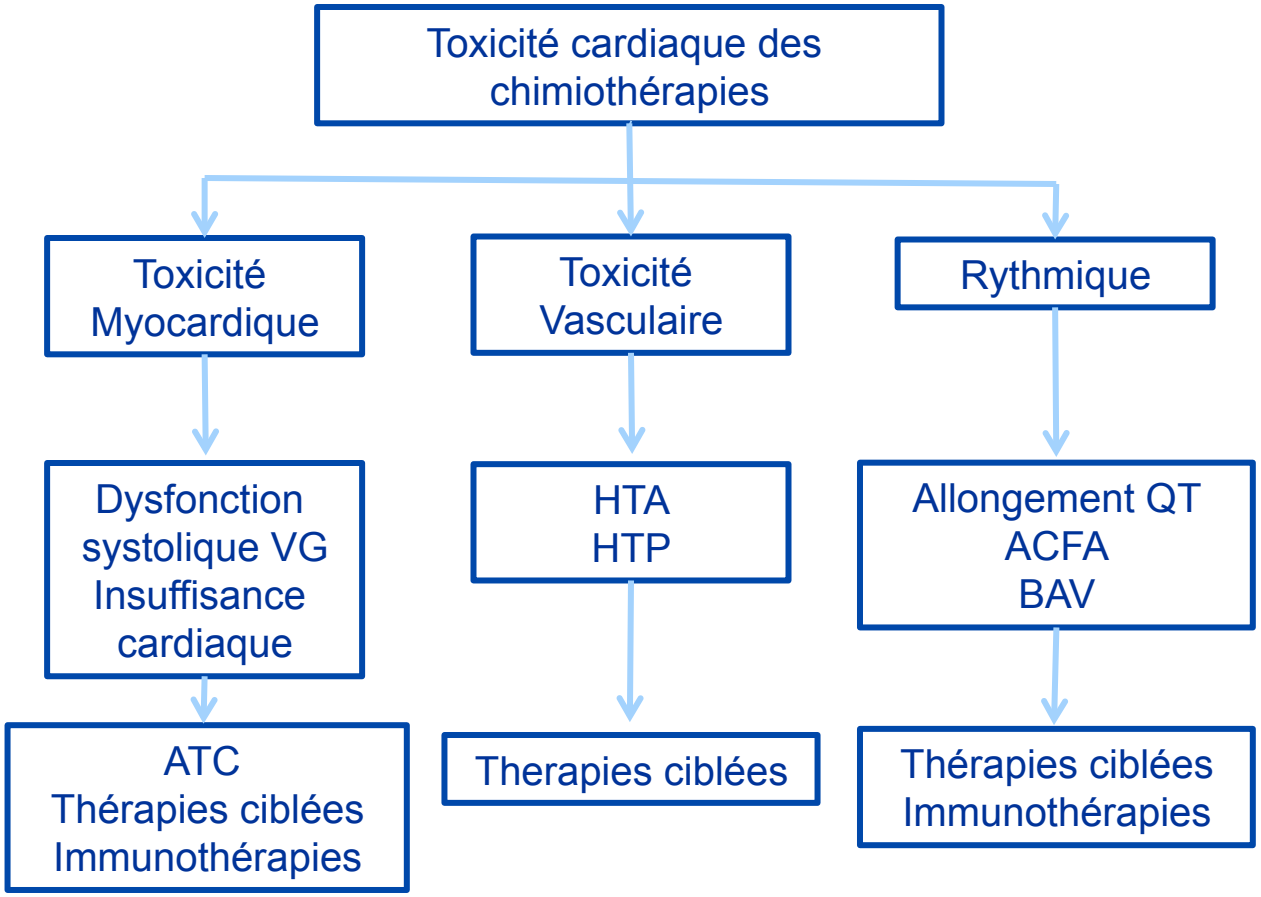
Unite de cardio-oncologie APHP.6
Hôpital Saint-Antoine, Paris


Shared Risk Factors:
Smoking
Obesity
Nonprudent Diet
Physical Inactivity
⇧CANCER RISK
CANCER
Radiation
Targeted Therapy
Surgery
Chemotherapy
⇧Cancer Risk:
- Less therapy offered because of CVD
- Cardiotoxicity limits therapy
Cancer Survivors:
High Long-Term Risk
⇧CARDIAC RISK
Perioperative Cardiac Events
Cardiotoxicity From Cancer Therapy
⇧ Cardiac Risk:
- Cardiotoxic cancer therapy
- Worsening risk factors
Clinical Cardiovascular Disease at Cancer Diagnosis
Subclinical Cardiovascular Disease at Cancer Diagnosis
Risk Factors Persist During Cancer Treatment
Risk Factors May Worsen During Cancer Treatment

How to prevent LV systolic dysfunction secundary to chemotherapy?



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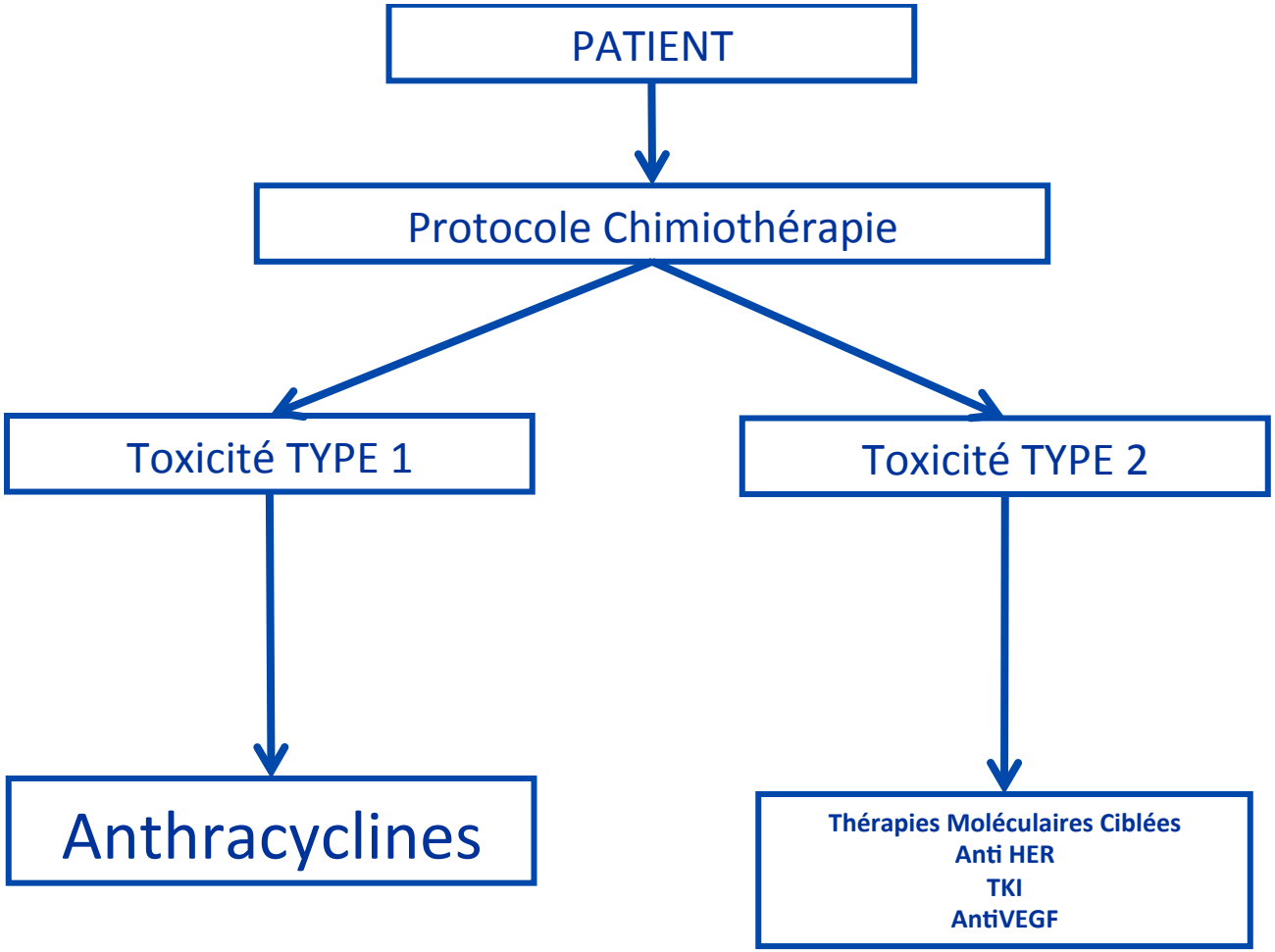
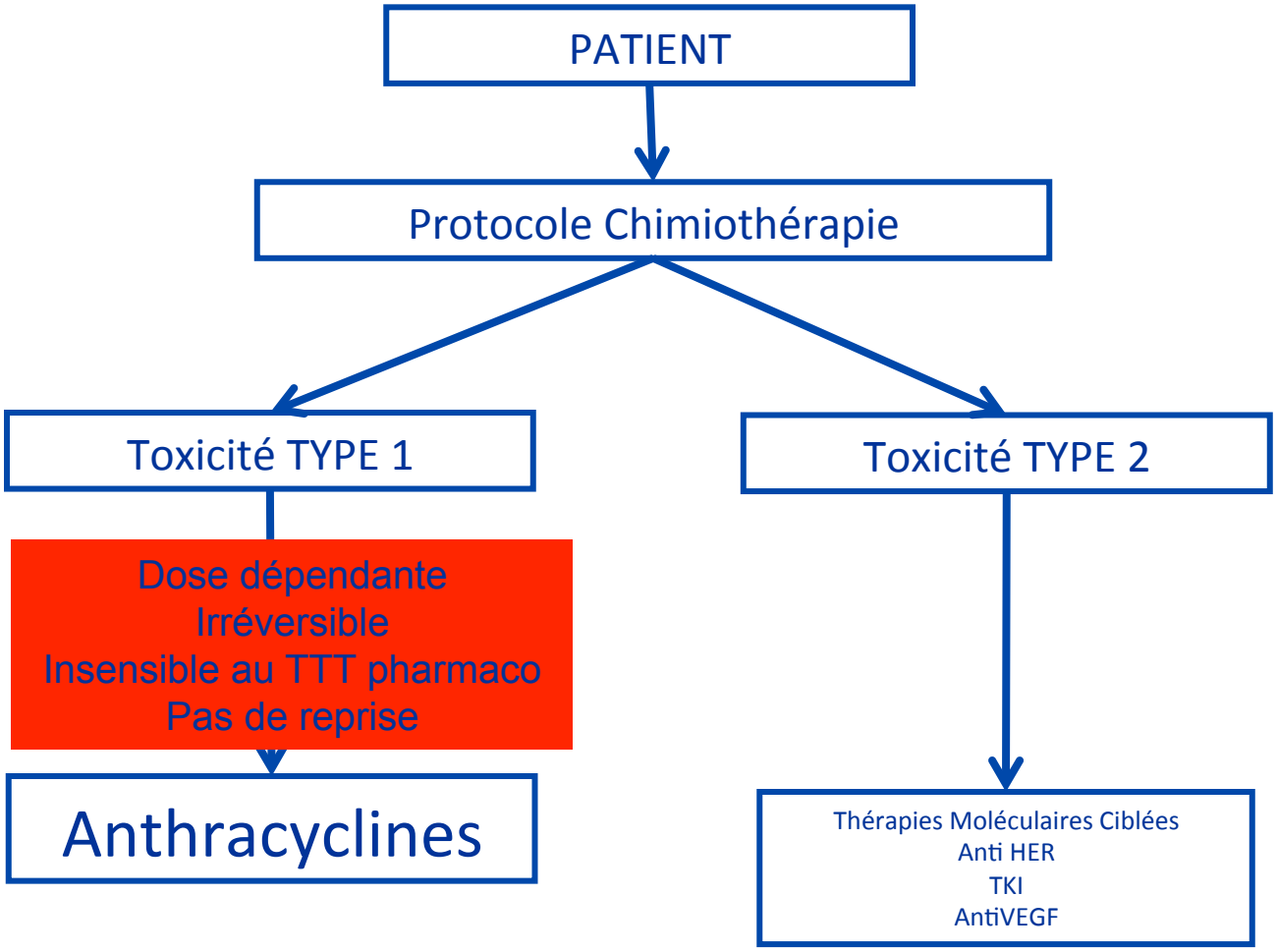


Adapté de Plana J Am Soc Echocardiogr 2014;27:911-39

How to prevent LV systolic dysfunction secundary to chemotherapy?



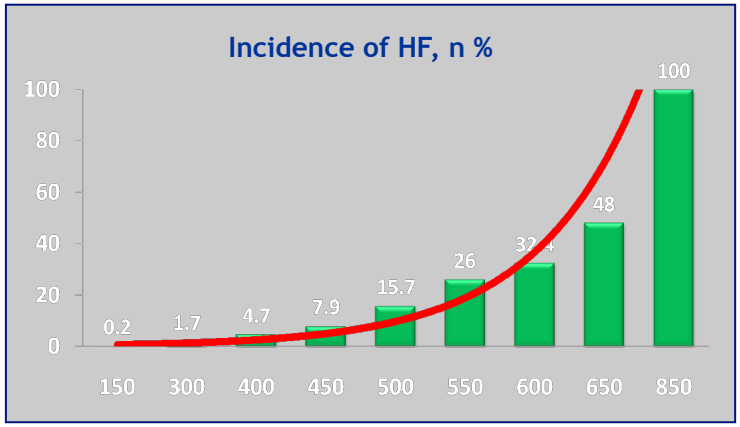
Adapté de Plana J Am Soc Echocardiogr 2014;27:911-39

Review and meta-analysis of incidence and clinical predictors of anthracycline cardiotoxicity

18 studies, 49 107 cancers patients
Median FU : 9 years

Clinically overt HF
6 % (95 % CI 3 to 9 %)

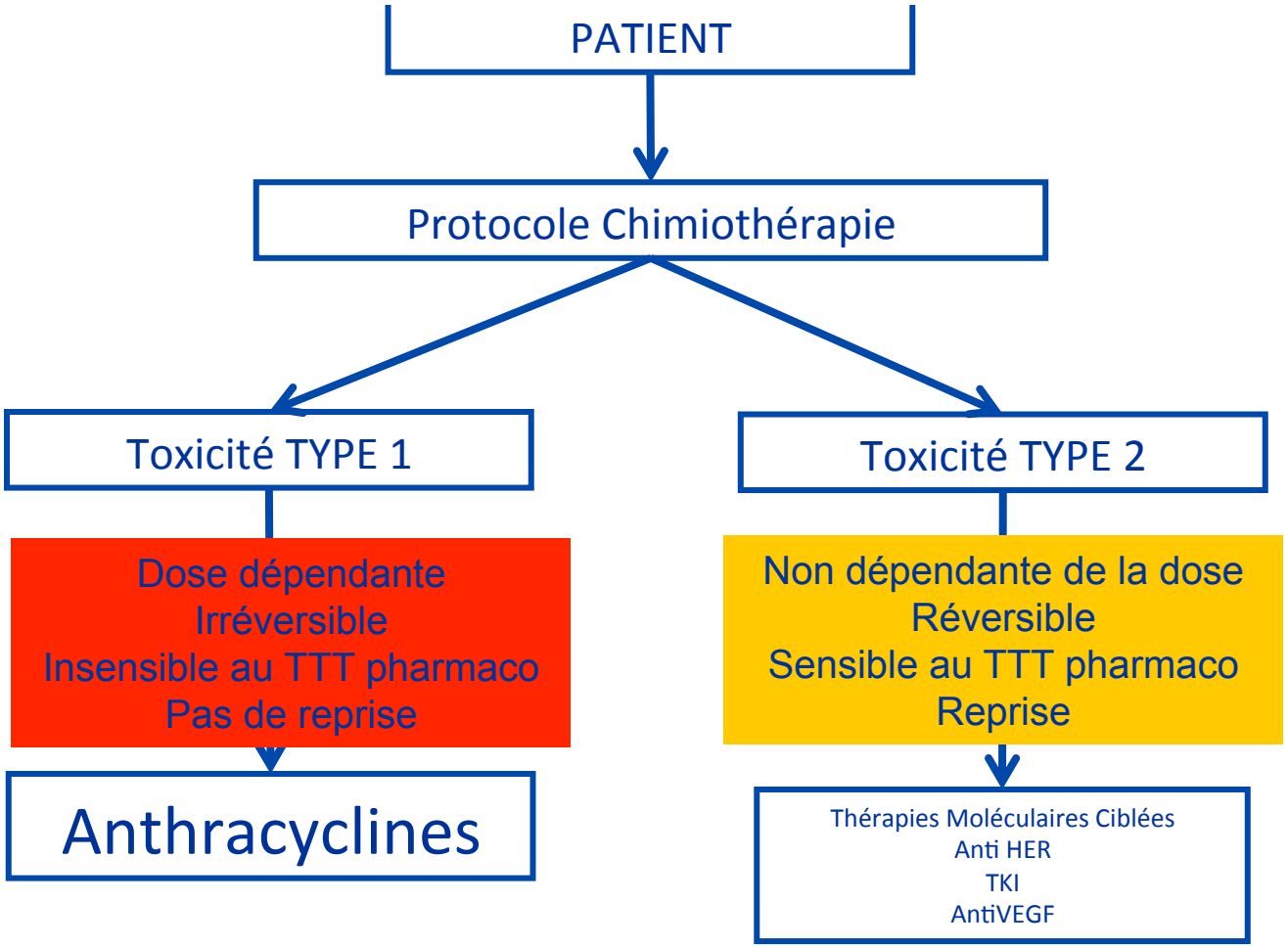
Sub Clinical cardiotoxicity
18 % (95 % CI 12 to 24 %)



Predictors of cardiotoxicity
Chest Radiotherapy
African-american ethnicity
Very Young or very Old age
Diabetes, Hypertension
Very High or very low BMI
Severe co morbidities

Lotrionte Am J Cardiol 2013 ; 112 : 1980 -1984

How to prevent LV systolic dysfunction secundary to chemotherapy?

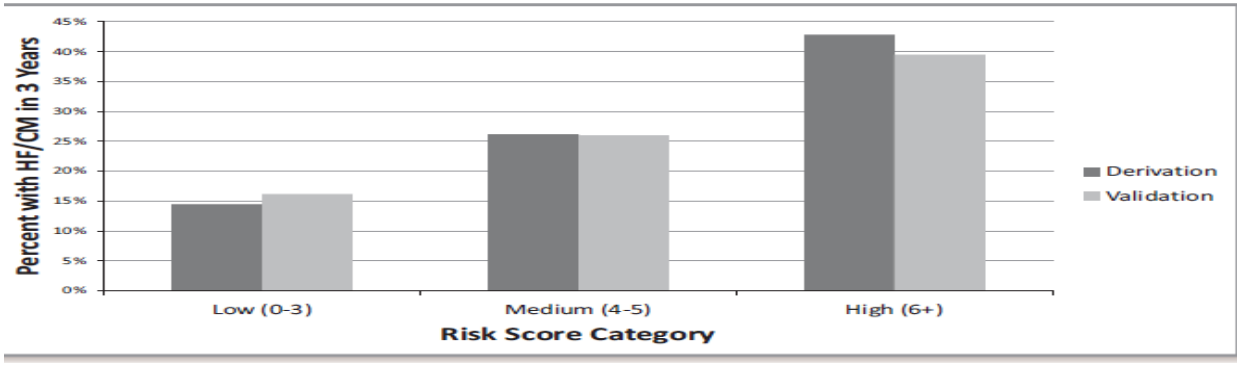


Adapté de Plana J Am Soc Echocardiogr 2014;27:911-39

Risk Prediction Model for Heart Failure and Cardiomyopathy After Adjuvant Trastuzumab Therapy for Breast Cancer

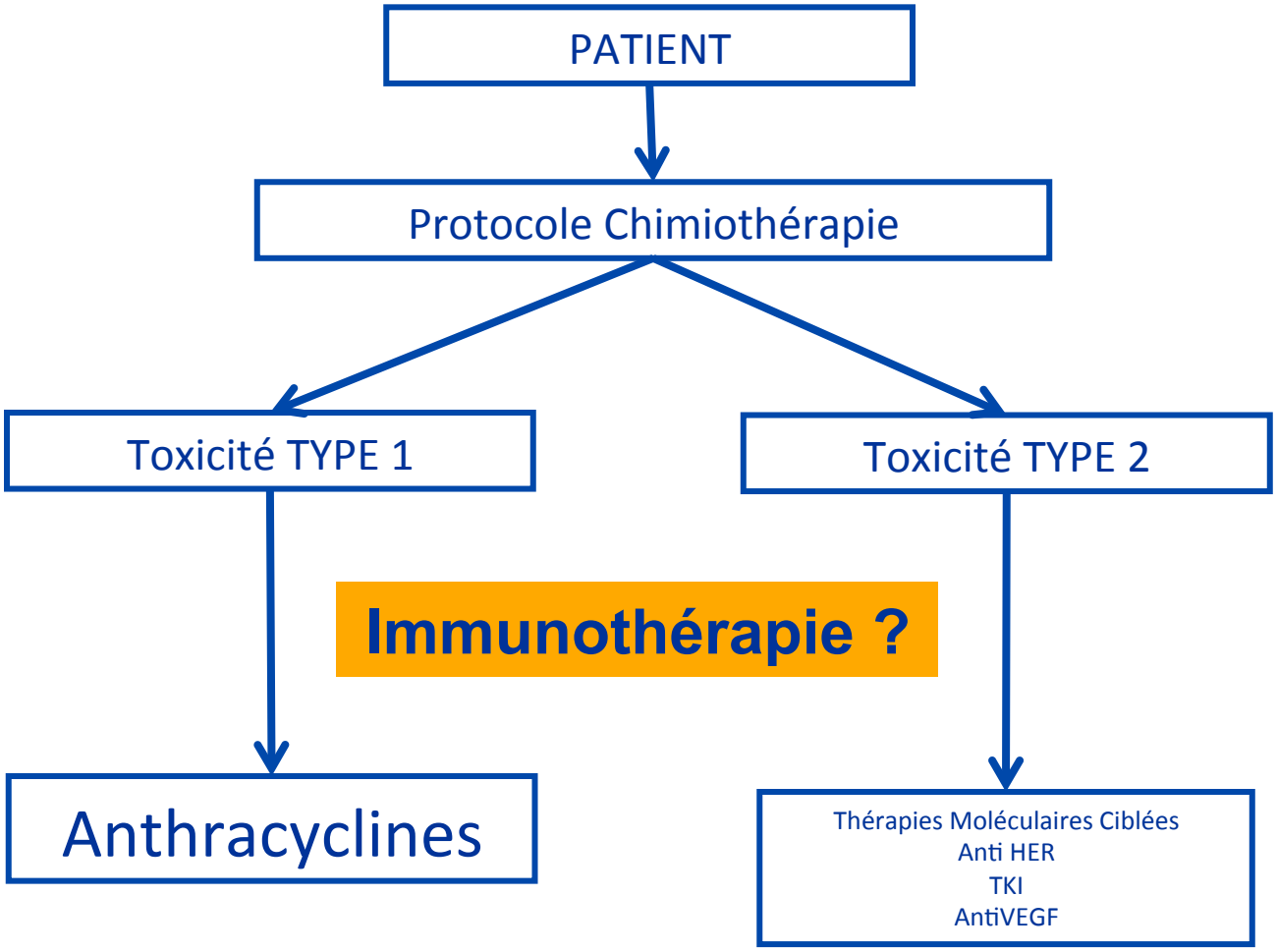
3-year cumulative HF/CM by risk score category

Risk Factor	Hazard Ratio (95% Confidence Interval)	Regression Coefficient	*P* Value	Points Assigned
Adjuvant therapy				
Anthracycline chemotherapy	1.93 (1.11 to 3.36)	0.66	0.020	2
Non-anthracycline chemotherapy	1.64 (0.99 to 2.73)	0.50	0.055	2
No identified chemotherapy	Reference	Reference		
Age category, y				
67 to 74	Reference	Reference		
75 to 79	1.36 (0.92 to 2.01)	0.31	0.125	1
80 to 94	2.04 (1.29 to 3.24)	0.71	0.003	2
Cardiovascular conditions and risk factors				
Coronary artery disease	2.16 (1.21 to 3.86)	0.77	0.009	2
Atrial fibrillation/flutter	1.69 (0.98 to 2.91)	0.53	0.058	2
Diabetes mellitus	1.50 (1.03 to 2.18)	0.41	0.034	1
Hypertension	1.44 (0.99 to 2.08)	0.36	0.054	1
Renal failure	1.99 (0.96 to 4.14)	0.69	0.065	2



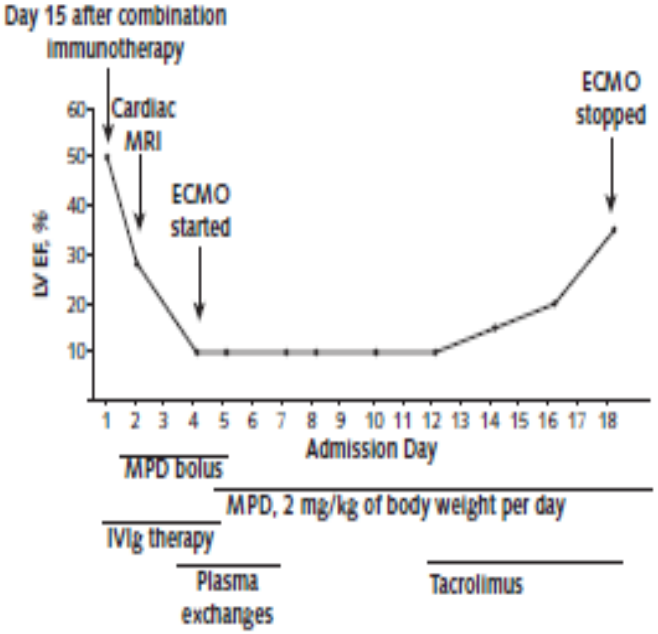
Ezaz G J Am Heart Assoc. 2014 ;3:e000472.

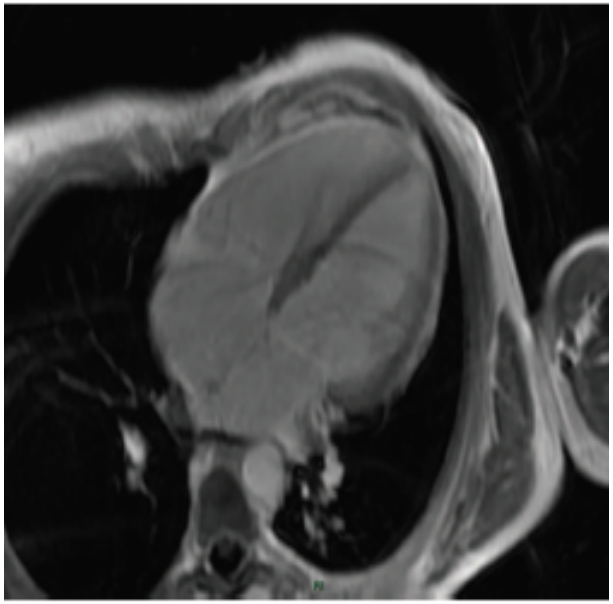
How to prevent LV systolic dysfunction secundary to chemotherapy?



Adapté de Plana J Am Soc Echocardiogr 2014;27:911-39

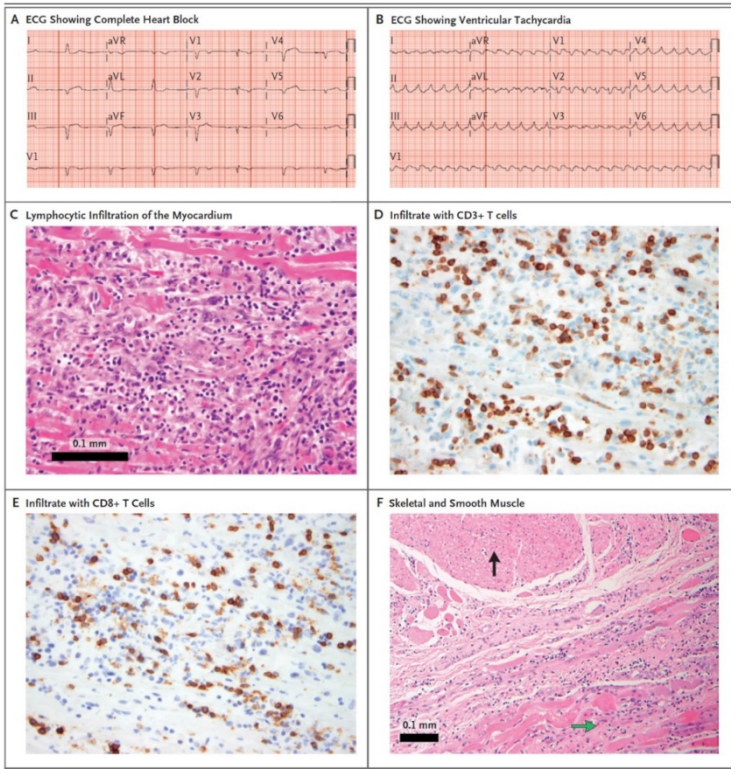
Survival After Fulminant Myocarditis induced by Immune-checkpoints inhibitors





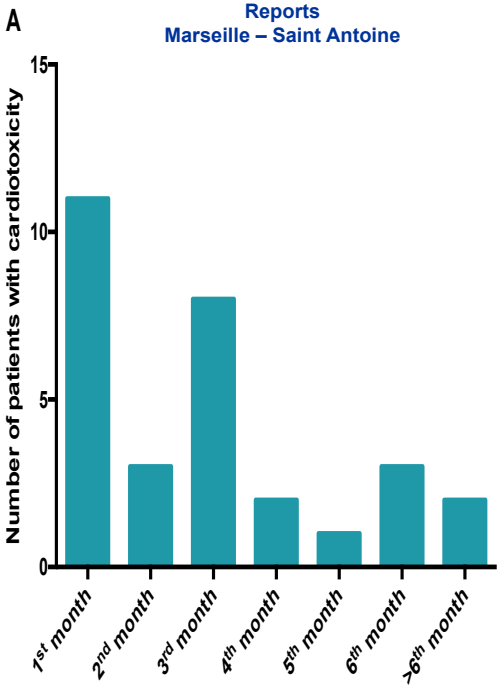
Arangalage Ann Intern Med. 2017

Fulminant Myocarditis with Combination Immune Checkpoint Blockade



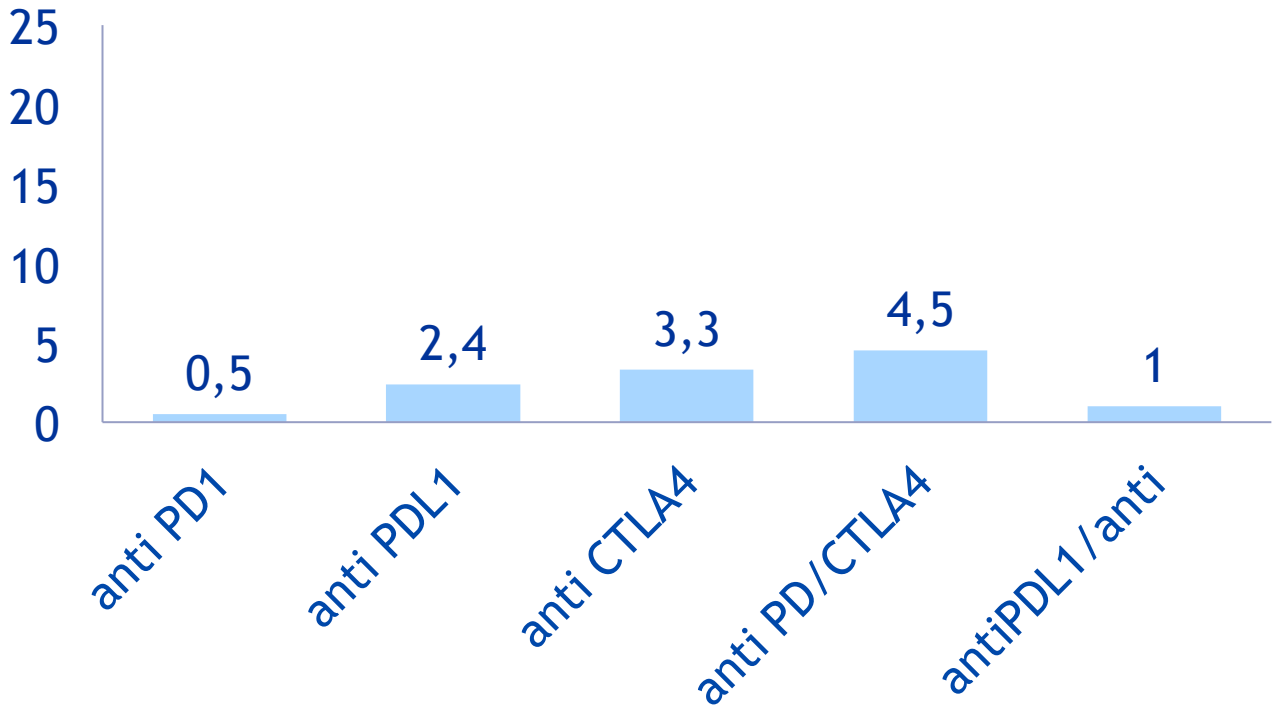
Johnson DB New Engl J Med 2016 ; 375 : 1749-1755

Immune Checkpoint Blockers-Related Cardiotoxicity: A Pooled Analysis of A New Case Series and Previous Reports
Marseille – Saint Antoine



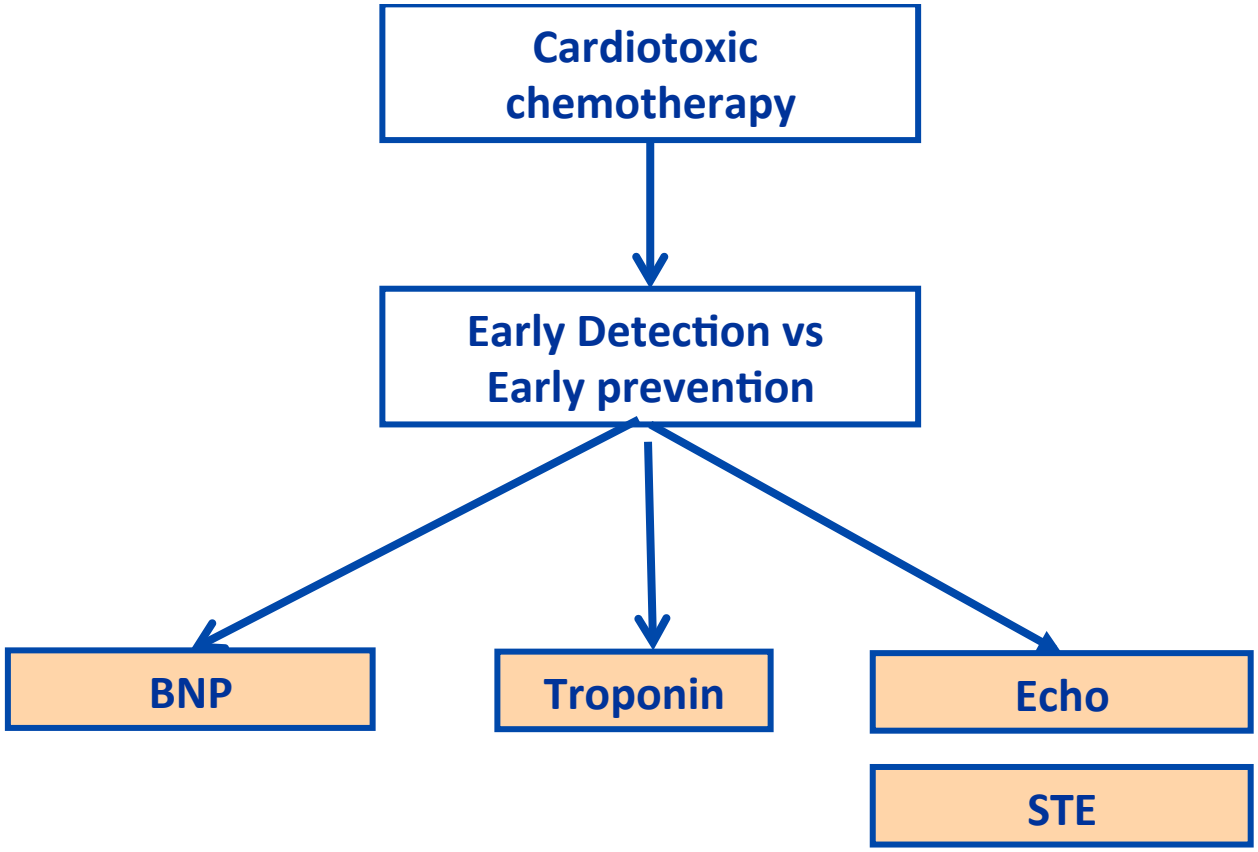
Escudier M, Circulation. 2017 ;136 : 2085-2087.

Myocarditis in Patients Treated With Immune Checkpoint Inhibitors
Myocarditis Incidence



Mahmood SS. J Am Coll Cardiol. 2018 Apr 24;71(16):1755-1764.

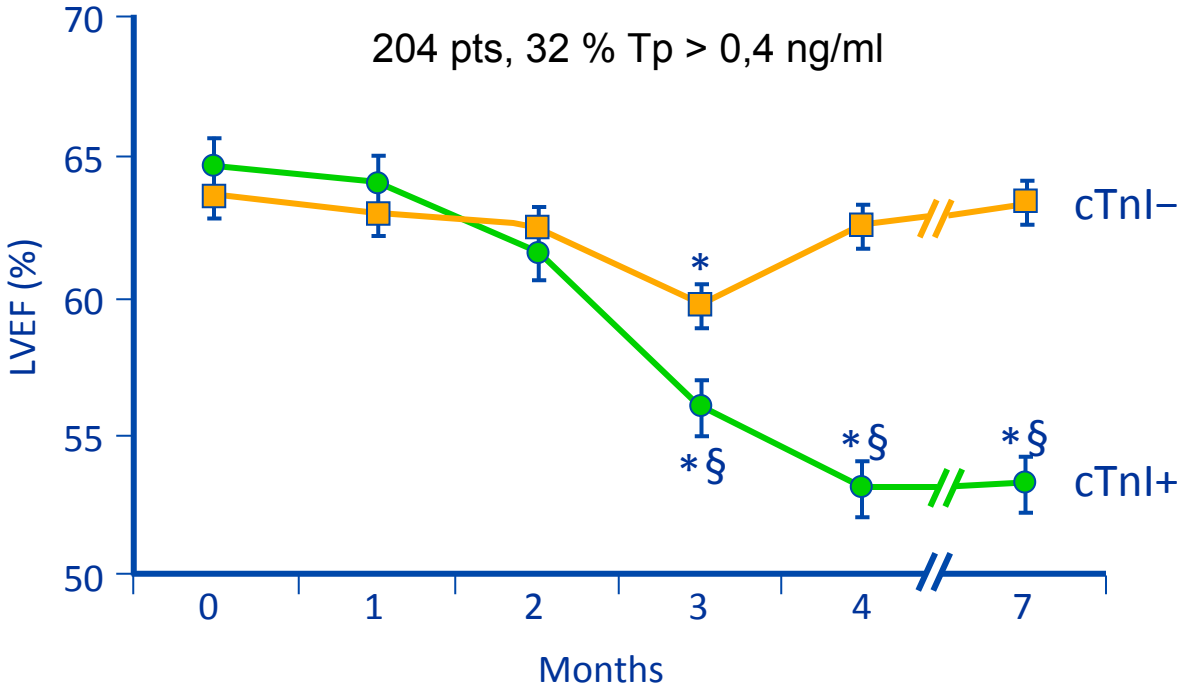
How to prevent LV systolic dysfunction secundary to chemotherapy?



Natriuretic peptides in the monitoring of anthracycline induced reduction in LVEF.

Author, year	Marker	Tumor / Chemo	Asym LVSD	Symp LVSD
Mercuro, 2007	BNP	Various/ATC	No association	No association
Dodes, 2008	NTpro BNP		No association	No association
Feola, 2011	BNP			Associated
Romano, 2011	NT proBNP,	NHDC		LVEFdysfunction
Fallah-Rad,2011	Nt pro BNP	BC/ATC, TZM	No elevation	
Sawaya, 2012	NT pro BNP	BC/ATC, TZM		Not associated
Kittiwarawut, 2013	NT pro BNP	BC /ATC	FS	Not available
Drafts, 2013	BNP	BC, NHL, A ML	No association	No Association

Left Ventricular Dysfunction Predicted By Early Troponin I Release



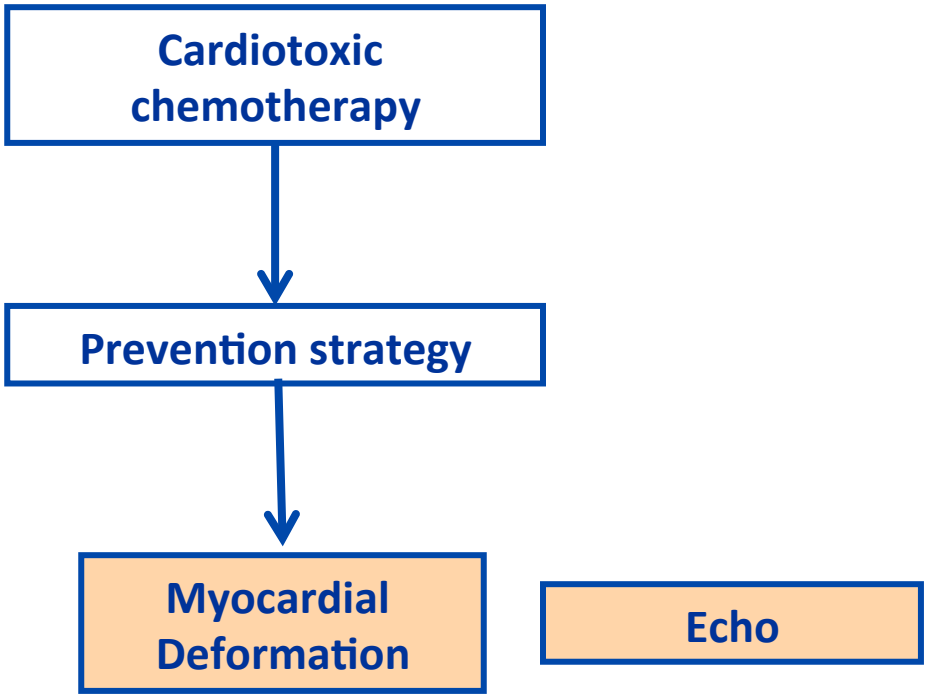
Cardinale et al. J Am Coll Cardiol 2000;36:517-522

Troponin and detection of cardiotoxicity

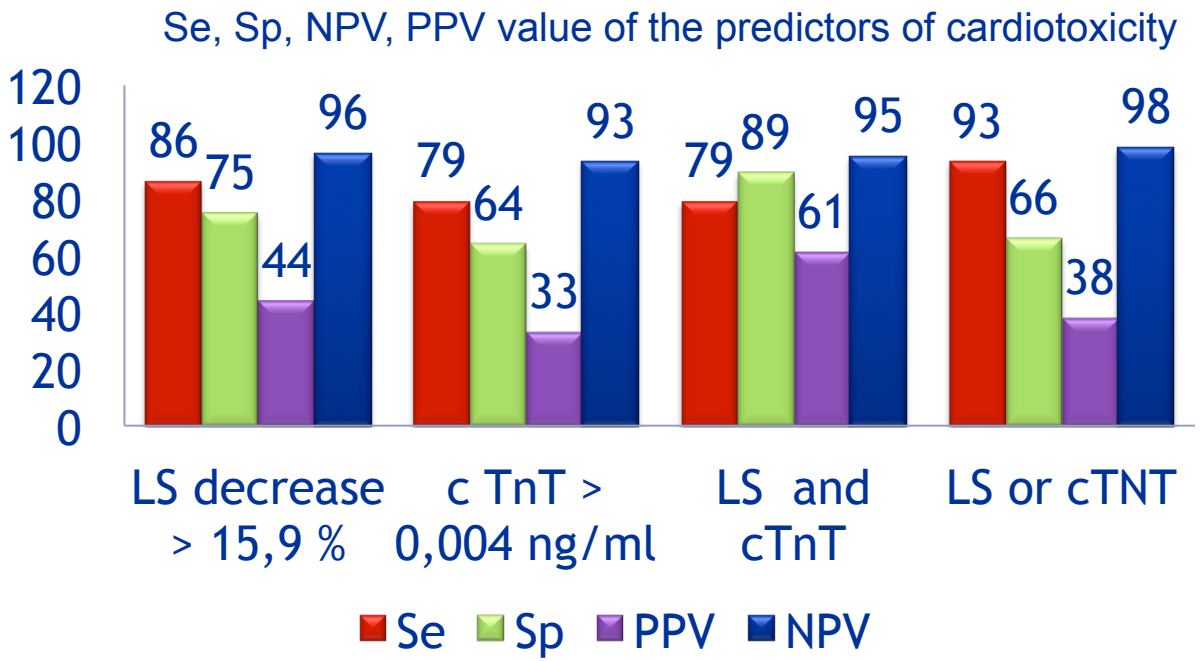
Author,year	Method, Cut off	Tumors / Chemo	% Tp > cut off	Main result
Cardinale, 2000	TnI, >0.4ng/ml	Various/ ATC	32 %	LVSD
Cardinale, 2002	TnI, >0.5ng/ml	BC/ATC	33%	LVSD
Sandri, 2003	TnI, 0.08micro/l	Various /ATC	32%	LVSD
Auner, 2003	TnT, ≥ 0.03ng/ml	Hemato /ATC	15 %	LVSD
Cardinale,2004	TnI,, >0.08ng/ml	HDC/ATC	30 %	Cardiac events
Kilickap, 2005	TnT, >0.1ng/ml	/ATC	34 %	DD
Horacek, 2008	TnI or T, > 0.4ug/l	AL/ATC	17.4%	LVSD, HF
Mercuro, 2007	TnI			
Nistico, 2007	TnT,	BC/ATC	0%	No association with LVSD
Dodes, 2008	TnT	ATC	0 %	No association with LVSD
Cardinale, 2010	TnI,	BC/ATC,TZM	17%	LVSD
Fallah-rad,2011	Tnt, >0,01ug/l	BC/ATC, TZM	No elevation	No association with LVSD
Sawaya, 2012	TnUS, >30pg/ml	BC/ATC, TZM	33%	LVSD
Mornos, 2013	TnT,	NHL,HL/ATC	NA	No association with LVSD
Kittiwarawut,2013	TnT,	BC/ATC	NA	No association with LVSD
Drafts, 2013	TnI, >0.6ng/ml	BC/AL, Lymp	26 %	No association with LVSD
Romano,2012	TnI	N HDC	0%	No association with LVSD

Secondary prevention

Cancer Therapeutics regimens associated with type I and type II Cancer therapeutics related cardiac dysfunction

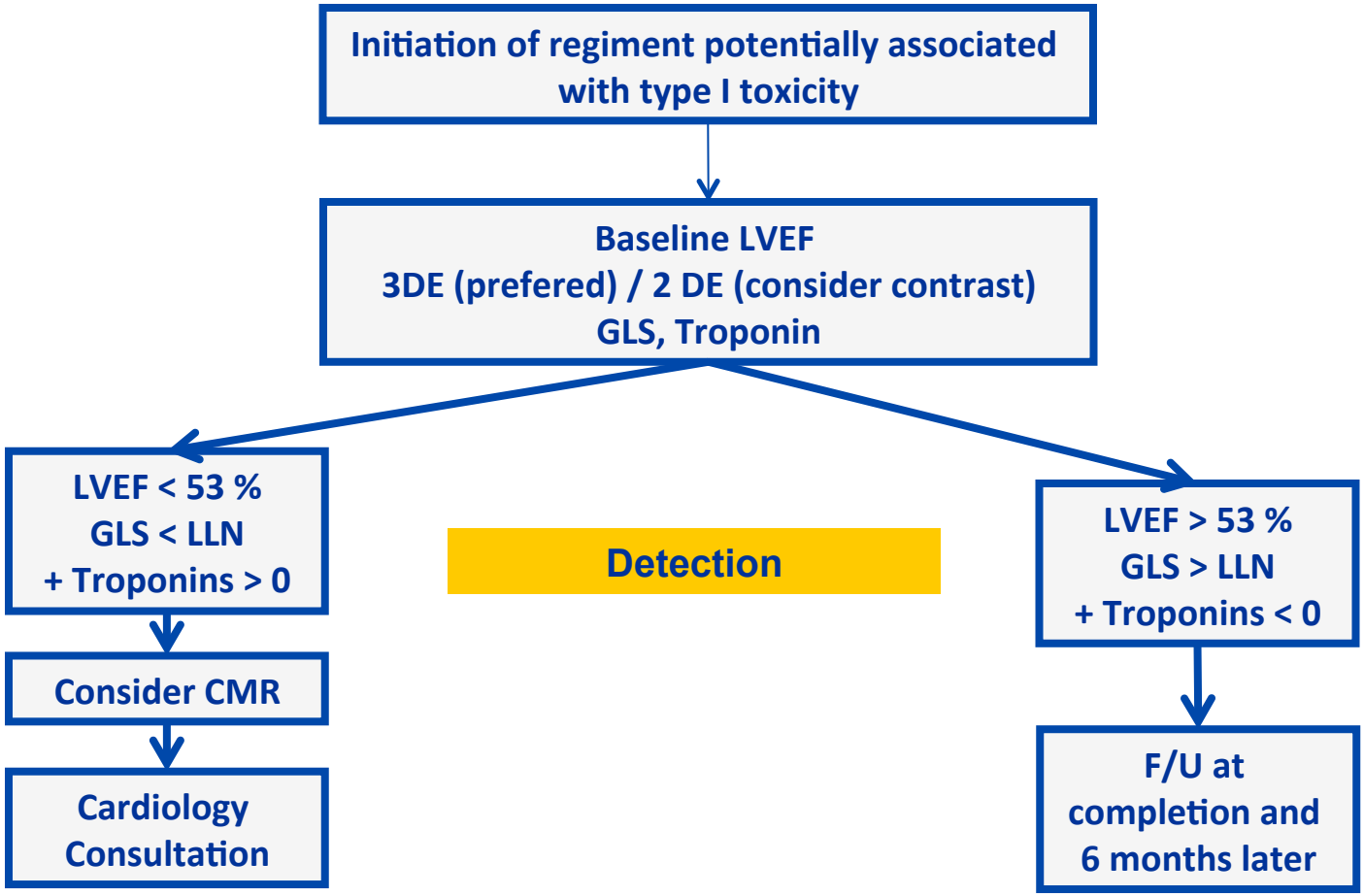


Two-dimensional speckle tracking echocardiography combined with high-sensitive cardiac troponin T in early detection and prediction of cardiotoxicity during epirubicine-based chemotherapy



Kang European Journal of Heart Failure 2014 16, 300–308

How to prevent LV systolic dysfunction secundary to chemotherapy?



Plana J Am Soc Echocardiogr 2014;27:911-39

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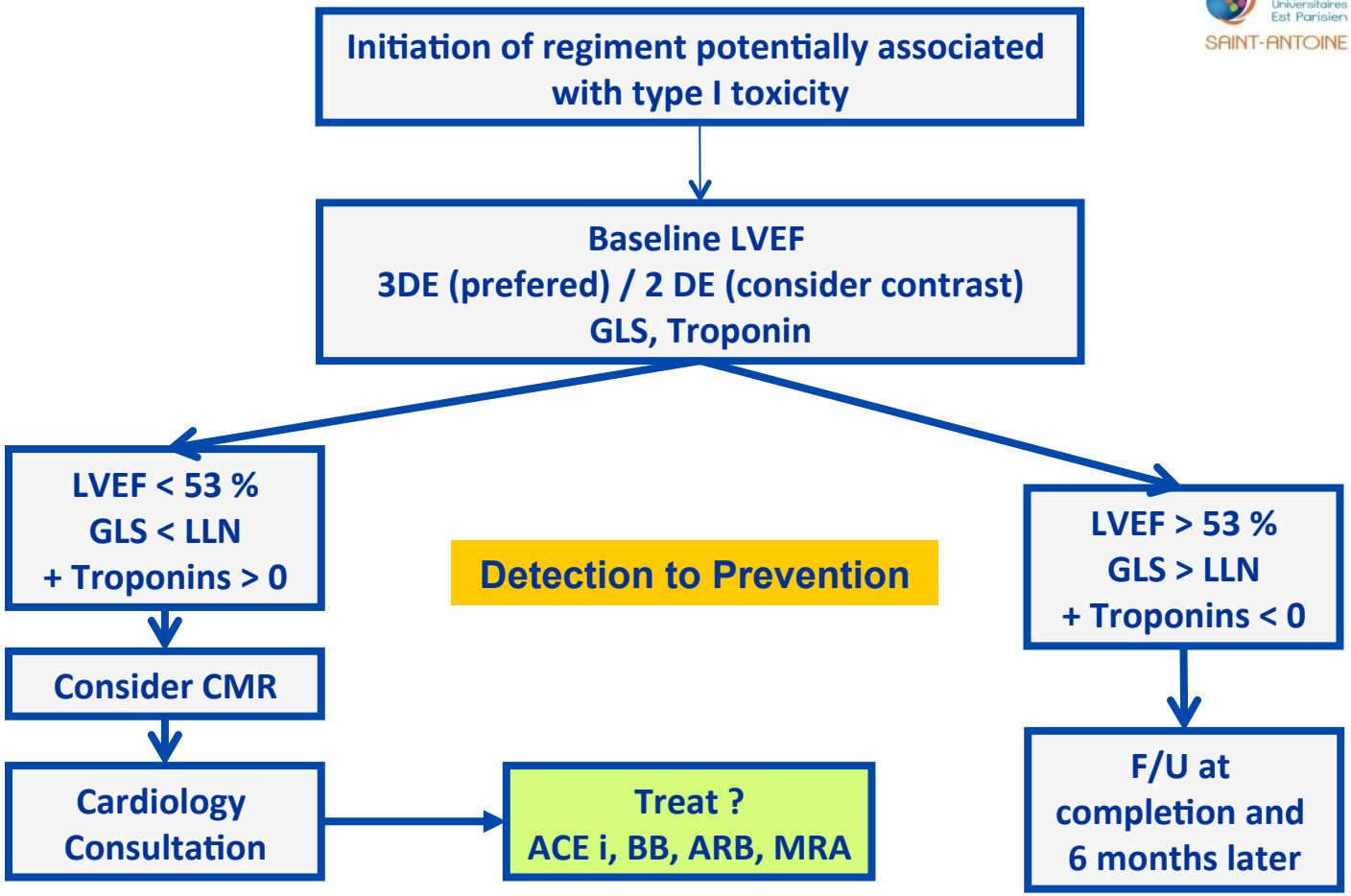

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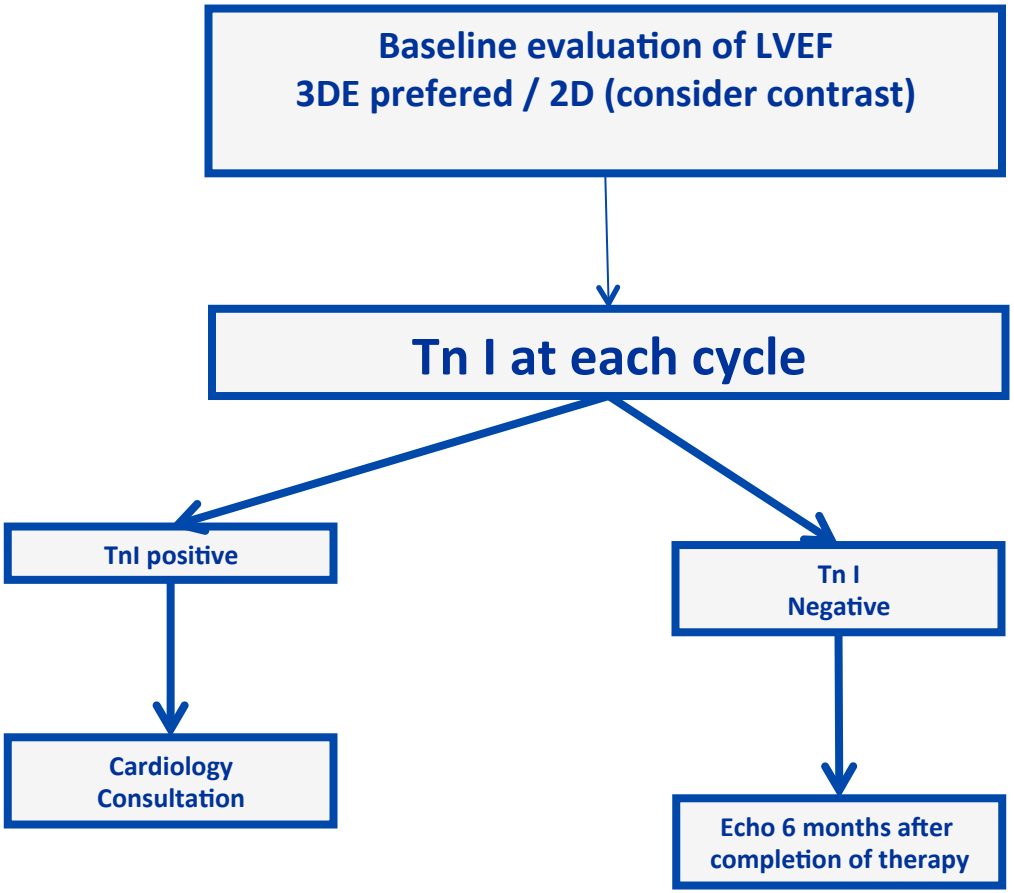

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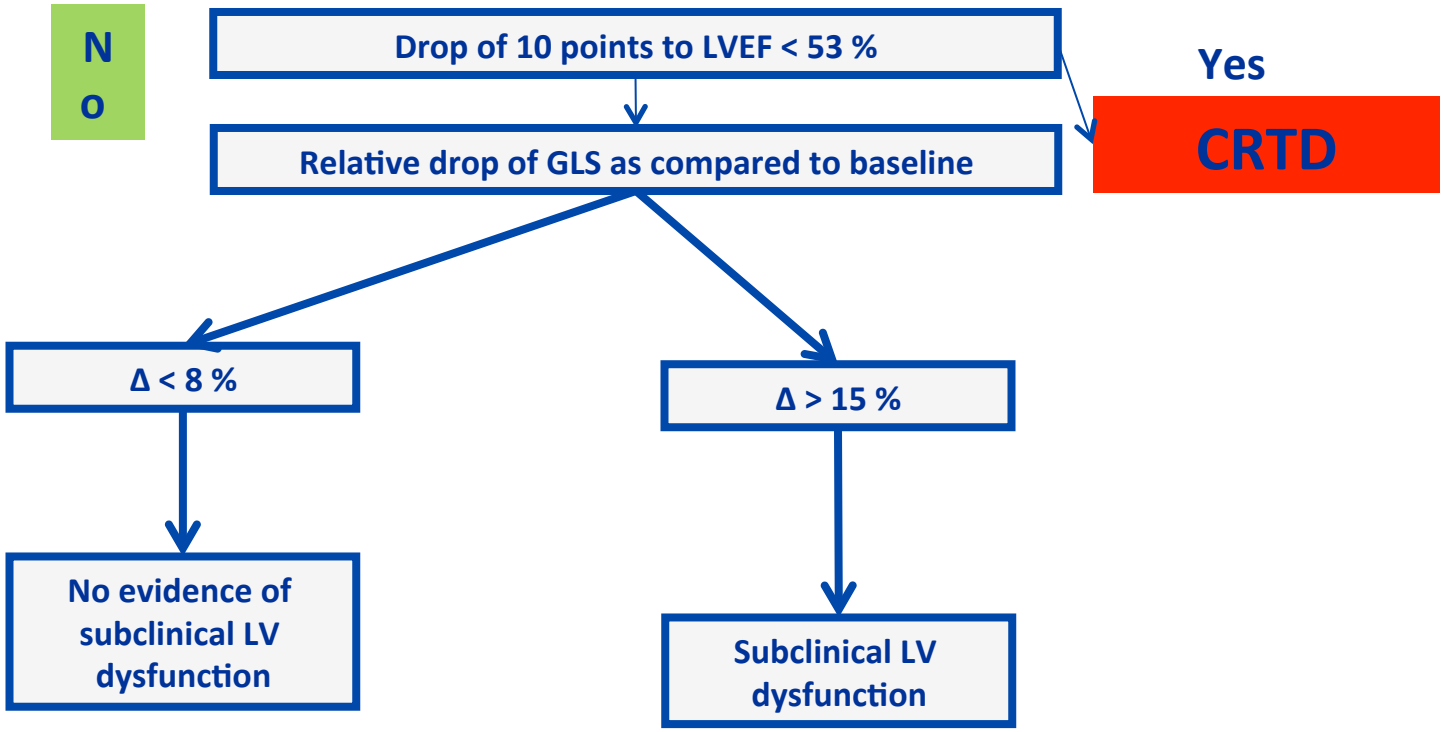
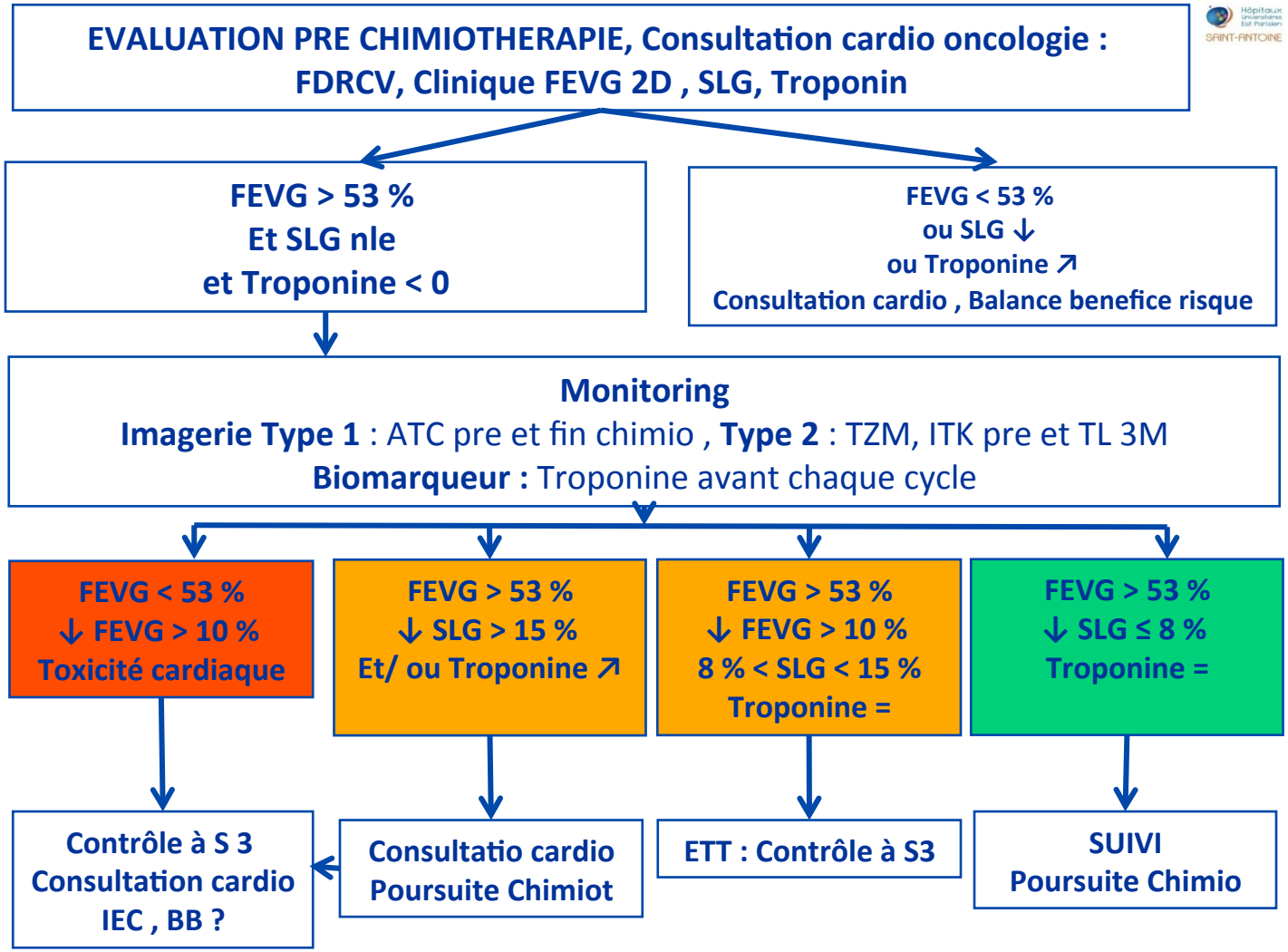


GLS consider Vendor, Gender, Age, loading conditions

Plana J Am Soc Echocardiogr 2014;27:911-39

How to prevent LV systolic dysfunction secundary to chemotherapy?



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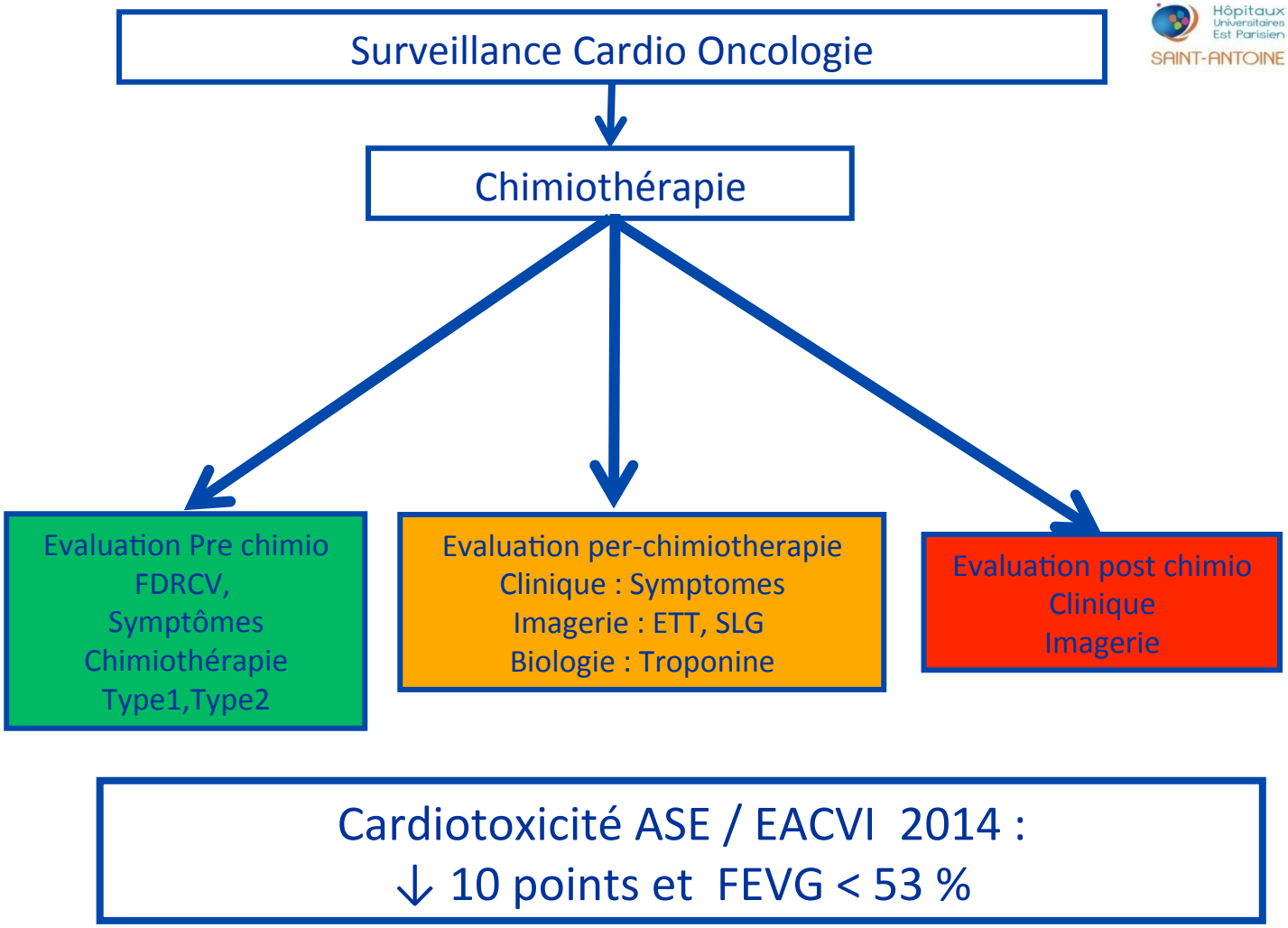
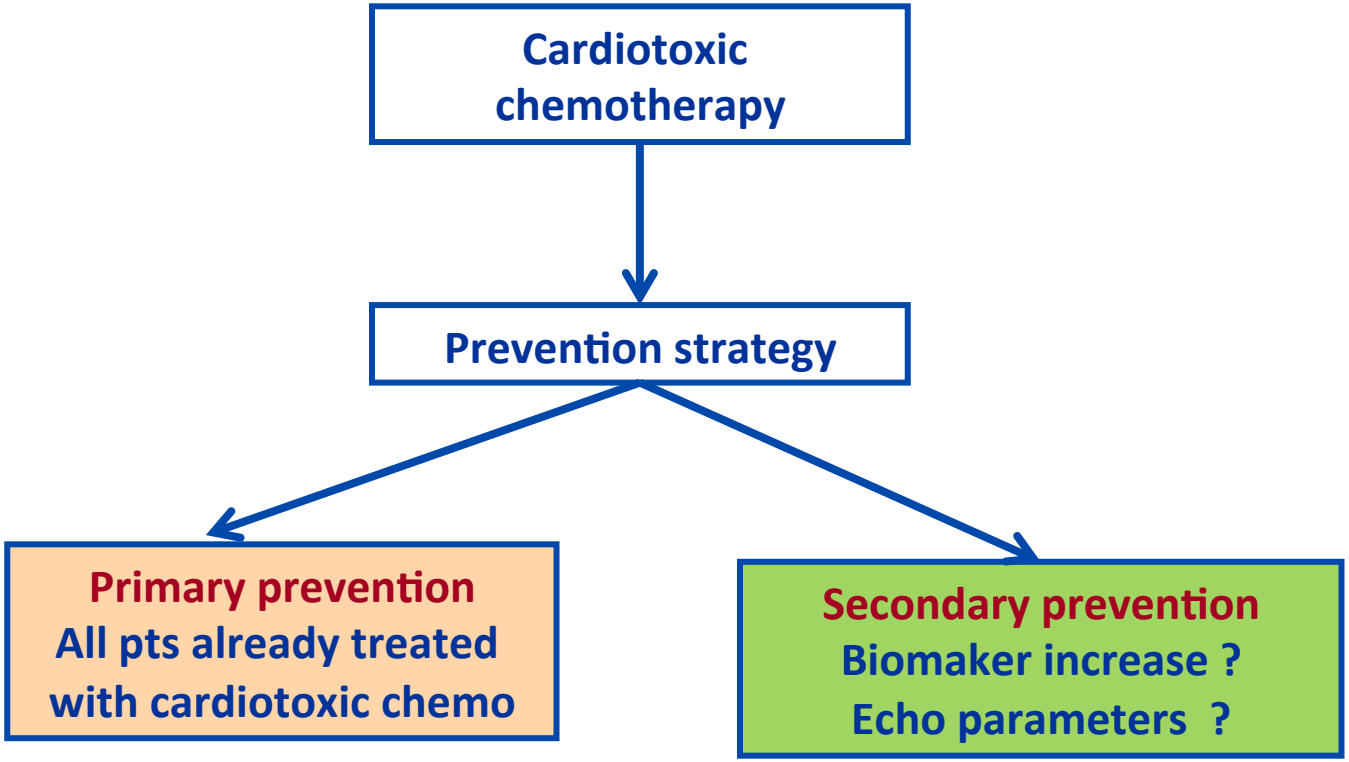
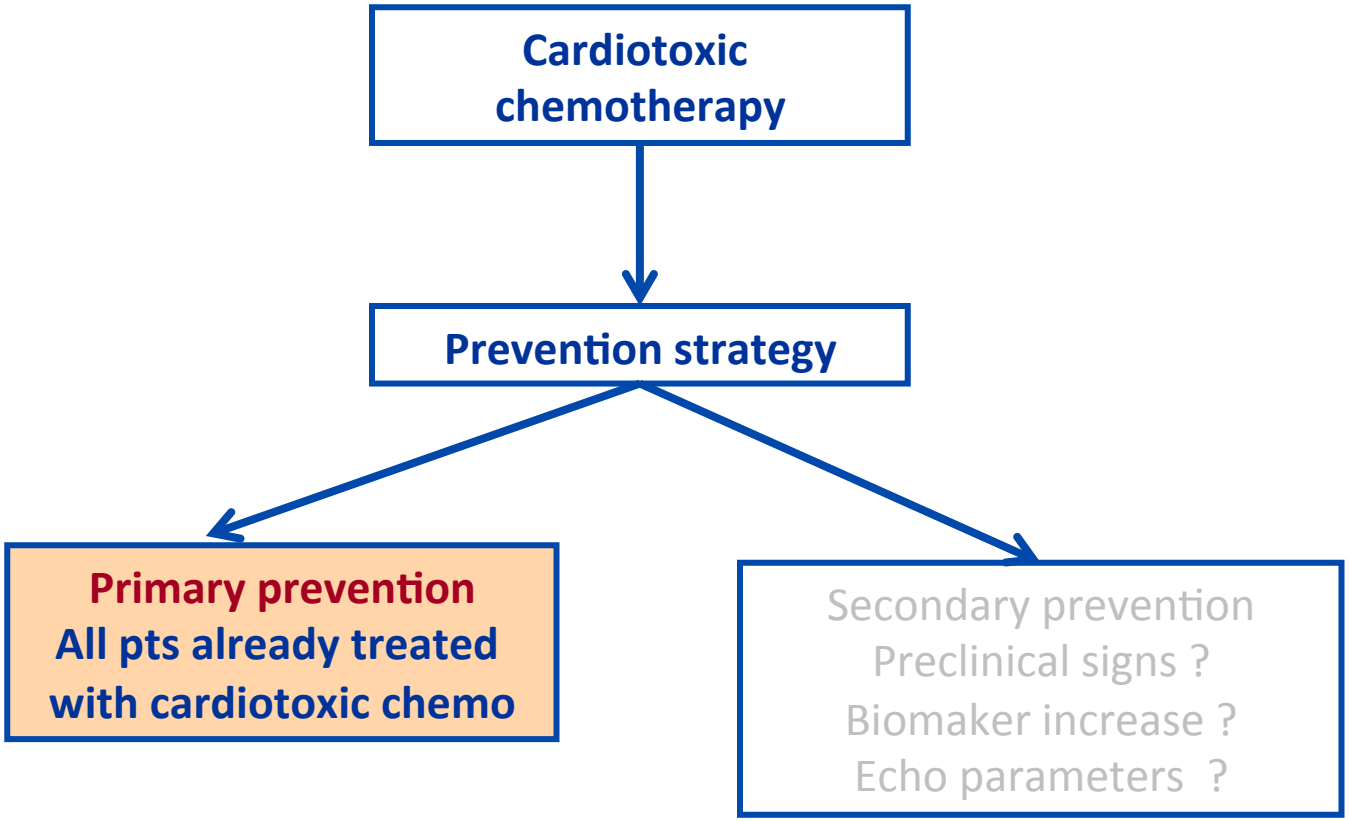


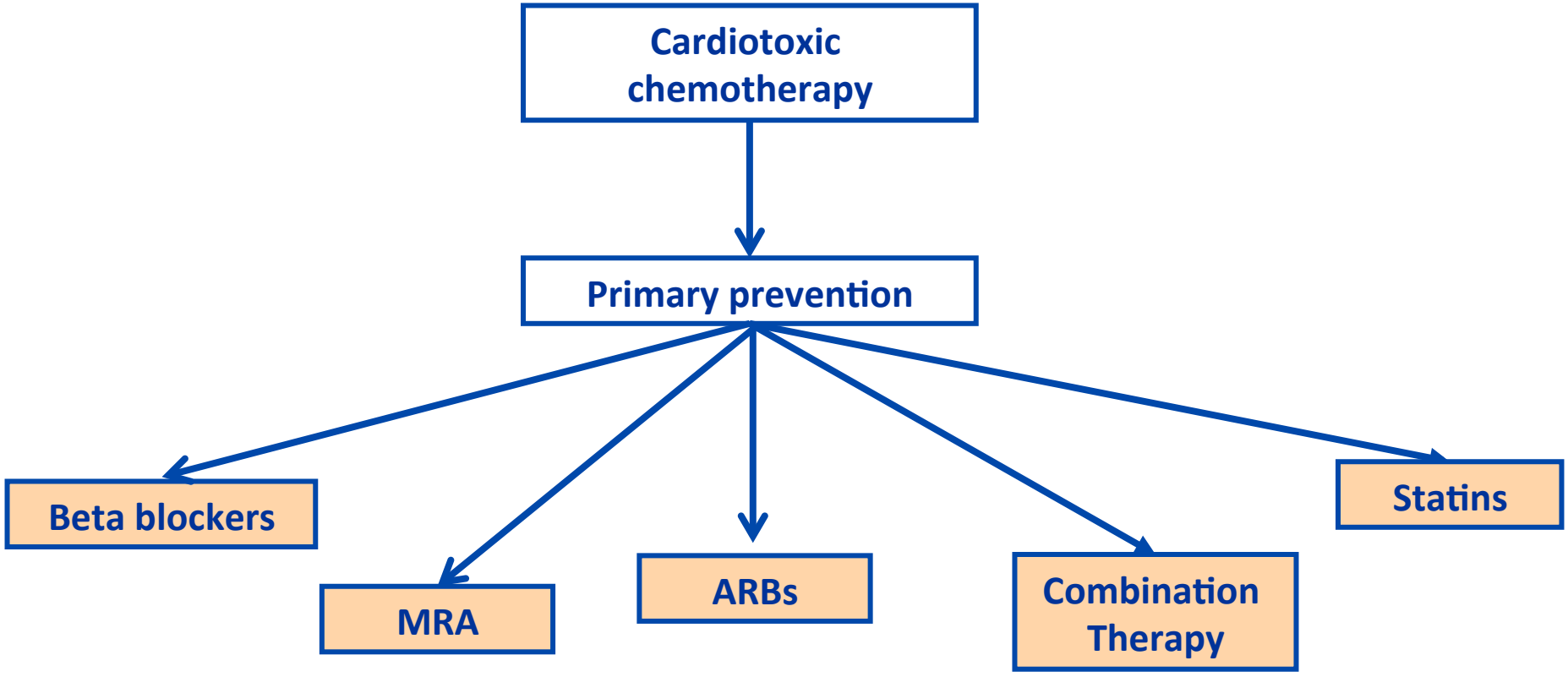
Primary vs Secondary prevention



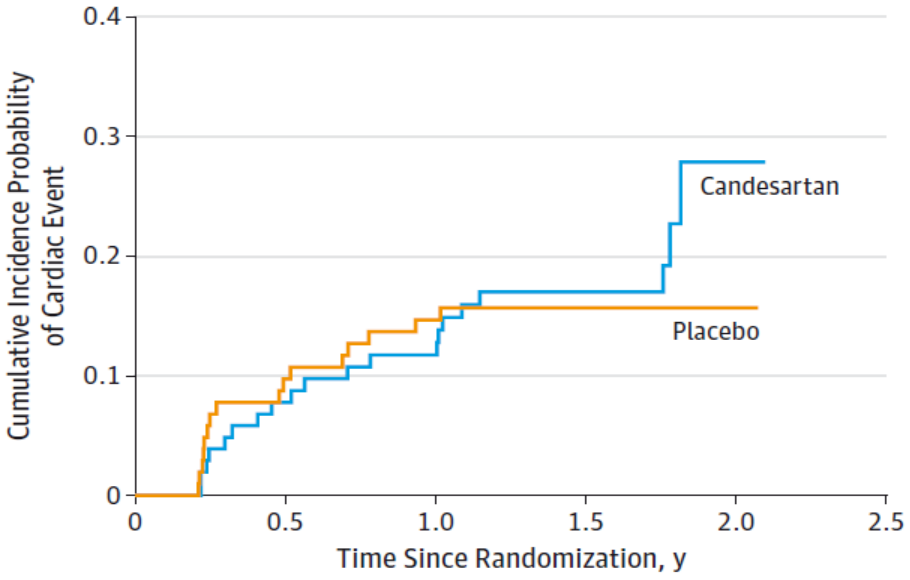
How to prevent LV systolic dysfunction secundary to chemotherapy?



Which strategy for primary prevention



Angiotensin II-receptor inhibition with candesartan to prevent trastuzumab related cardiotoxic effects in patients with early breast cancer

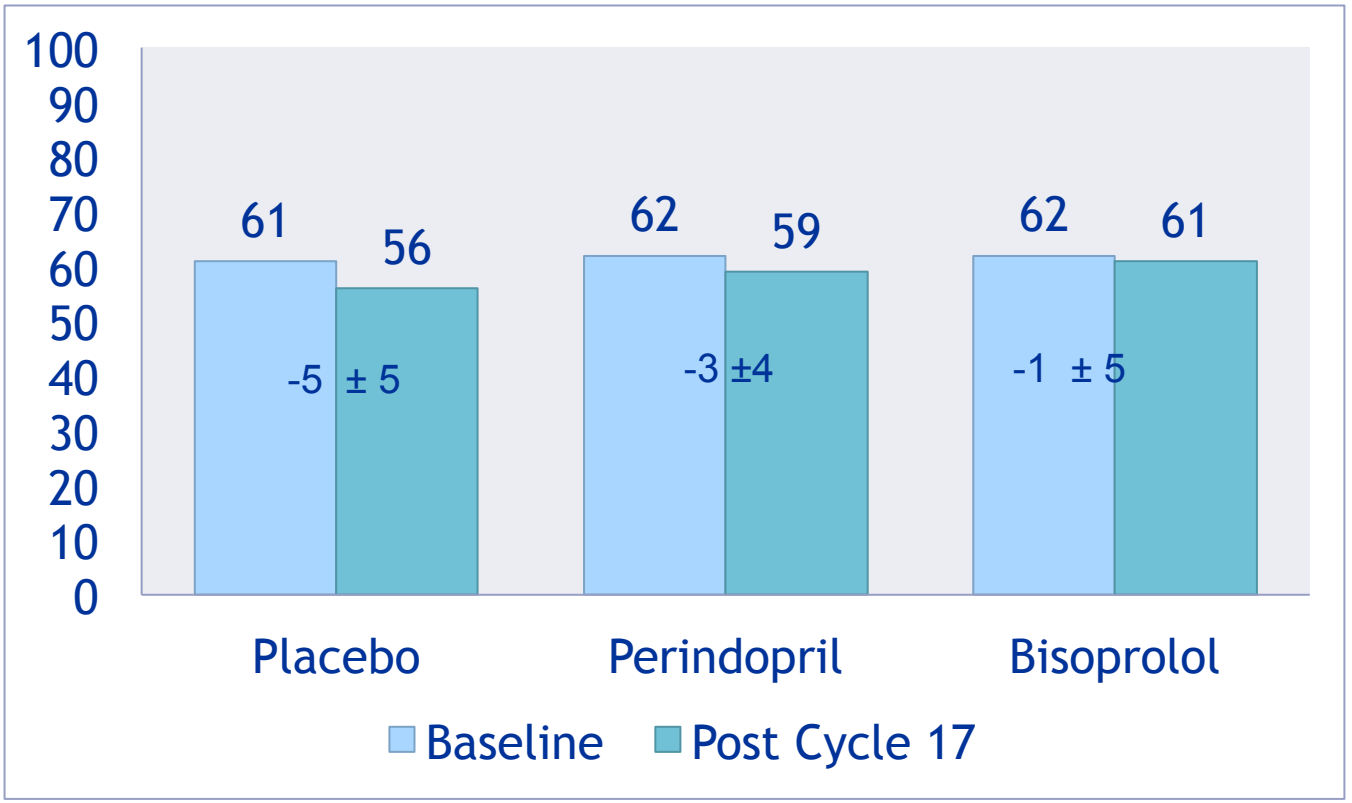


No. at risk						
Candesartan	103	93	84	68	1	0
Placebo	103	92	85	83	4	0

Cumulative 2-year incidences of cardiac events for the patients assigned to candesartan and those assigned to placebo

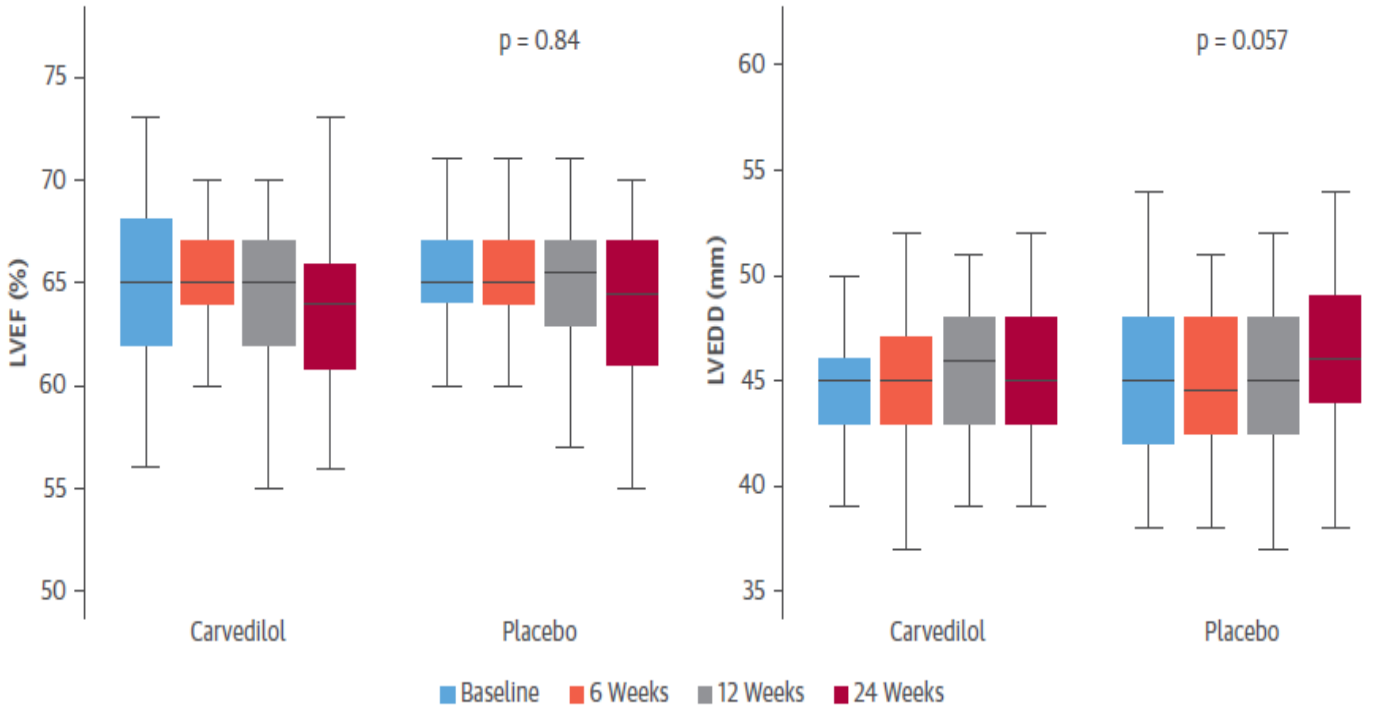
Boekhout A JAMA Oncology 2016 ;2:1030-1307

Multidisciplinary Approach to Novel Therapies in Cardio-Oncology Research (MANTICORE 101-Breast): A Randomized Trial for the Prevention of Trastuzumab-Associated Cardiotoxicity



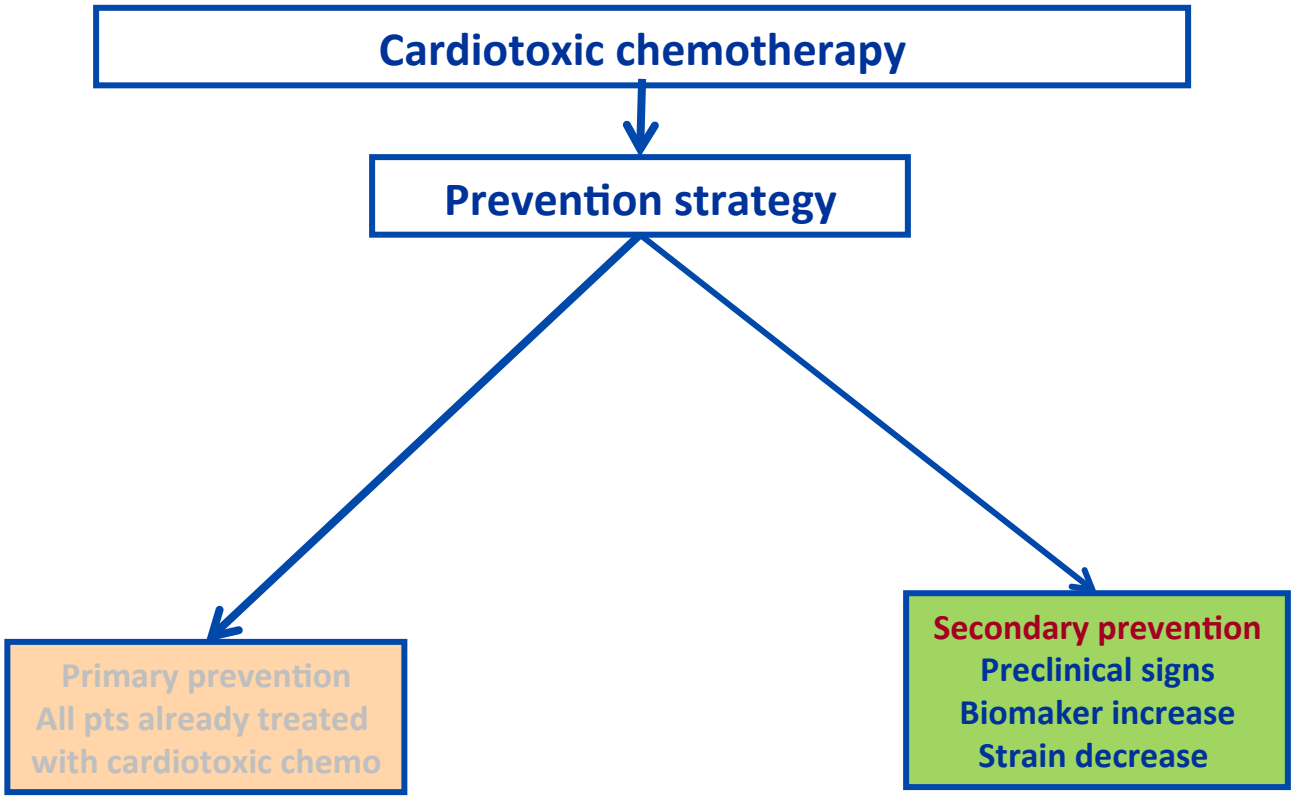
Pituskin J Clin Oncol. 2017 Mar 10;35:870-877

Comparison of placebo and carvedilol in the echo parameters during follow-up

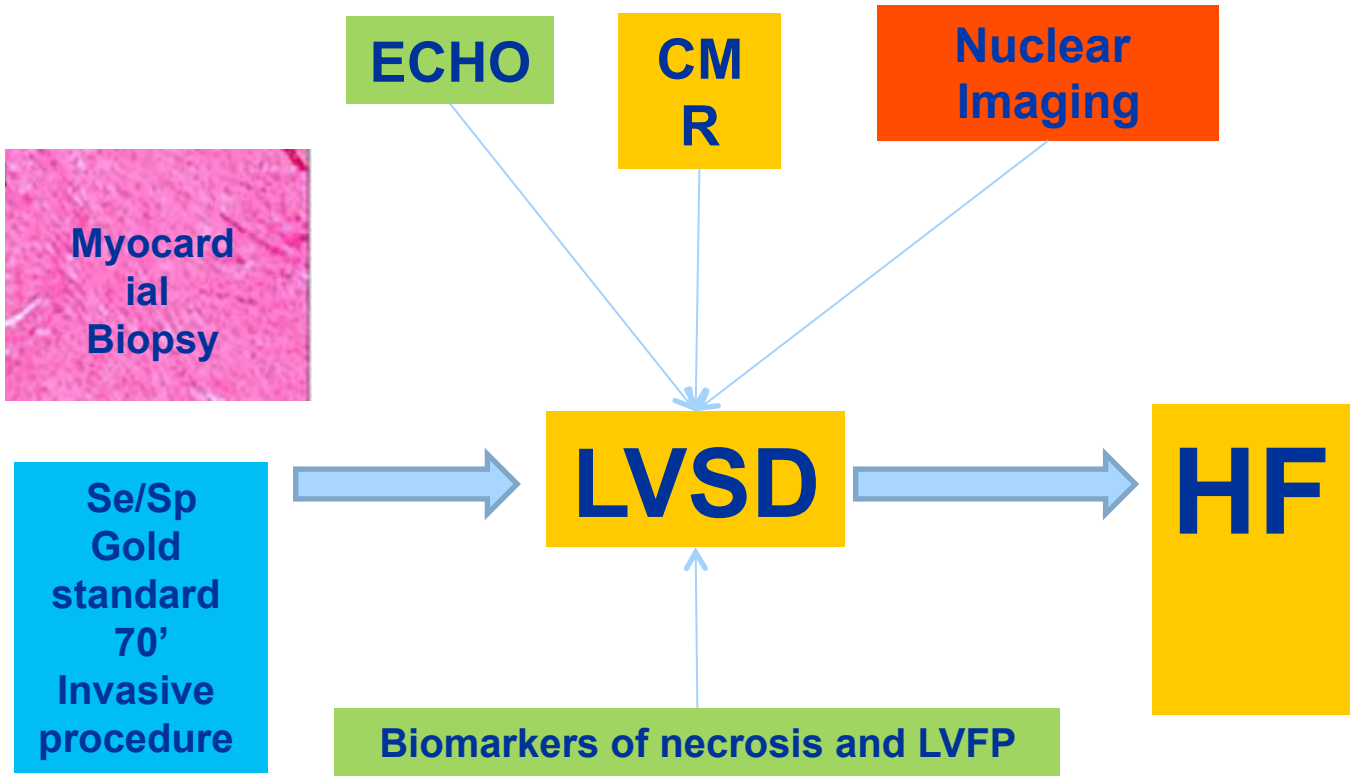


Avila J Am Coll Cardiol 2018;71:2281–90

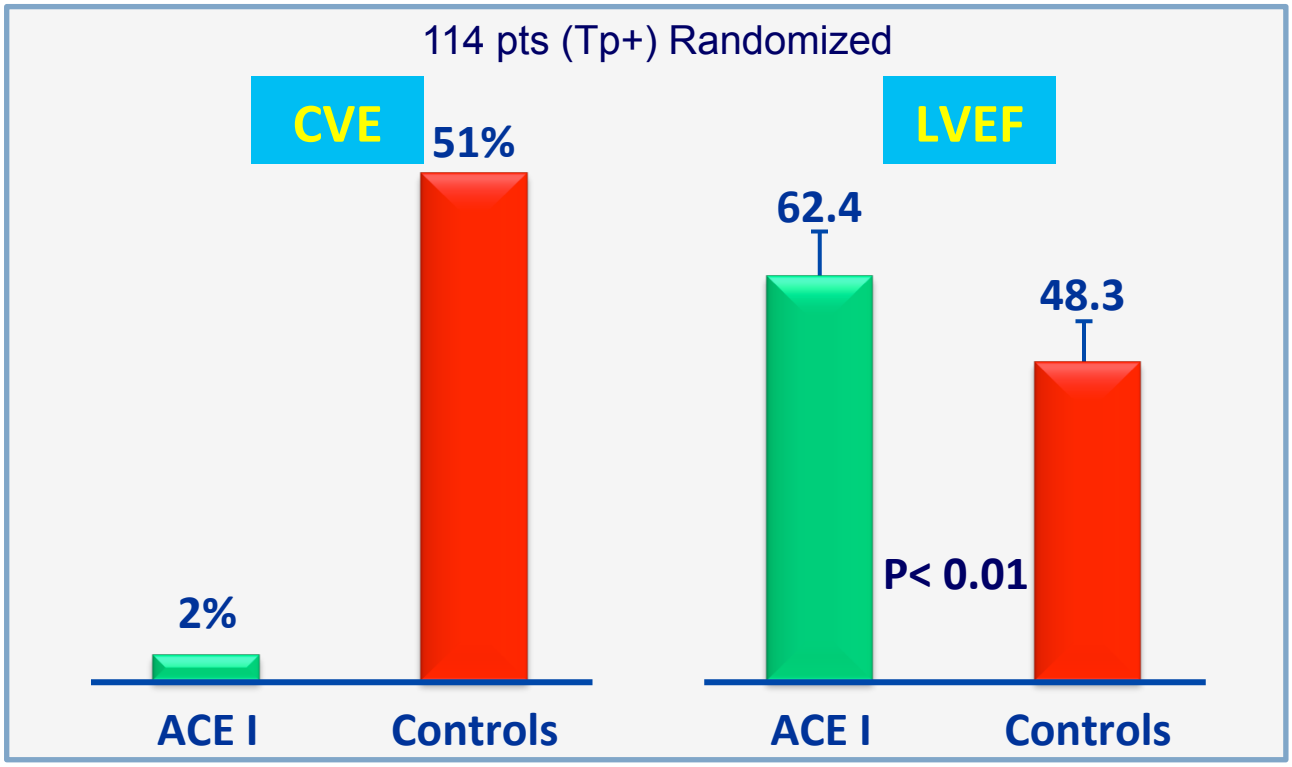
Cancer Therapeutics regimens associated with type I and type II Cancer therapeutics related cardiac dysfunction



What do we have in clinical practice



Prevention of Cardiotoxicity with ACE Inhibitors

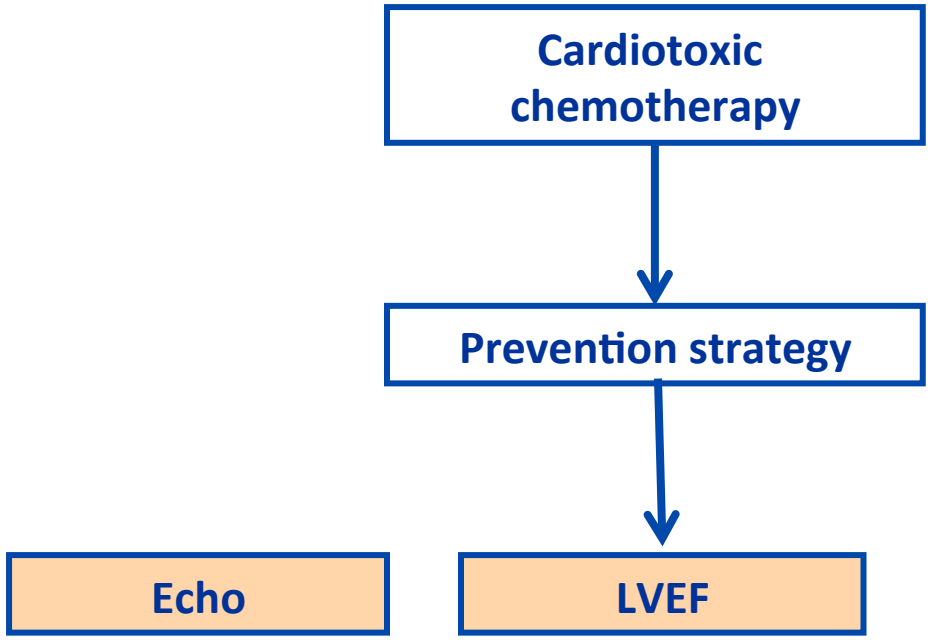


CVE=Cardiovascular event

Cardinale D. Circulation. 2006;114: 2474-81

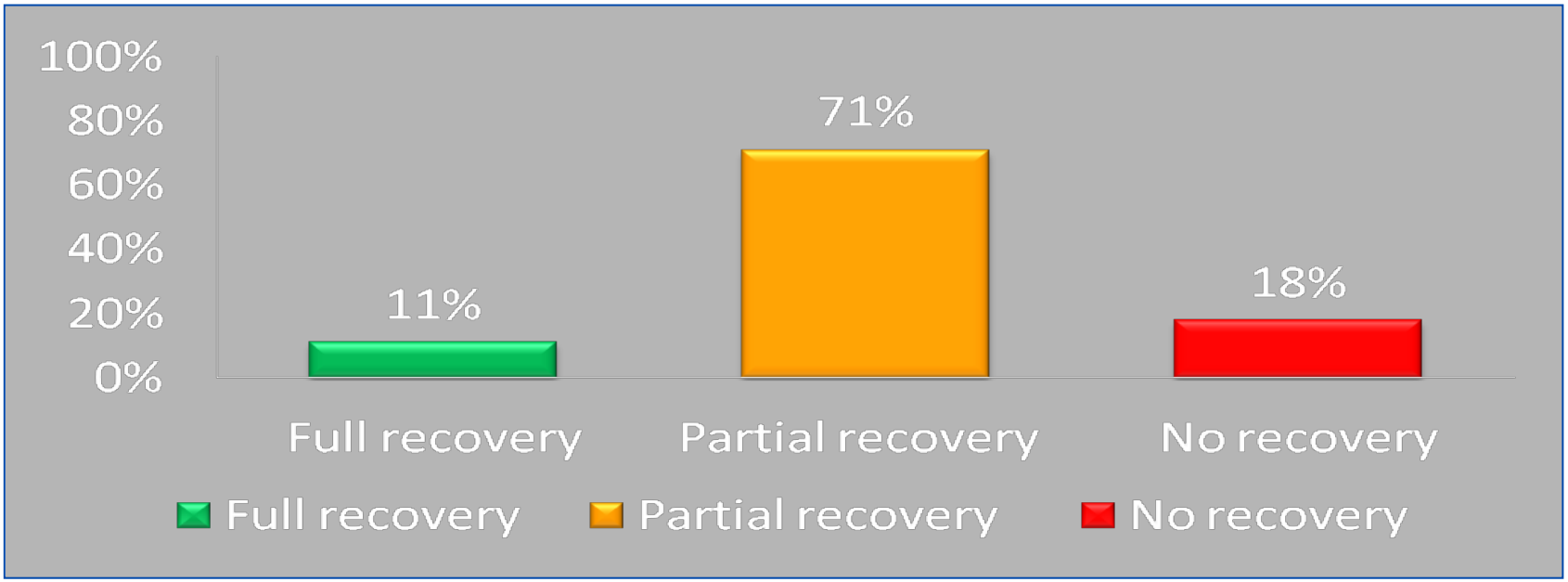
Secondary prevention

Cancer Therapeutics regimens associated with type I and type II Cancer therapeutics related cardiac dysfunction



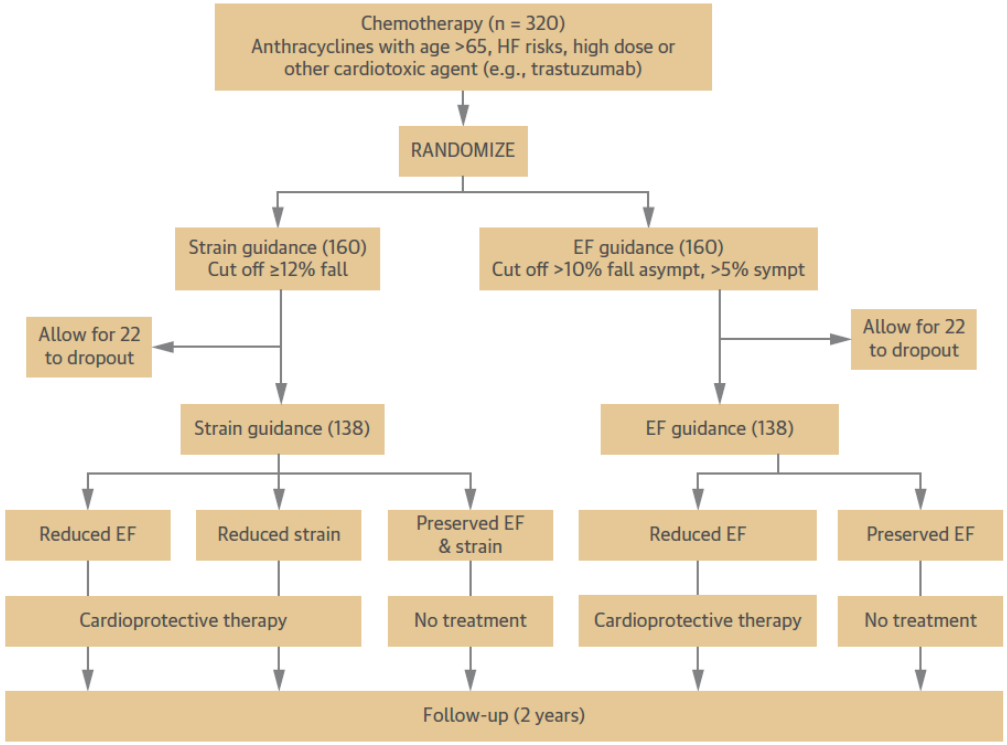
Early detection of ATC cardiotoxicity and improvemetnt with HF
2625 pts, Echo, ACE i + BB

9 % LVEF drop > 10 % unit + LVEF < 50 %



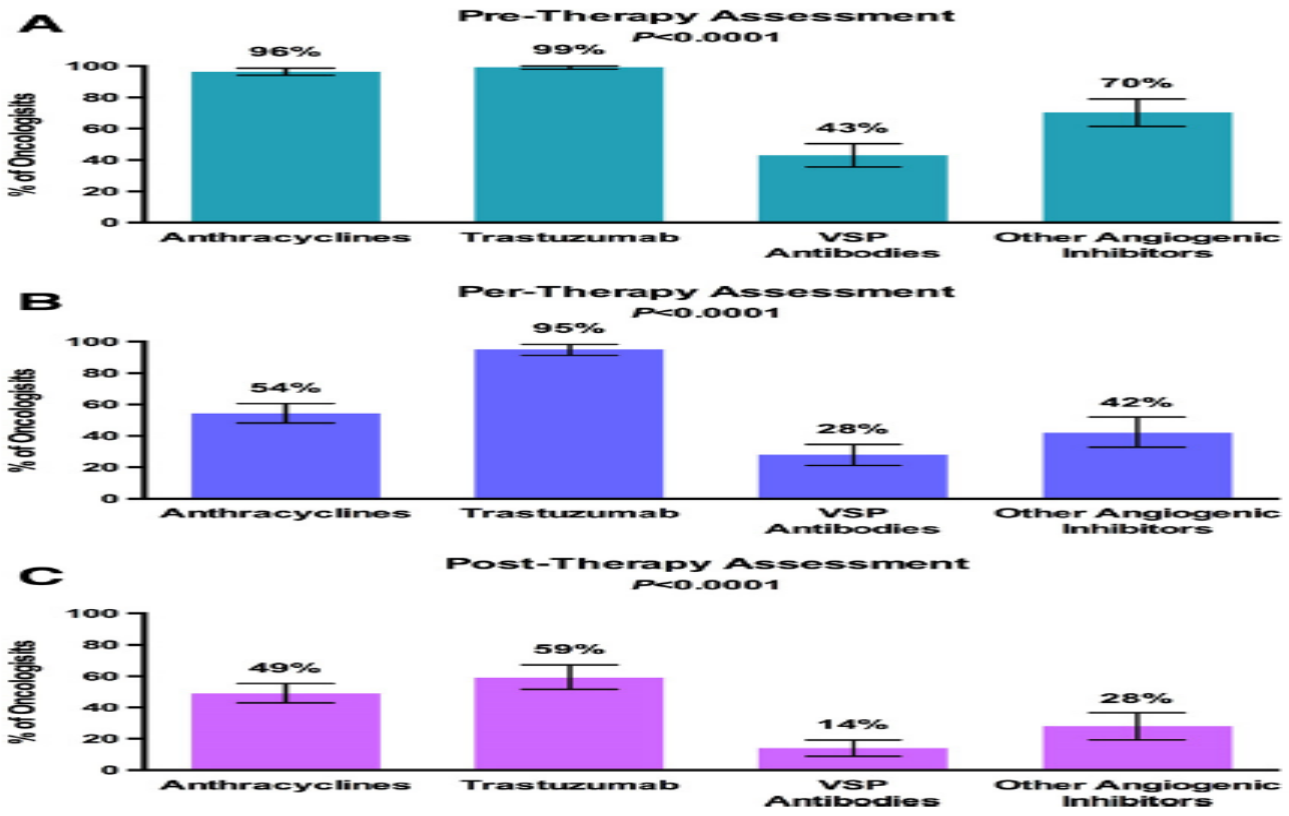
Cardinale D. Circulation. 2015;131: 1981-8

The Strain Surveillance of Chemotherapy for Improving Cardiovascular Outcomes: The SUCCOUR Trial. .



Negishi T JACC imaging 2018 ;11:1098-1105.

Practices in management of cancer treatment-related cardiovascular toxicity: A cardio-oncology survey.



Jovenaux L. Int J Cardiol. 2017 ;241:387-392.

Conclusion

1- Anthracycline , Molecular tageted Agent and Immunotherapy are associated with an increased risk of HF

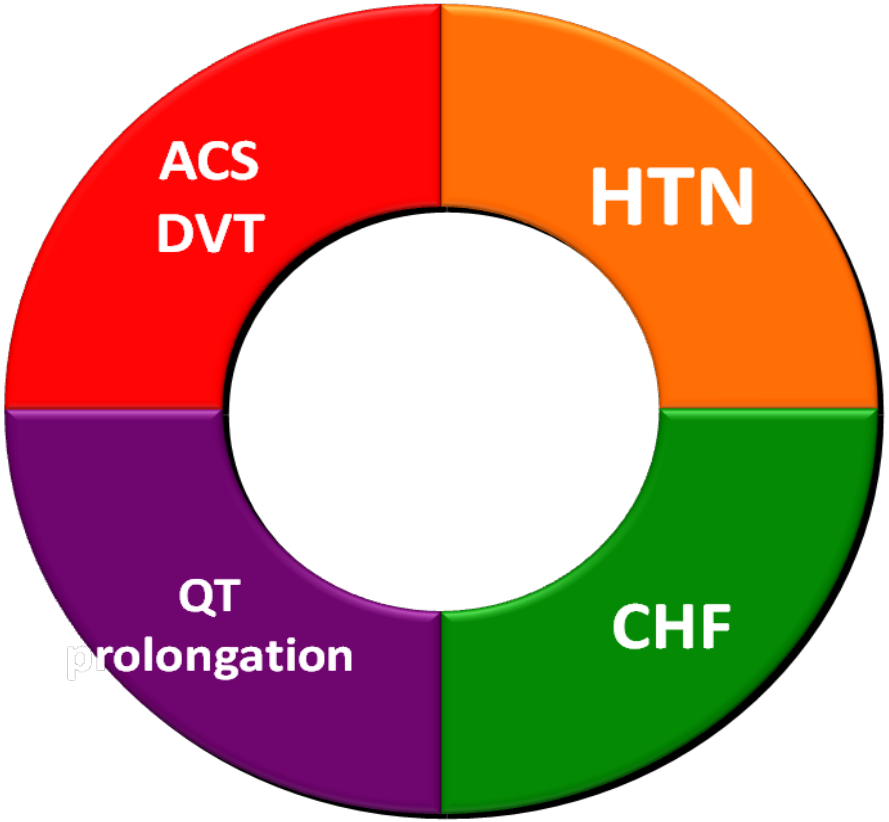
3- Guidelines on detection of cardiotoxicity

2- Limited data on cardioprotection in patients receiving trastuzumab or molecular targeted agents

3- No date on the best way to assess cardiotoxicity in cancer patients treated with Immunotherapy

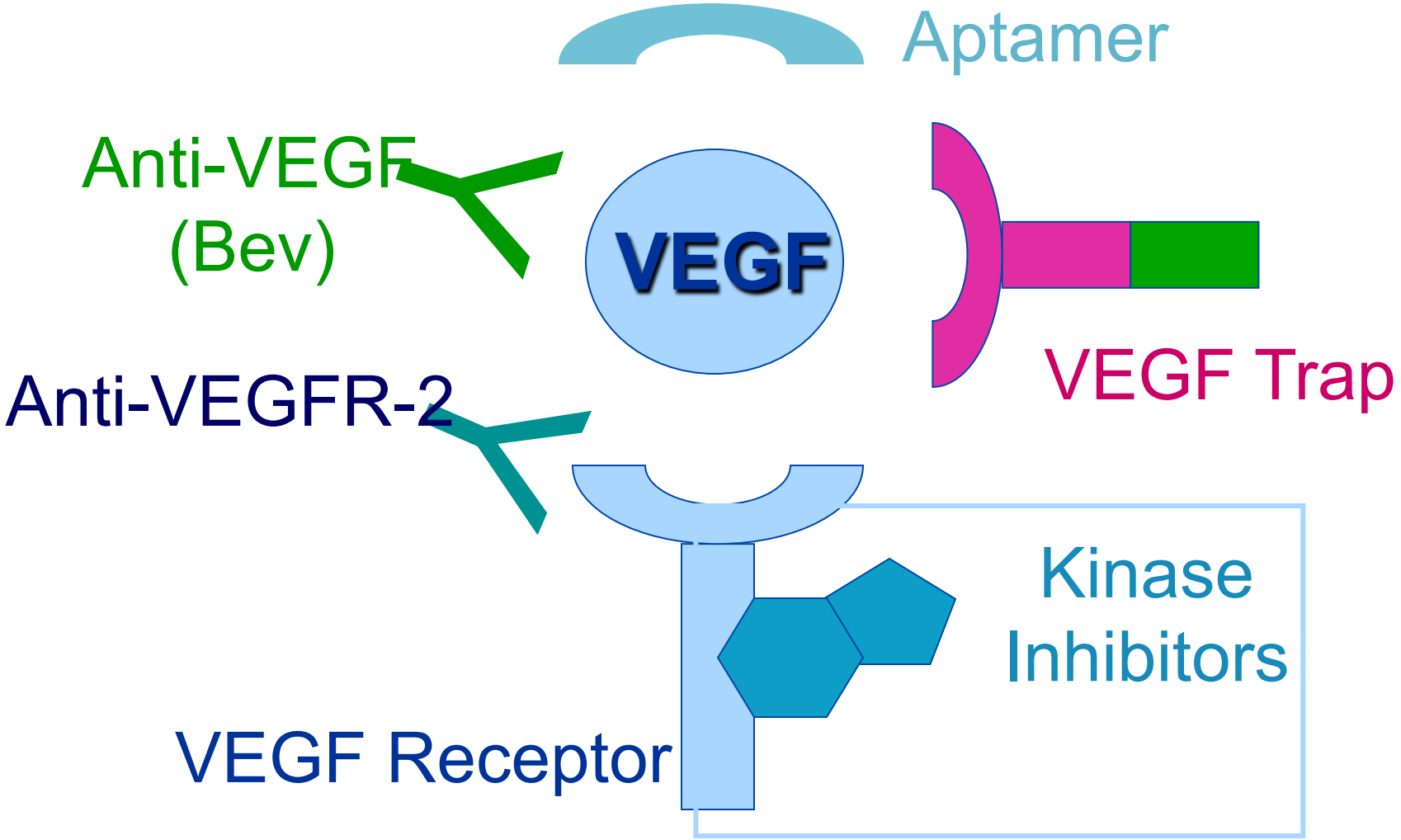
4- Clinical prospective trials addressing prevention prophylatic are warranted

Cardiotoxicity



- Peripheral Artery disease
- Pulmonary Hypertension
- Atrial Fibrillation
- Acute Myocarditis

Targeting the VEGF Pathway



How to prevent LV systolic dysfunction secondary to chemotherapy?

Chimiotherapie	Incidence HTA Tous Grades	Incidence grade > 3
Aflibercet	46 %	18 %
Axitinib	30 %	5 %
Bevacizumab	22 %	11 %
Cediranib	72 %	33 %
Motesanib	56 %	25 %
Pazopanib	37 %	8 %
Sorafenib	17 %	4 %
Sunitinib	24 %	8 %
Vandetanib	21 %	2 %

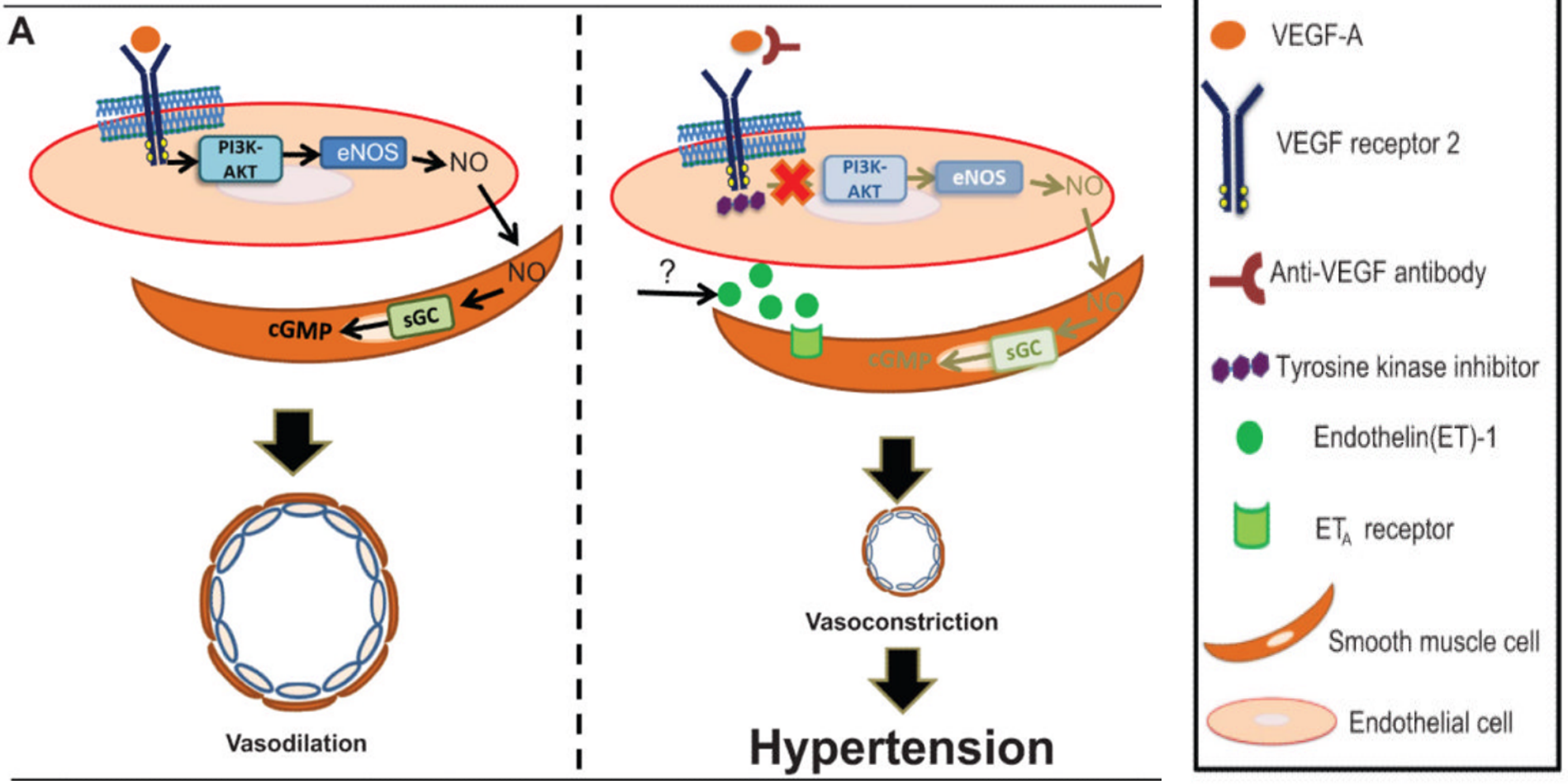
Maintland et al. J Natl Cancer Inst 2010;102,596-604

Protéinurie et thérapie moléculaire ciblées

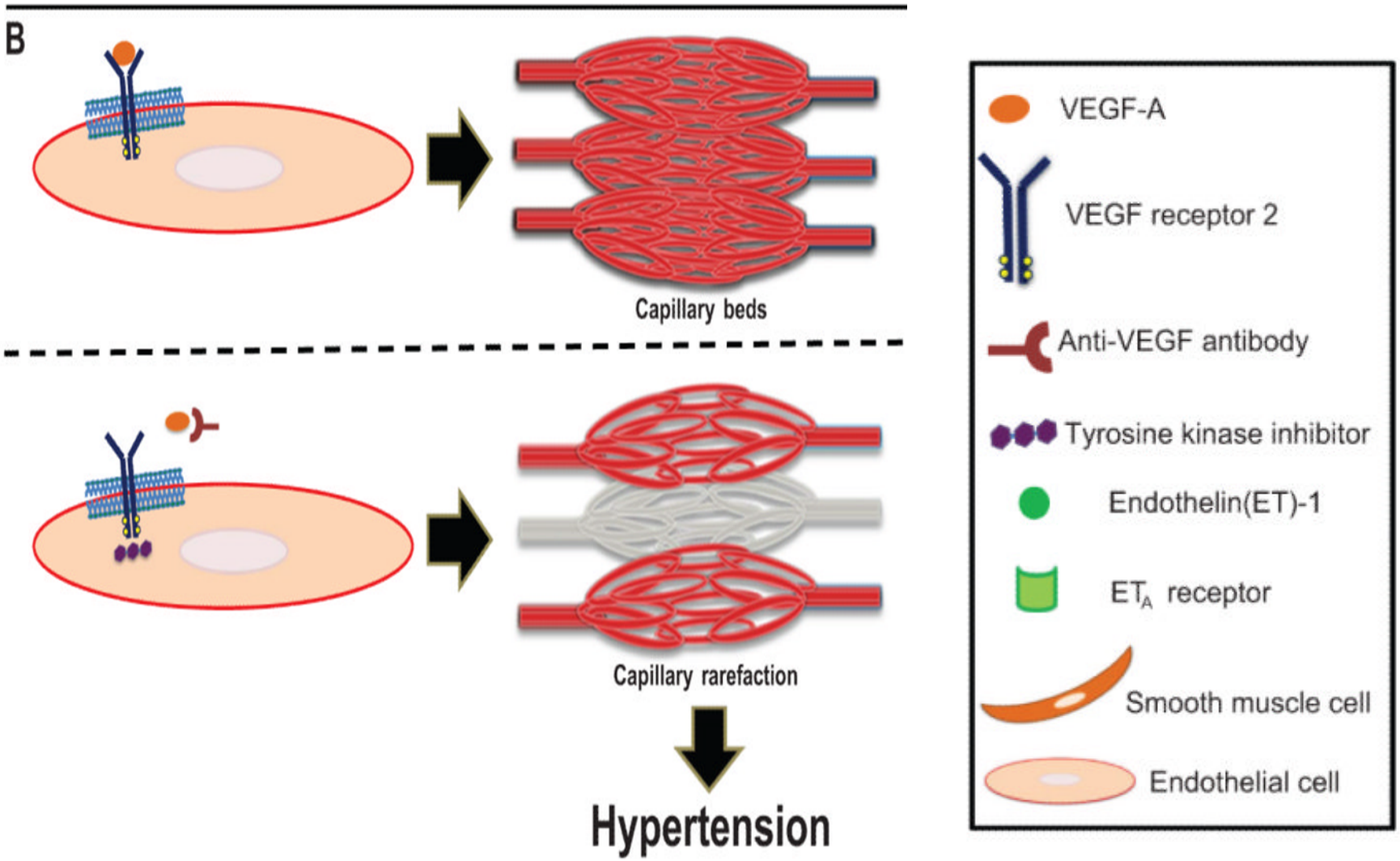
Chimiotherapie	Incidence Proteinurie Tous grades	Incidence Proteinurie grade > 3
Aflibercet		18
Axitinib	Protéinurie	5
Bevacizumab	13 a 52 %	0,4 a 0,9 %
Cediranib		33 %
Motesanib		25 %
Pazopanib		8 %
Sorafenib	NA	NA
Sunitinib	NA	NA
Vandetanib	Protéinurie	2 %

Maintland et al. J Natl Cancer Inst 2010;102,596-604

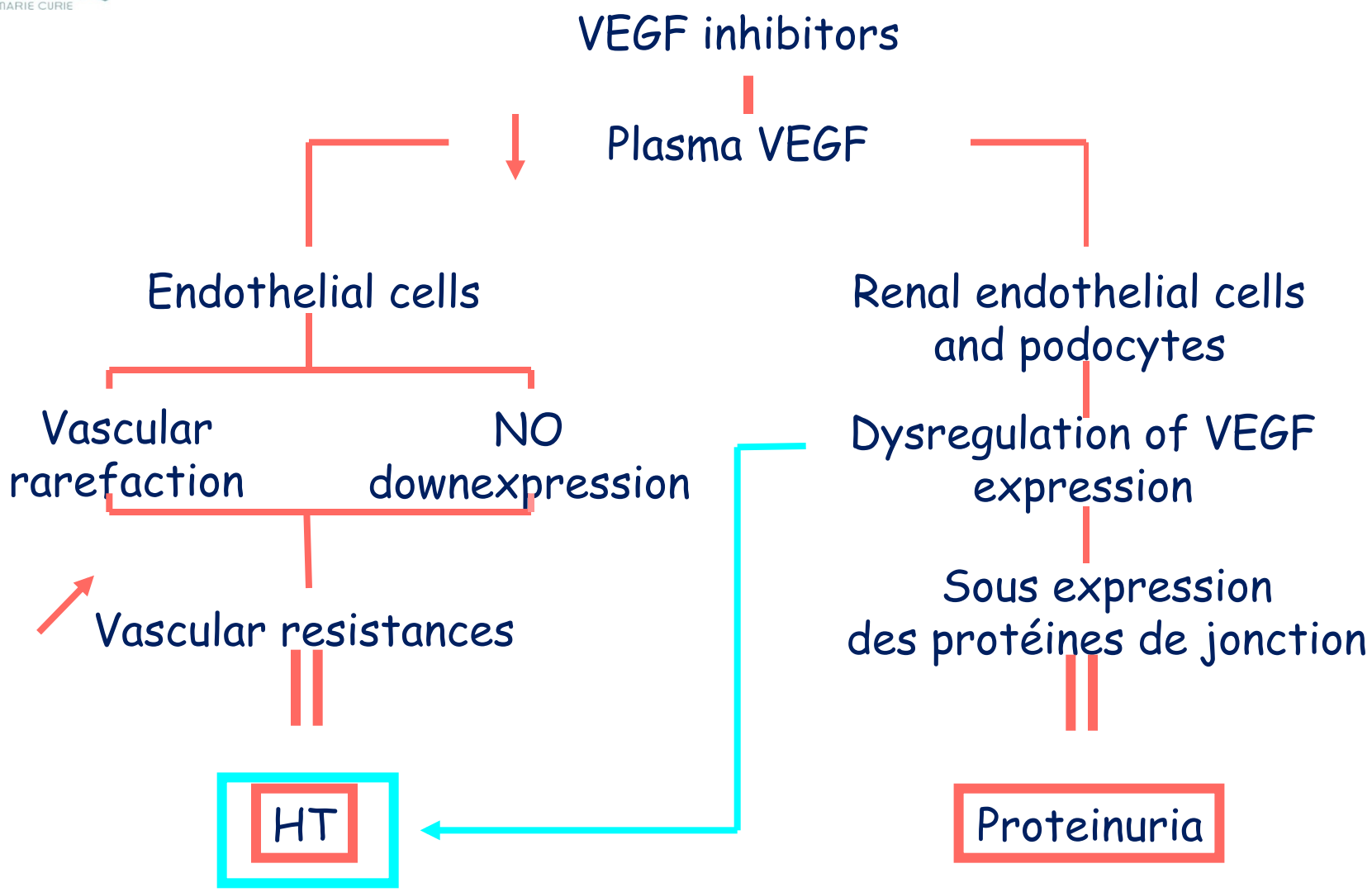
Mécanismes Hypertension Artérielle
Voie Du NO



Mécanismes Hypertension Artérielle
Raréfaction Capillaire



How to prevent LV systolic dysfunction secundary to chemotherapy?



Izzedine

Mesure de la pression artérielle

1- Eviter exercise physique avant la mesure de la pression arterielle

2- Eviter dans les 30 mn qui precedent la mesure la consommation d'alccol, cafeine et nicotine

3- Patient installe confortablement depuis au moins 5 mn, idealement 15 mn avant la mesure

4- Installation patient : couche ou assis (eviter jambes croisees aui peuvent majorere la PA de 2–8mmHg)

5- Position du bras : Retirer chemise, bras appuye sur table, soutenu

6- brassard tensionnel adapte, positionne a hauteur du coeur

7- Moyenne de 2 mesures a 3 mn d'intervalle

NCI-CTC version 4

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Prehypertension PAS 120-139 mmHg Ou PAD 80-89 mmHg	HTA stade 1 PAS 140-159 mmHg PAD 90-99 MMhg	HTA stade 2 PAS ≥ 160 mmHg Ou PAD ≥ 100	HTA compliquée	**Décès**
Pas de TTT	**TTT HTA nécessaire**	**TTT HTA nécessaire**	**TTT HTA urgent**	

Prise en charge de la HTA sous regorafenib
Principe généraux

NCI CTCAE v 4	Regorafenib	Modification Dose	Dose Cycle suivant
Grade 0-2	Poursuivre	Non	Pas de chgt
Grade 3	Retarder jusqu'à grade ≤ 2	Réduire d'un pallier	Tox ≤G2 discuter augmentation dose
Grade 4	Retarde jusqu'à grade ≤ 2	Réduire d'un pallier Envisager interruption définitive	

Dose 0	Dose 1	Dose 2
160 mg	120 mg	80 mg

Si Arrêt nécessaire du REGO > 4 semaine, stop prescription

Antihypertensive agents and angiogenic inhibitors

ACEI, ARB, diuretic, beta-blockers, alpha blockers, nitrate derivates, calcium channel blockers

Low interaction potential

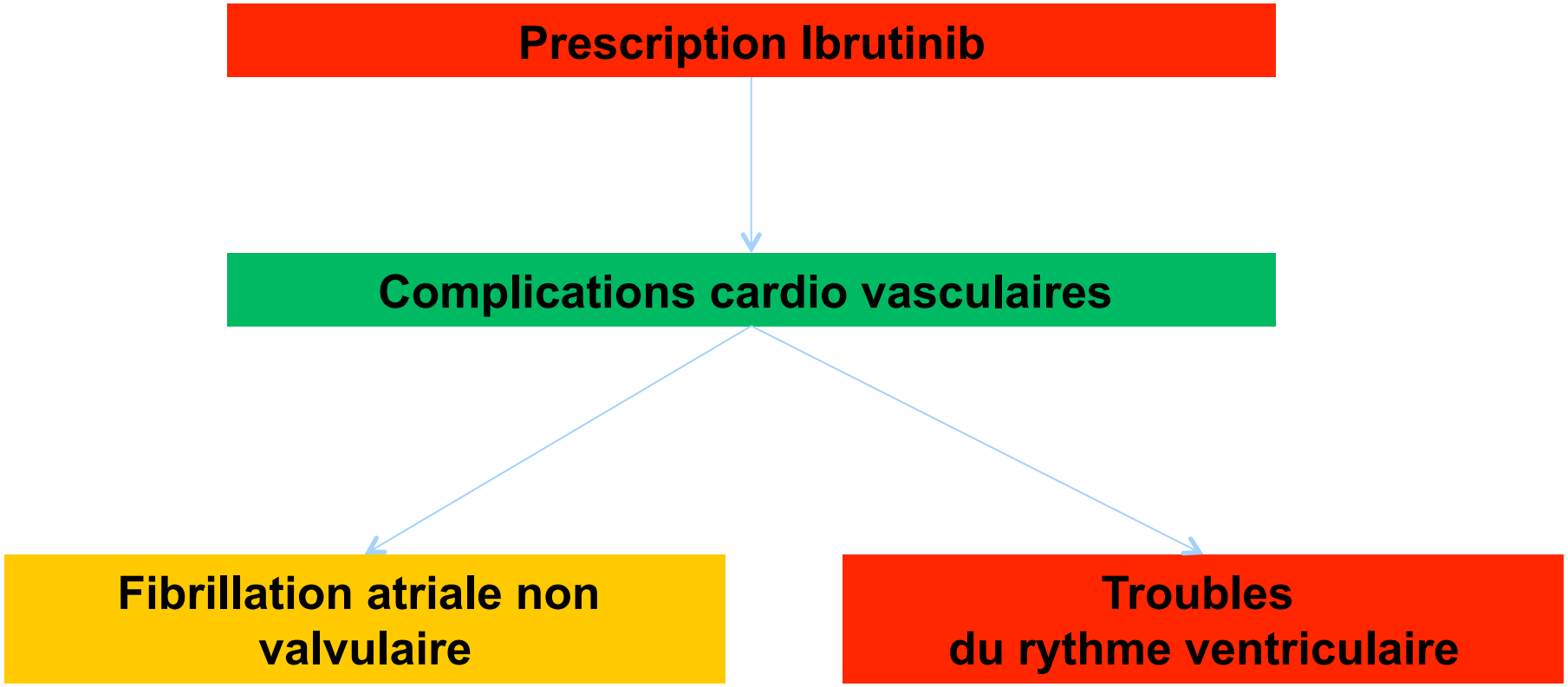
Nifedipine, calcium channel blockers

Use cautiously

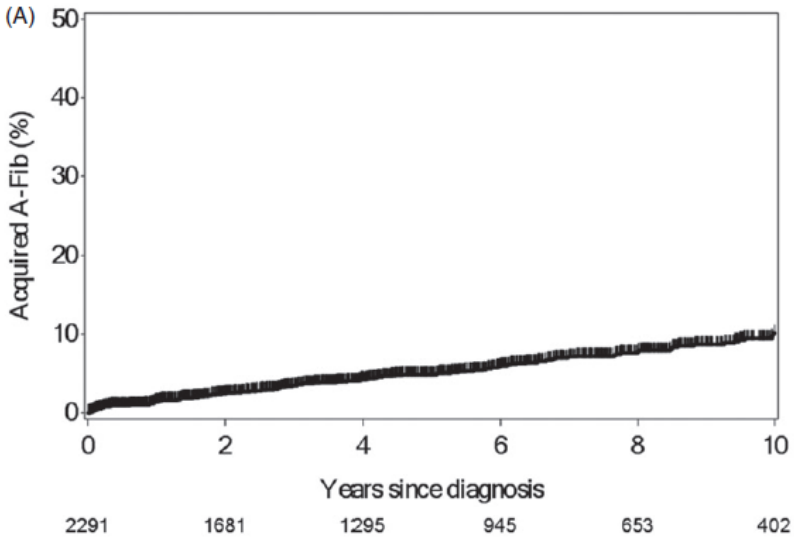
Verapamil
Diltiazem
CYP3A4 inhibitors

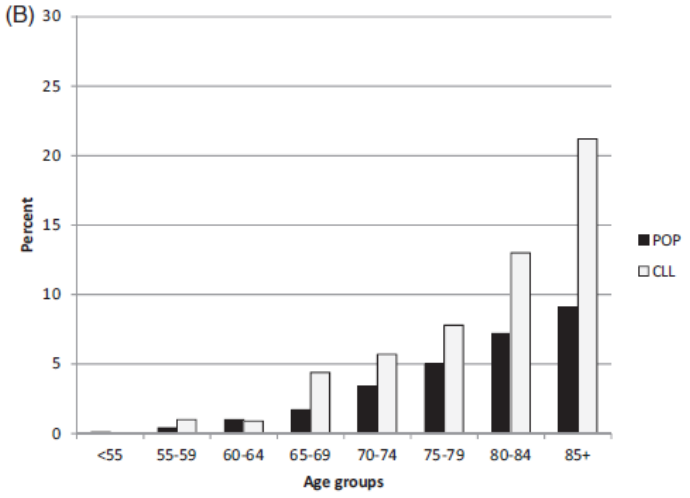
Contraindicated with AI (sunitinib,Sorafenib)

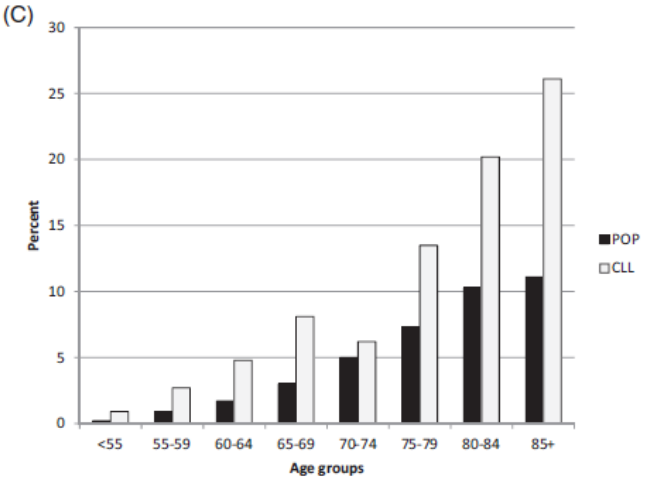
Izzedine H et al. Ann Oncol 2009;20,807-815


Prescription Ibrutinib
Complications cardio vasculaires
Fibrillation atriale non valvulaire
Troubles du rythme ventriculaire

Atrial fibrillation in pts with LLC

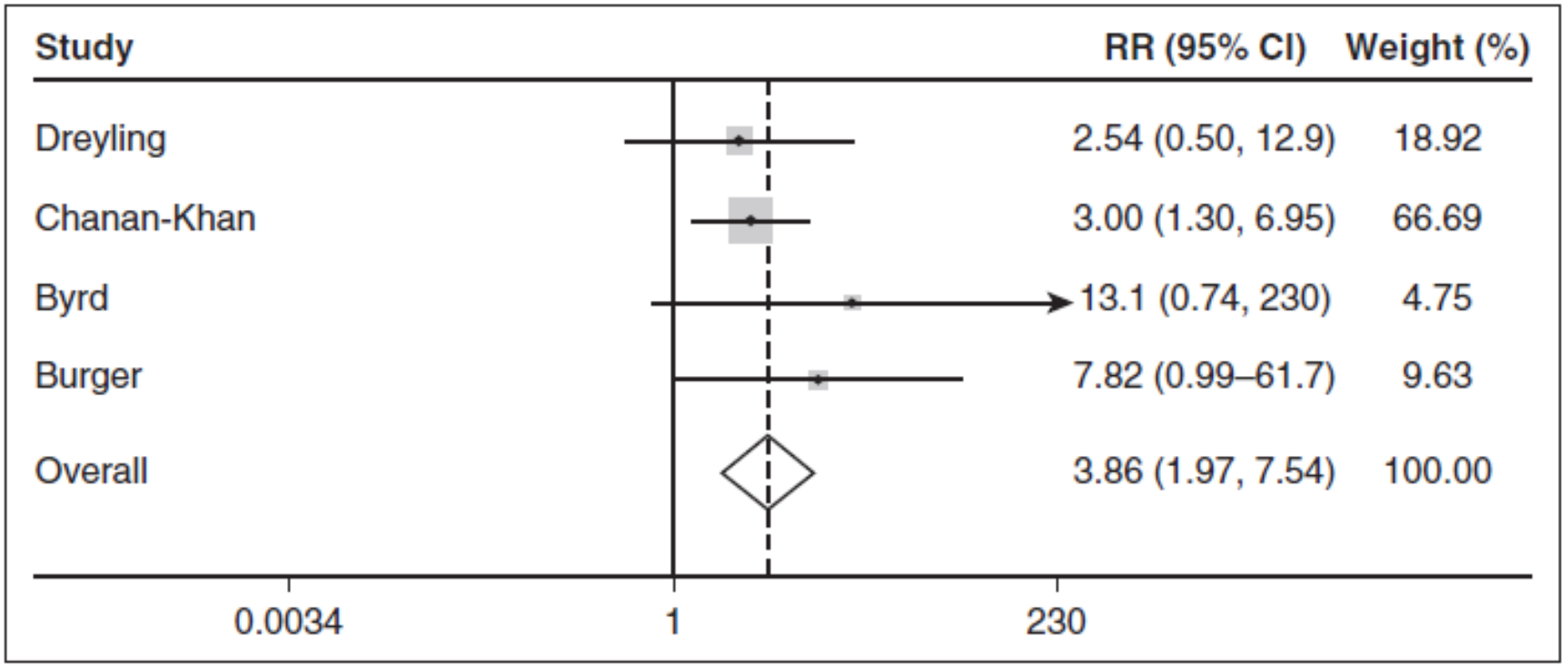






Shanafelt Leukemia & Lymphoma2017 , 58:7,

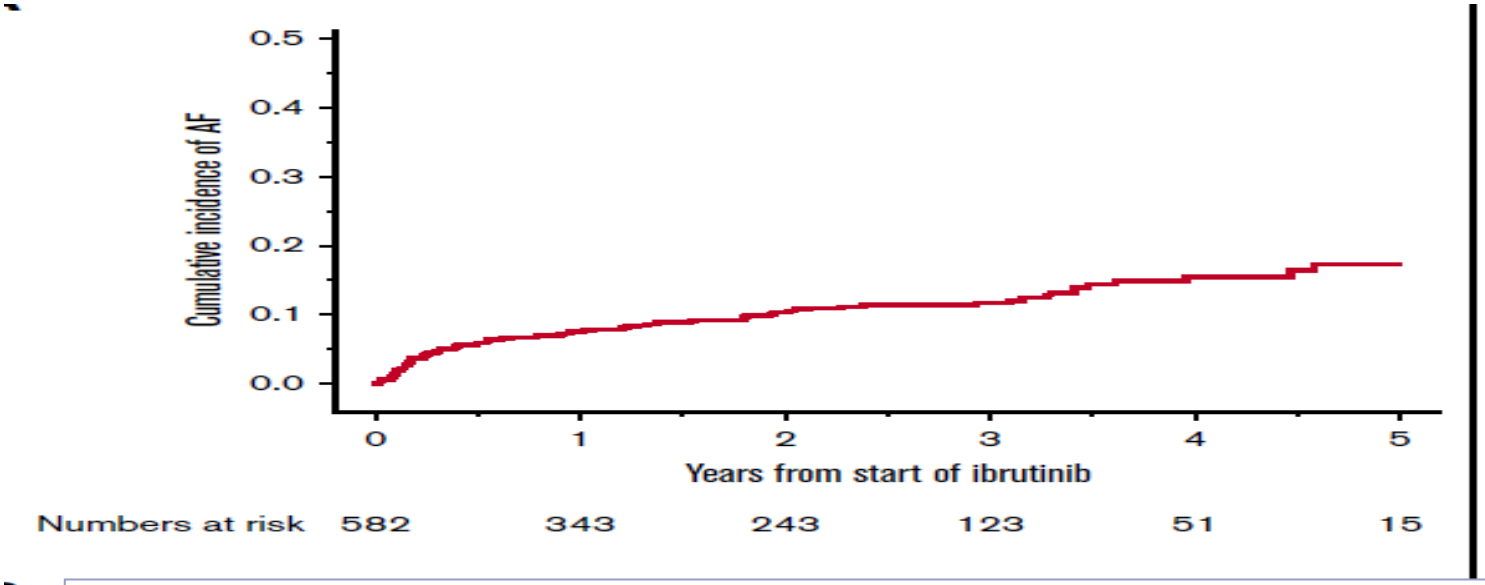
The risk of atrial fibrillation with ibrutinib use: a systematic review and meta-analysis

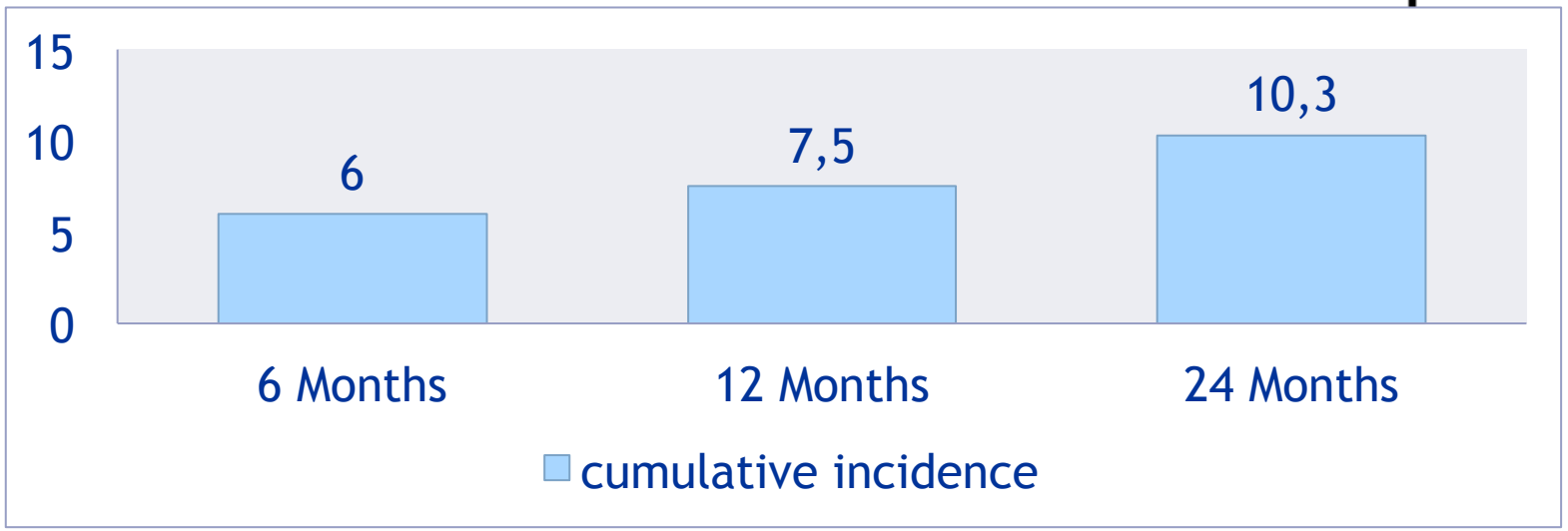


RR 3.9 (2-7.5) p< 0.001

Leong BLOOD, 2016 ;128, 140-141

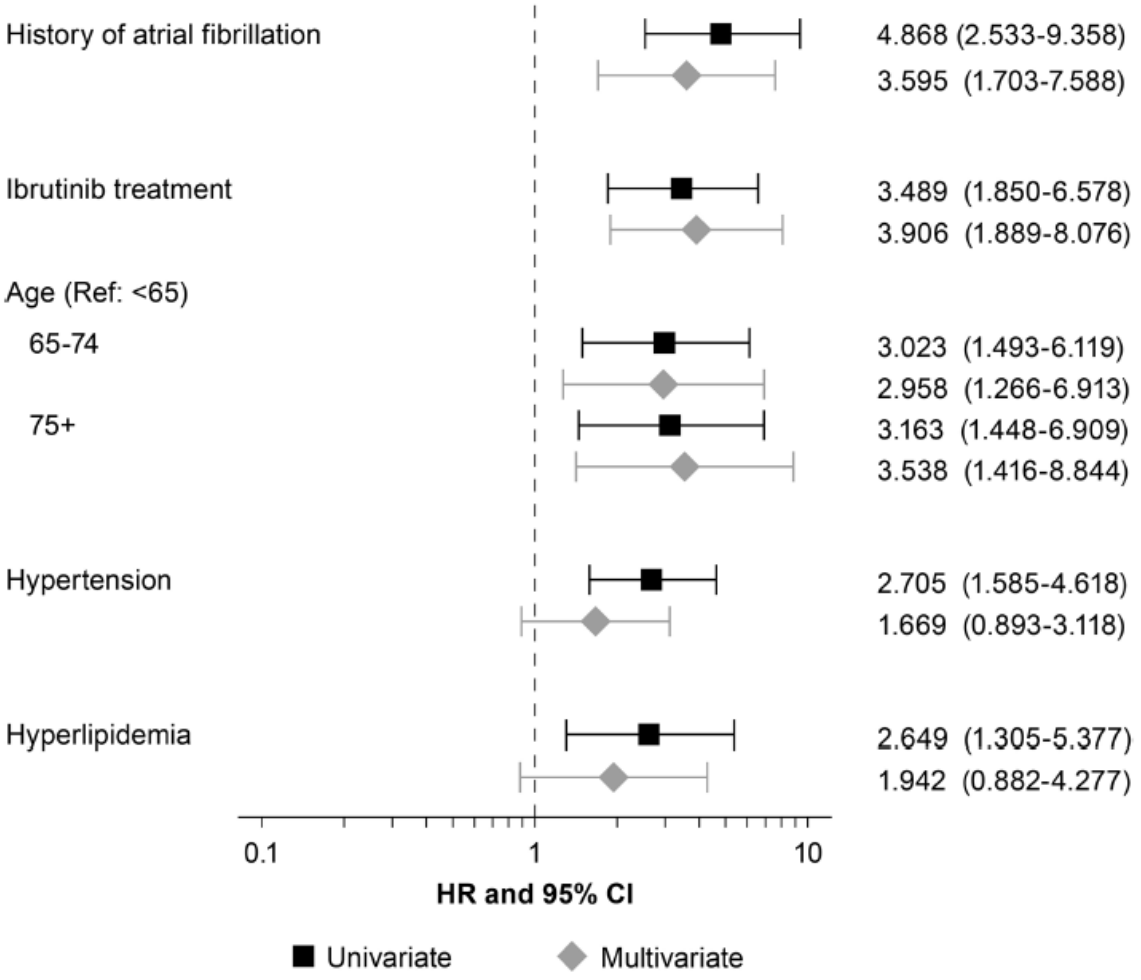
Cumulative incidence, risk factors, and management of atrial fibrillation in patients receiving ibrutinib





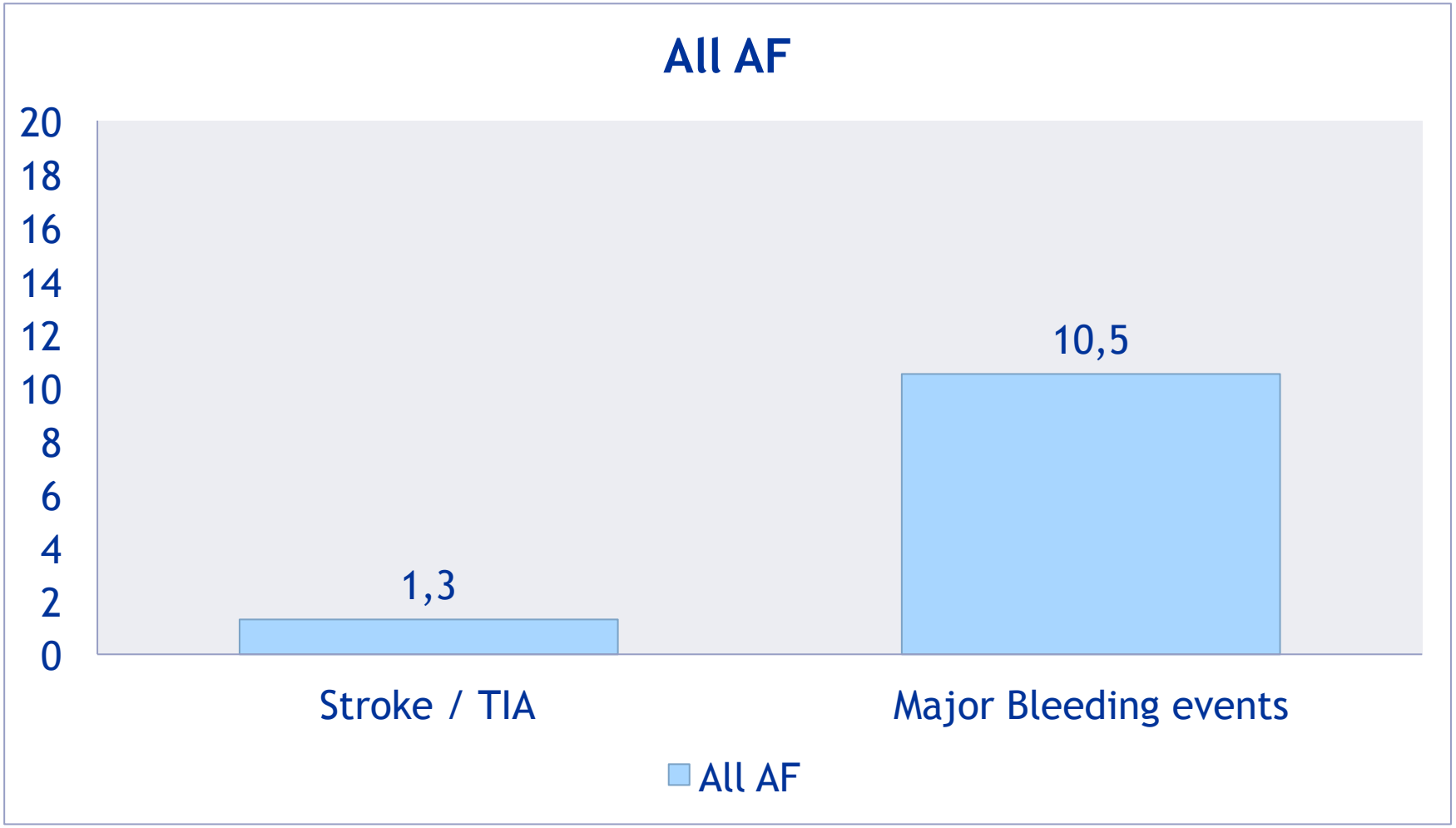
Wiczer blood Advances 2017 ; 1,20 :

Characterization of atrial fibrillation adverse events reported in ibrutinib randomized controlled registration trials
Significant factors for development of AF



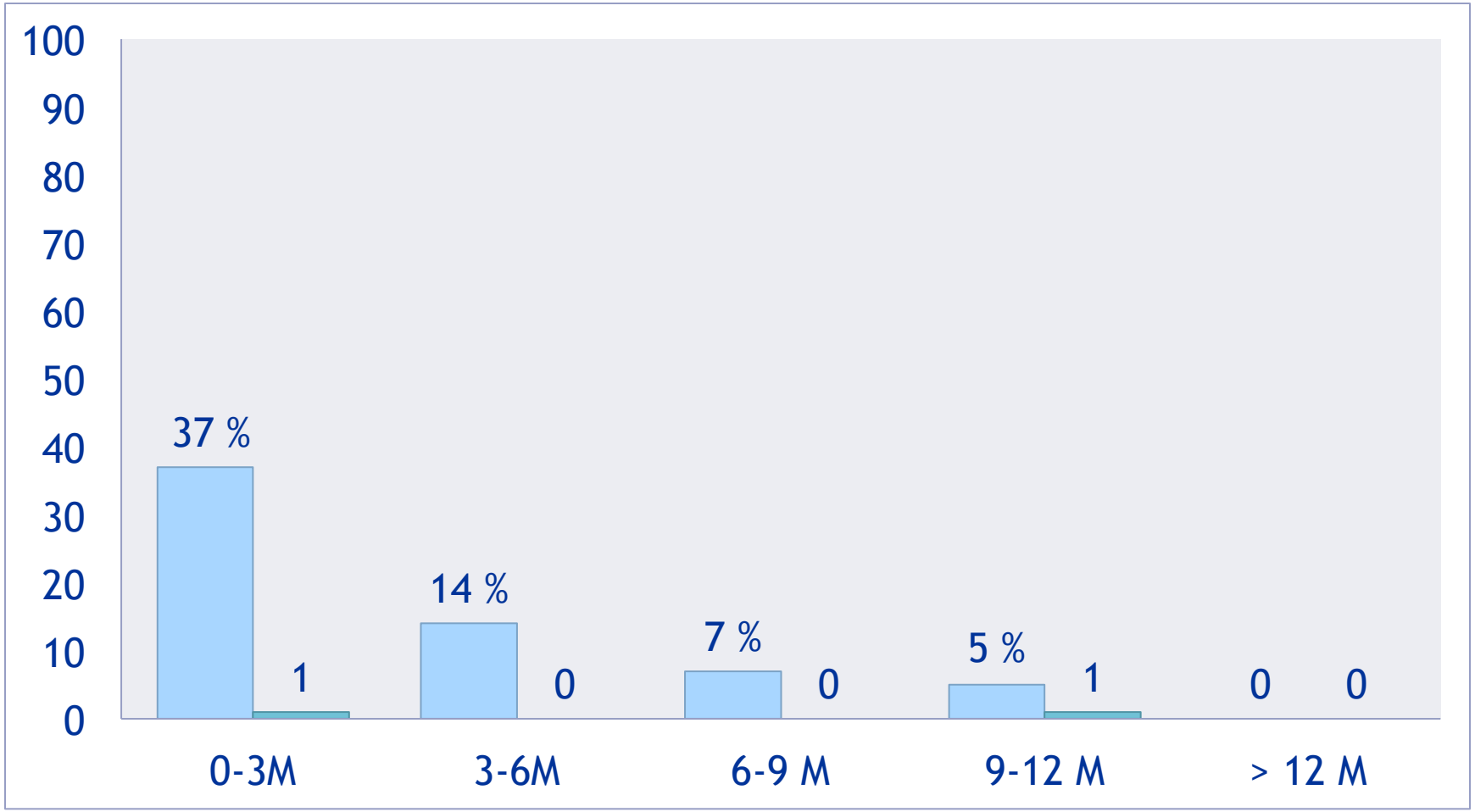
Brown Haematologica 2017 ;102:179

Cumulative incidence, risk factors, and management of atrial fibrillation in patients receiving ibrutinib



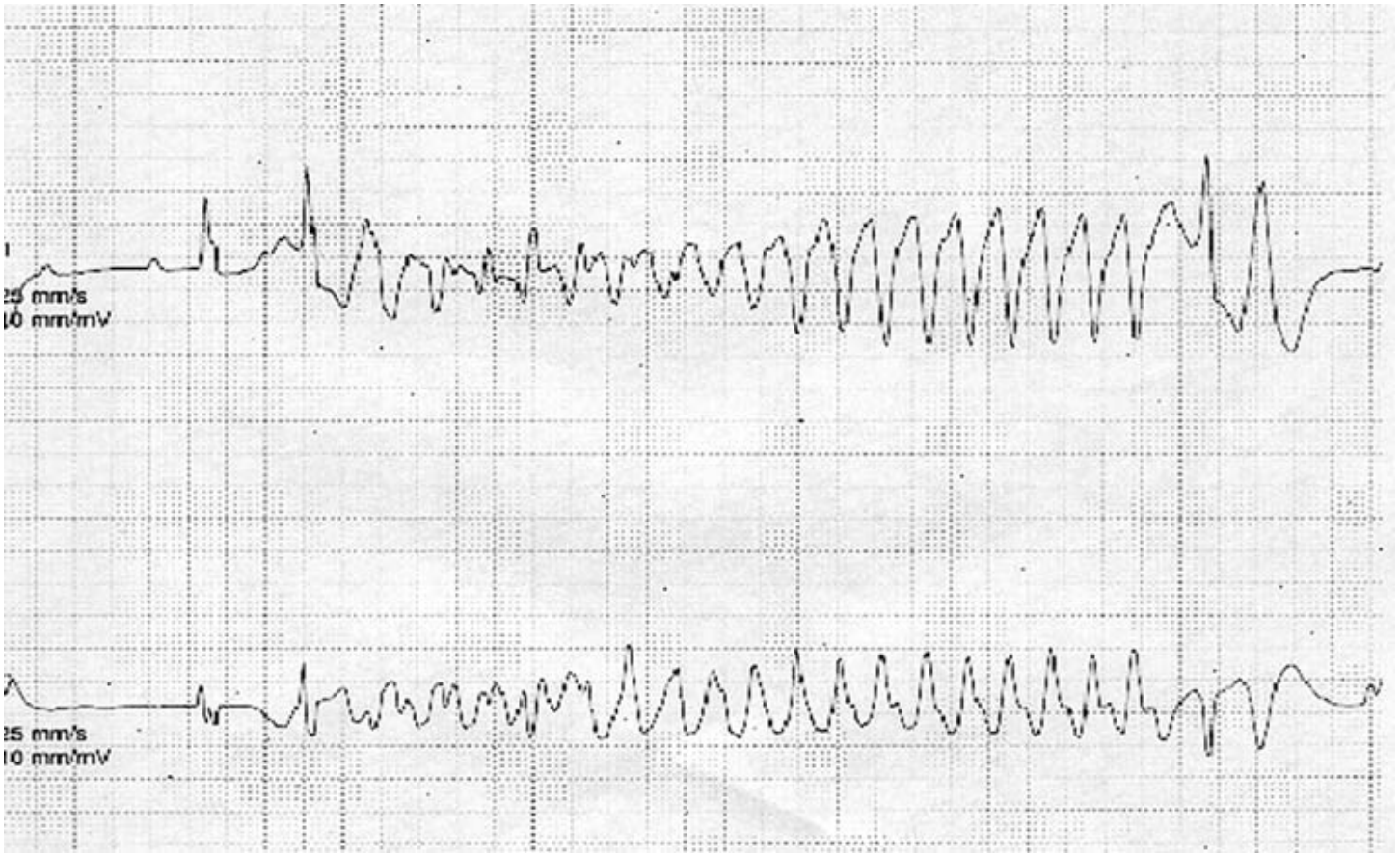
Wiczer blood Advances 2017 ; 1,20 :

Incidence and risk factors of bleeding-related adverse events in patients with chronic lymphocytic leukemia treated with ibrutinib



Lipsky AH Haematologica. 2015 ;100 :1 571-8

Torsades de pointes - ECG



QT mesure vs QT corrige

Feature	Formula
Bazett	QTc=QT(HR/60)1/2
Fridericia	QTc=QT(HR/60)1/3
Framingham	QTc=QT+0,154 (1-RR)
Hodges	QT+105(1/RR-1)

Strevel et al. J Clin Oncol, 2007; 25 : 3362

Facteurs associés à une prolongation du QT

Cause
Congenital : Syndrome du QT long
Cardiopathie : HVG, Dysfonction VG, cardiopathie ischémique, Trouble conductif
Métabolique : HypoK+,HypoMG, HypoCA+, Hypothyroidie
Psychotropes : amitriptyline,haloperidol
Antibiotiques : Clarithromycin, Quinilone
Antihistaminiques : Terfenadine
Autre : Domperidone, Cisapride, droperidol, Tacrolimus , Tamox 5 hybdroxy trytamine antagonist

Strevel et al. J Clin Oncol, 2007; 25 : 3362

How to prevent LV systolic dysfunction secundary to chemotherapy?

Initiation traitement
Examen clinique : Asymptomatique ?
HTA ?, ICA ?, DT ?
Ordonnance ?
Inhibiteur CYP3A4 ?
ECG : QT m / QTc F
metabolisme : K+ / Mg 2+ Fonction hépatique

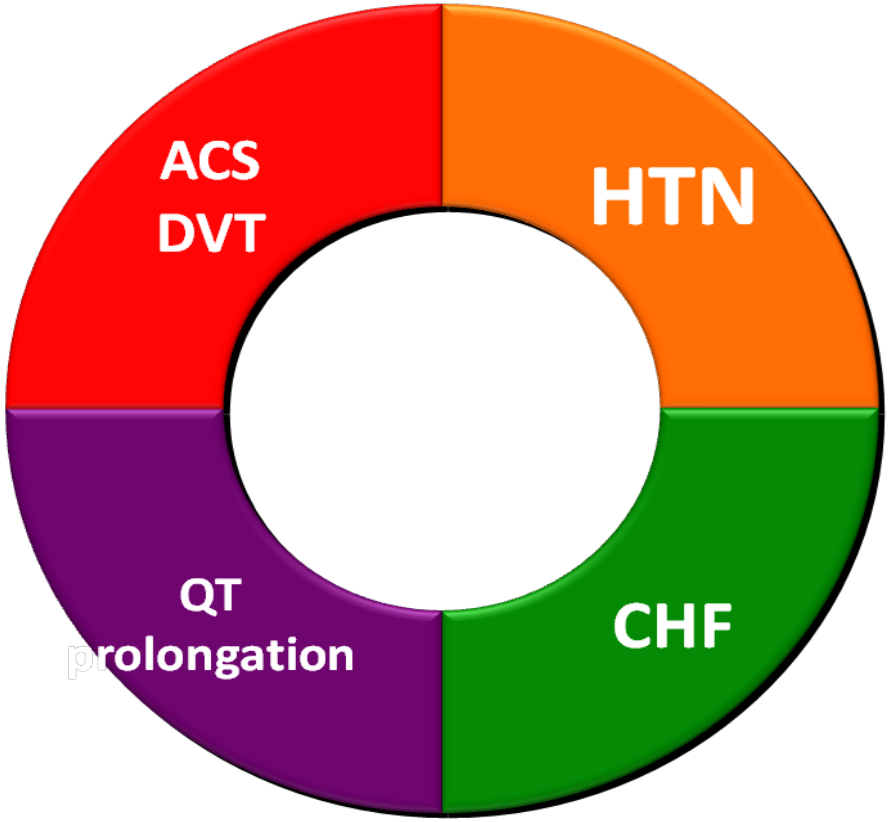
Suivi
Examen clinique : Asymptomatique ?
ECG : D7, periodique, apres changement dose
surveillance K+ / Mg 2 +

Stop Nilotinib
Si Symptomatique
If QTc > 450 msec

Prise en charge

QTcF	Posologie Nilotinib	Action
> 480 msec	Stop Nilotinib	Vérifier et corriger K +,Mg2+ Vérifier interaction médicamenteuse Vérifier Interaction CYP
< 450 msec	Reprendre Nilotinib Dose Initiale	ECG a chaque changement de dose
Si 450 < QtcF < 480 msec	Diminuer Posologie 400 mg/j	ECG a chaque changement de dose

Cardiotoxicity in Hematology



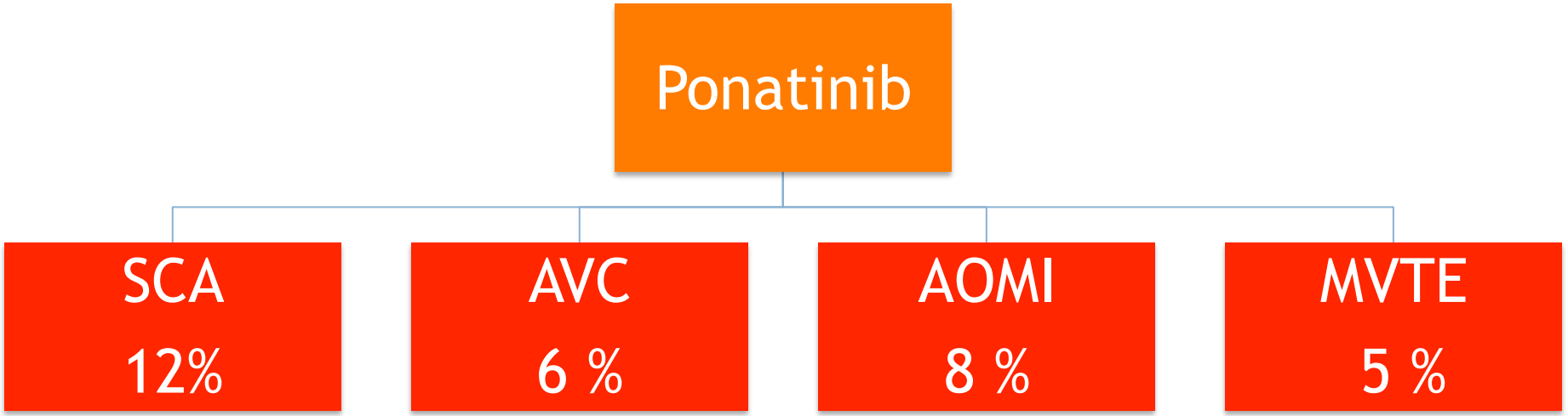
Peripheral Artery disease

Long-term benefits and risks of frontline nilotinib vs imatinib for chronic myeloi leukemia in chronic phase: 5-year update of the randomized ENESTnd trial

	Nilotinib 300 mg x 2 N=279 N(%)		Nilotinib 400 mg x 2 N=277 N(%)		Imatinib 400 mg N=280 N(%)	
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
HTN	29 (10,4)	4 (1,4)	23 (8,3)	3 (1,1)	12 (4,3)	1 (0,4)
Symp QTc prolongation	5 (1,8)	2 (0,7)	7 (2,5)	2 (0,7)	8 (2,9)	4 (1,4)
Ischemic heart disease	11 (3,9)	6 (2,2)	24 (8,7)	17 (6,1)	5 (1,8)	4 (1,4)
Cardiovascular events	4 (1,4)	3 (1,1)	9 (3,2)	6 (2,2)	1 (0,4)	1 (0,4)
Peripheral artery disease	7 (2,5)	4 (1,4)	7 (2,5)	3 (1,1)	0	0

Leukemia 2016 ; 30 : 1044 – 1054

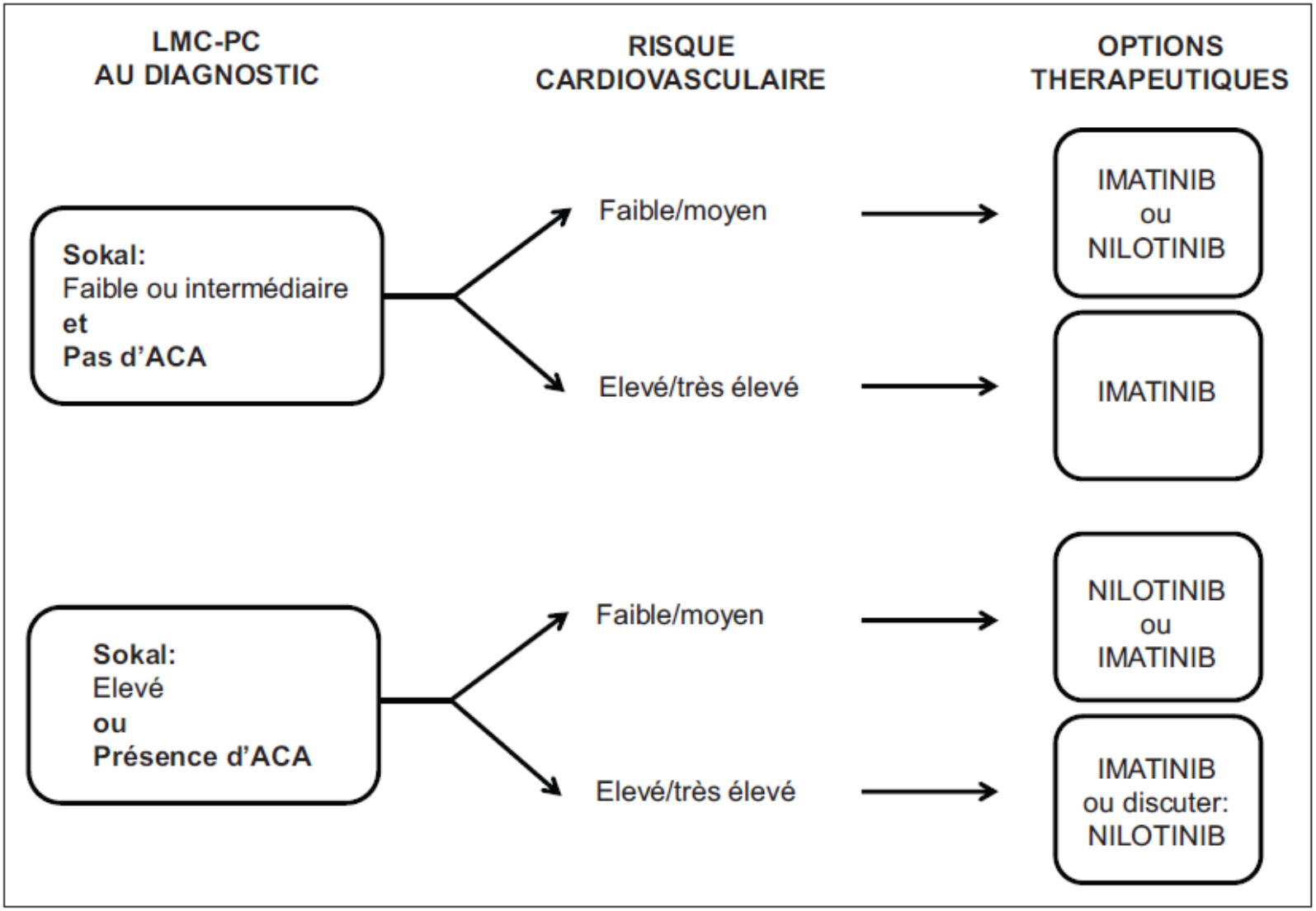
Ponatinib et évènement cardio vasculaire



Classification ESC 2012 du risque de mortalité cardiovasculaire globale à 10 ans

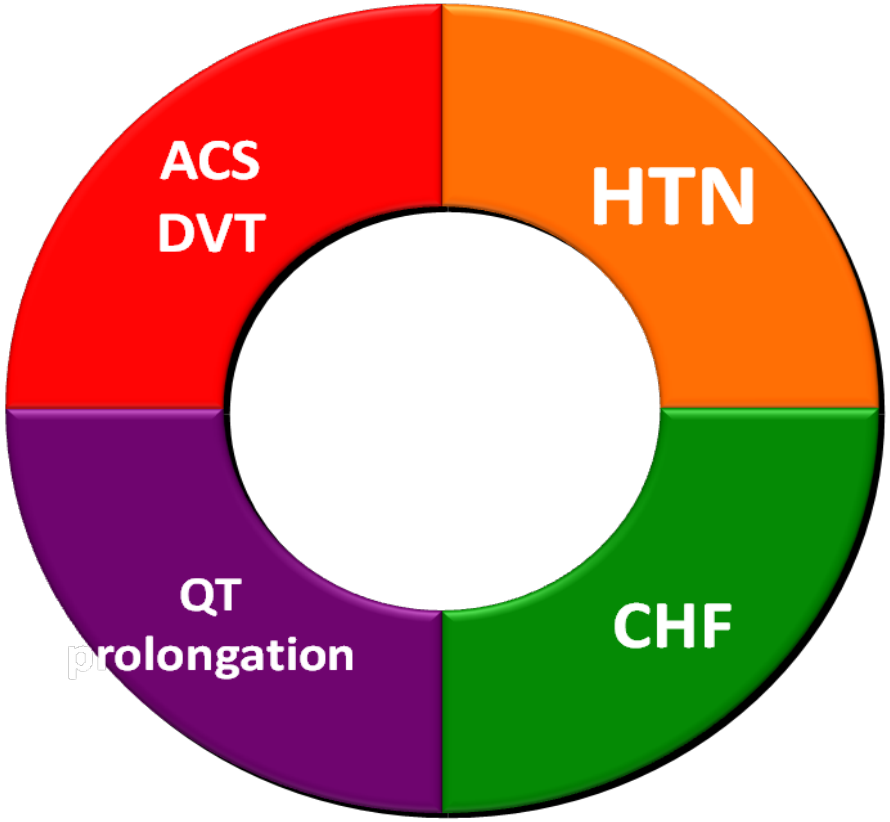
Groupe de risque	Au moins 1 des items suivants
Très élevé	Maladie cardiovasculaire documentée Infarctus du myocarde Syndrome coronarien Accident vasculaire cérébral ischémique Artériopathie périphérique Revascularisation artérielle Diabète avec au moins 1 autre facteur de risque cardiovasculaire majeur ou atteinte microvasculaire Insuffisance rénale chronique sévère SCORE[a] $\geq$ 10 %
Élevé	Un facteur de risque majeur très élevé (HTA sévère, dyslipidémie familiale) Diabète sans autre facteur de risque cardiovasculaire majeur et sans atteinte microvasculaire Insuffisance rénale chronique modérée SCORE[a] $\geq$ 5 % et $\leq$ 10 %
Moyen	SCORE[a] $\geq$1 % et $\leq$ 5 %
Faible	SCORE[a] $\leq$ 1 %

Gestion du risque d'événements cardiovasculaires sous nilotinib



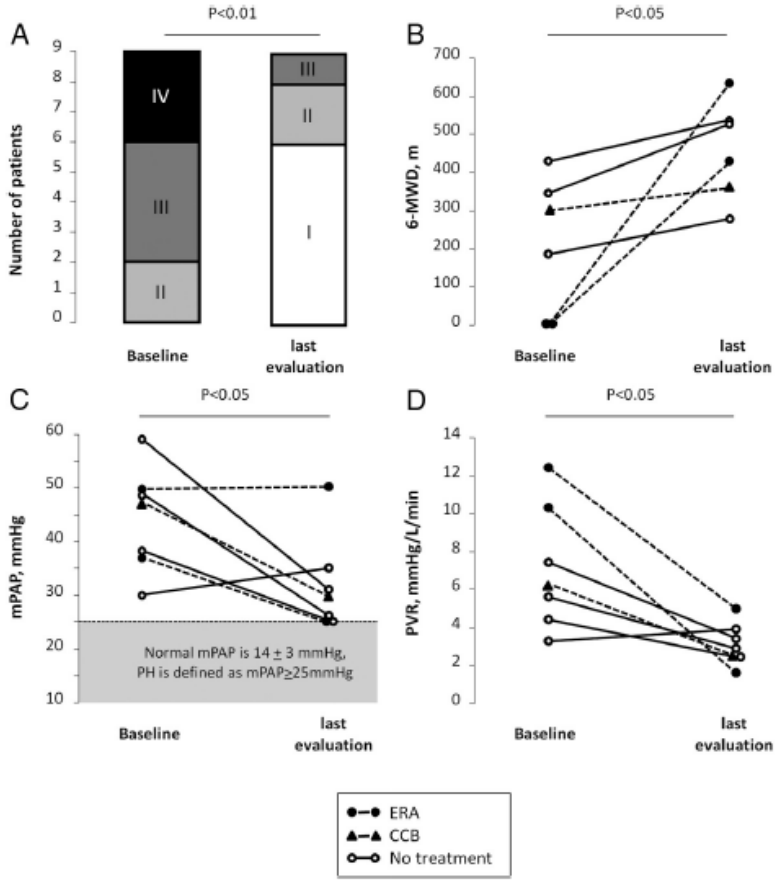
Rea Bull Cancer 2016 ; 103 : 180 -

Cardiotoxicity in Hematology



Pulmonary Hypertension

Pulmonary Hypertension and Dasatinib



Montani et al. Circulation 2012;125,2128-2137

Conclusions

1- Anthracycline :
Stratégie de depistage et de prevention

2- Thérapies moléculaires ciblées :
Reversibilite, Modulation de la posologie

3- Toxicités emergentes : AOMI, HTP

Global longitudinal strain at low-dose anthracyclines chemotherapy, for the prediction of subsequent cardiotoxicity

Parameters	AUC	95 % CI
GLS V1	0,76	0,58- 0, 88
GLS V2	0,82	0,52-0,99
Ab GLS	0,72	0,45-0,92
Δ GLS	0,74	0,48-0,94
LVEF V2	0,70	0,51-0,85

GLS V2 : - 17,45 after 150 mg/m2

Charbonnel, Eur Heart J Cardiovasc Imaging 2017 Jan 6. [Epub ahead of print]

Global Longitudinal Strain as a predictor of cardiotoxicity
Absolute value of GLS

Author	Pts	Definition of cardiotoxicity	CT rate	Echo	Threshold
Charbonnel	48 ± 10, 86 NHL, A+ R 15 %	↓ LVEF > 10 u to < 53 %	7 % 266 mg	150 mg/m	>-17,45%, GE Se 67 %, Sp 97 %
Sawaya	50± 10 , 81 BC A+T+R 60 %	↓ LVEF ≥5% to < 55% +S Or ↓ LVEF ≥10 % to < 55%	32 % 240 mg	3 M	> -19%, GE Se 74% Sp 73 %
Negishi	50± 11 81 BC, A+T+R 62 %	↓ LVEF ≥10 %	30 % 240 mg	6 M	> -20,5 %, GE Se 96% Sp 66 %

Adapted from Charbonnel, Eur Heart J Cardiovasc Imaging 2017 Jan 6. [Epub ahead of print
And Thavendiranathan J Am Coll Cardiol 2014; 25: 2571-68

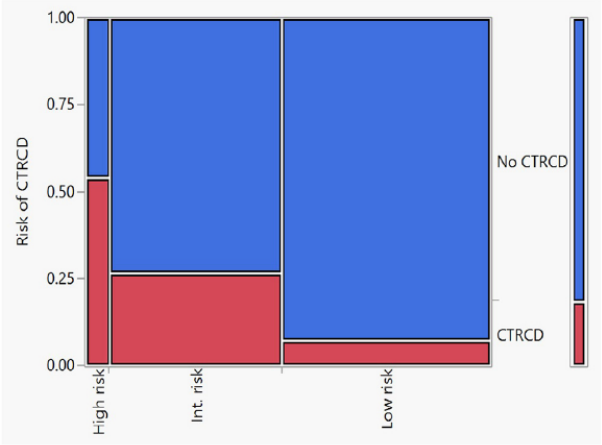
Global Longitudinal Strain as a predictor of cardiotoxicity
Relative reduction in GLS

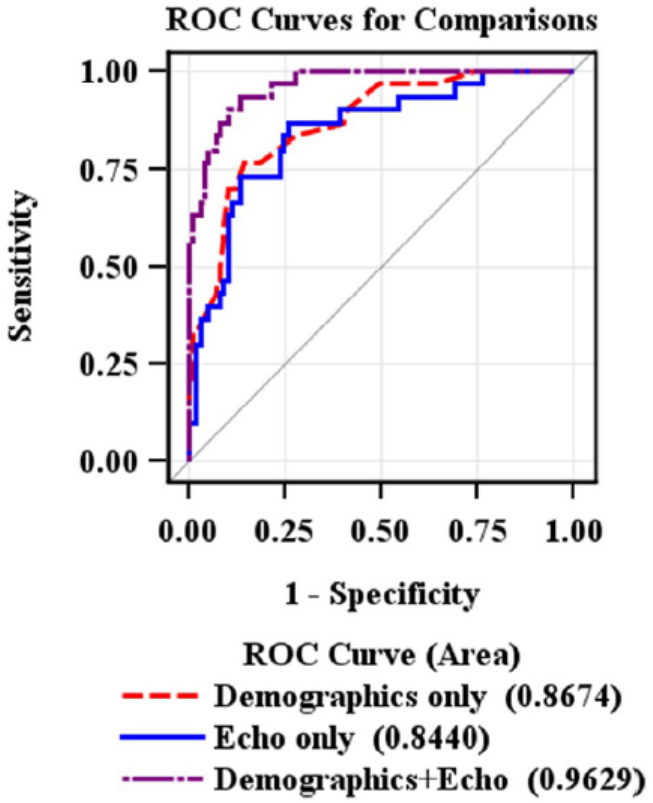
Author	Pts	Definition of cardiotoxicity	CT rate	Echo	Threshold
Fallah	47± 9 42 BC, A+T+R 97 %	↓ LVEF ≥ 10 % to < 55% +S	24 % 240mg/m	3 M	Δ 10,1 %, GE Se 79% ,Sp 82 %
Negishi	50 ± 11 81 BC, A+T+R 62	↓ LVEF ≥ 10 %	30 % 240mg/m	6 M	Δ 11 %, GE Se 65 % Sp 94 %
Sawaya	47± 9 49 BC ,A+T+R 12 %	↓ LVEF ≥5% to < 55% +S Or ↓ LVEF ≥10 % to < 55%	21 % 240mg/m	3 M	Δ 10 %, GE Se 86 %, Sp 86 %
Baratta	47 ± 16 36 B/H ,A+T+R 0 %	↓ LVEF ≥5% to < 55% +S Or ↓ LVEF ≥10 % to < 55%	19,4 % 139mg/ m2	3 M	Δ 15 %, GE Se 86 %, Sp 86 %
Mornos	51 ± 11 74 B/H ,A+ R 0 %	↓ LVEF ≥5% to < 55% +S Or ↓ LVEF ≥10 % to < 55%	13 % 178mg/ m2	6 W	Δ 13,1 %, GE Se 79 %, Sp 73 %
Kang	54 ± 14 75 H ,A	↓ LVEF ≥5% to < 55% +S Or ↓ LVEF ≥10 % to < 55%	18,7 % 300mg/ m2	3 c	Δ 15,9 %, GE Se 86 %, Sp 75 %
Baratta	47 ± 16 36 B/H ,A+T+R 0 %	↓ LVEF ≥10 % to < 55%	19,4 % 268mg/ m2	3 c	Δ 9 %, GE Se 84 %, Sp 80 %

Adapted from Charbonnel, Eur Heart J Cardiovasc Imaging 2017 Jan 6. [Epub ahead of print]

How to prevent LV systolic dysfunction secundary to chemotherapy?

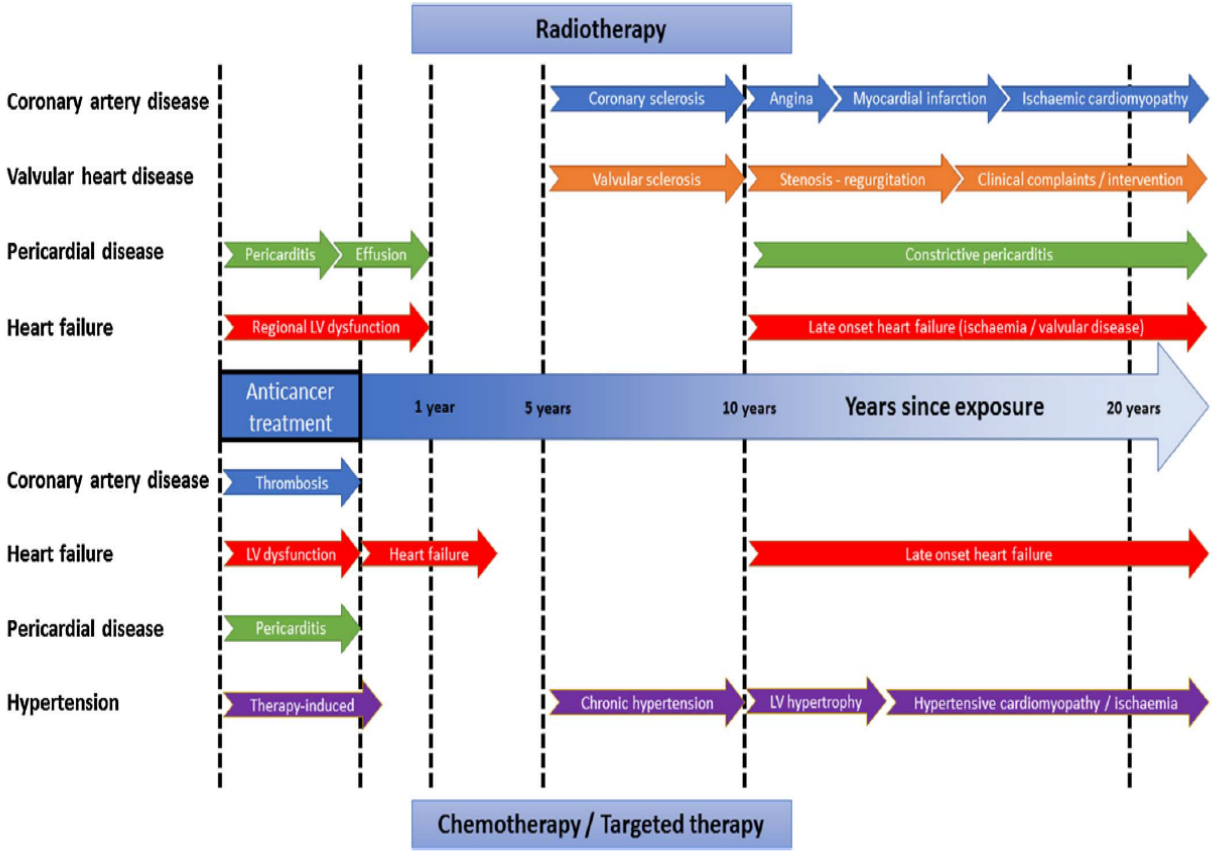
Usefulness of Integrating Heart Failure Risk Factors Into Impairment of Global Longitudinal Strain to Predict Anthracycline-Related Cardiac Dysfunction.





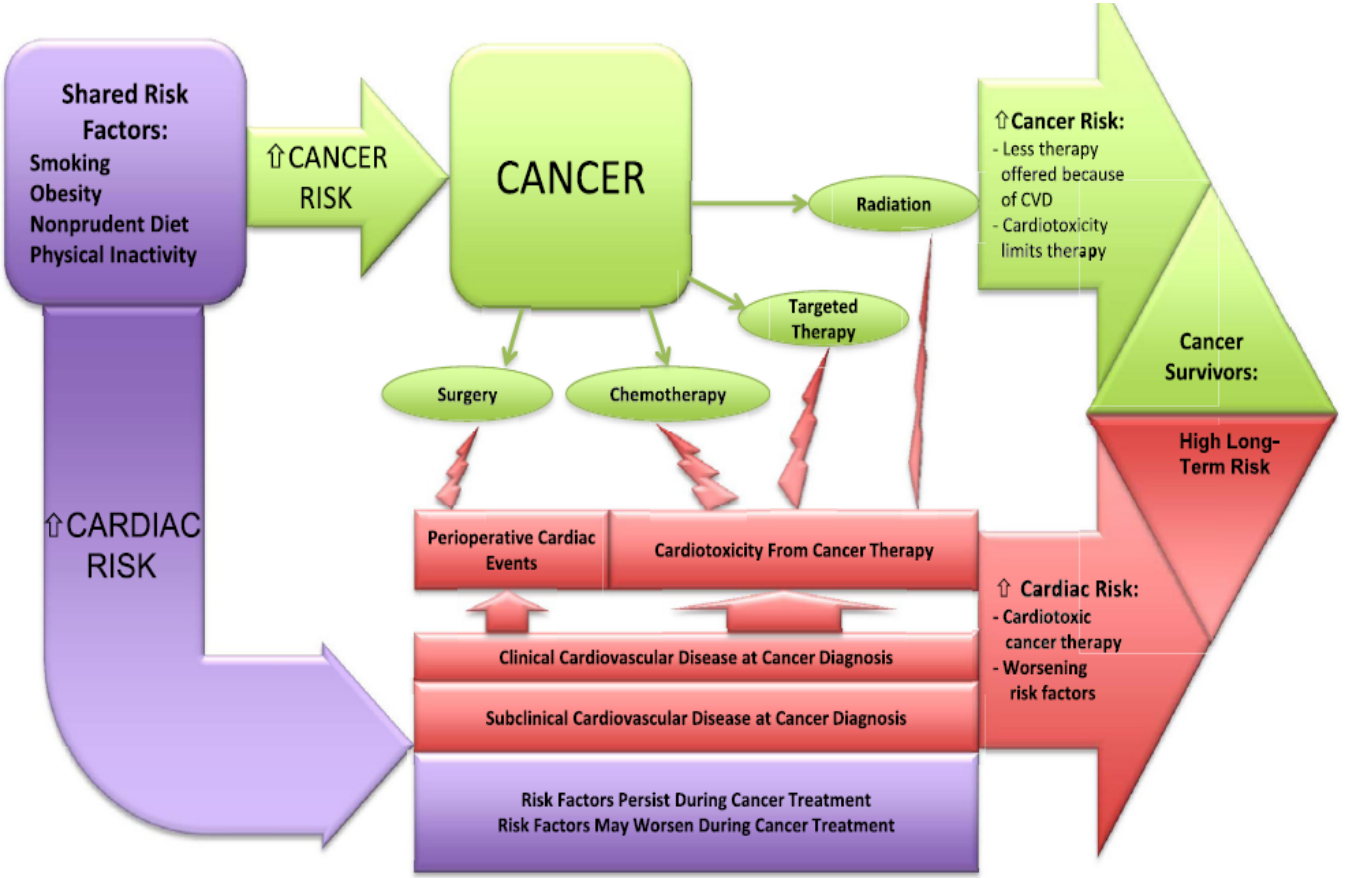
Milks MW, Am J Cardiol. 2018 ;121:867-873.

Long-term cardiovascular health in adult cancer survivors

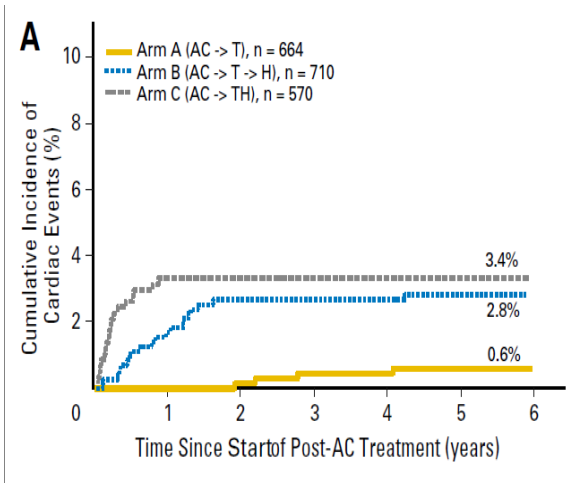


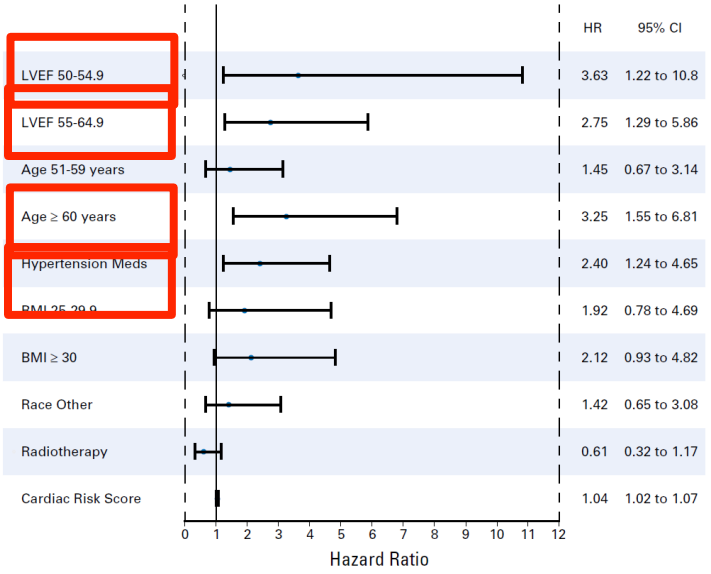
Naaktgeboren Maturitas 2017 ; 105 : 37–45

How to prevent LV systolic dysfunction secundary to chemotherapy?



Long-Term Cardiac Safety Analysis of NCCTG N9831 (Alliance) Adjuvant Trastuzumab Trial





Advani J Clin Oncol 2015 ; 34:581-587

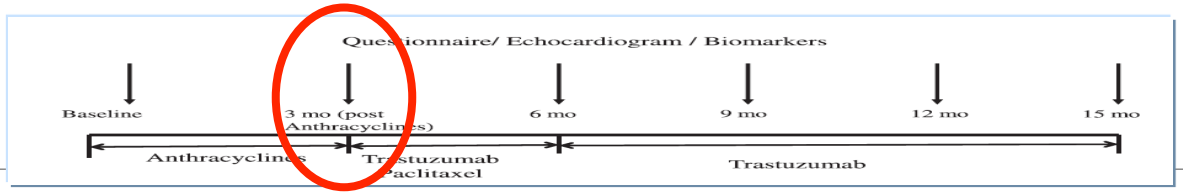
Cumulative Incidence of heart failure or cardiomyopathy during first 3 years after diagnosis by cancer therapy

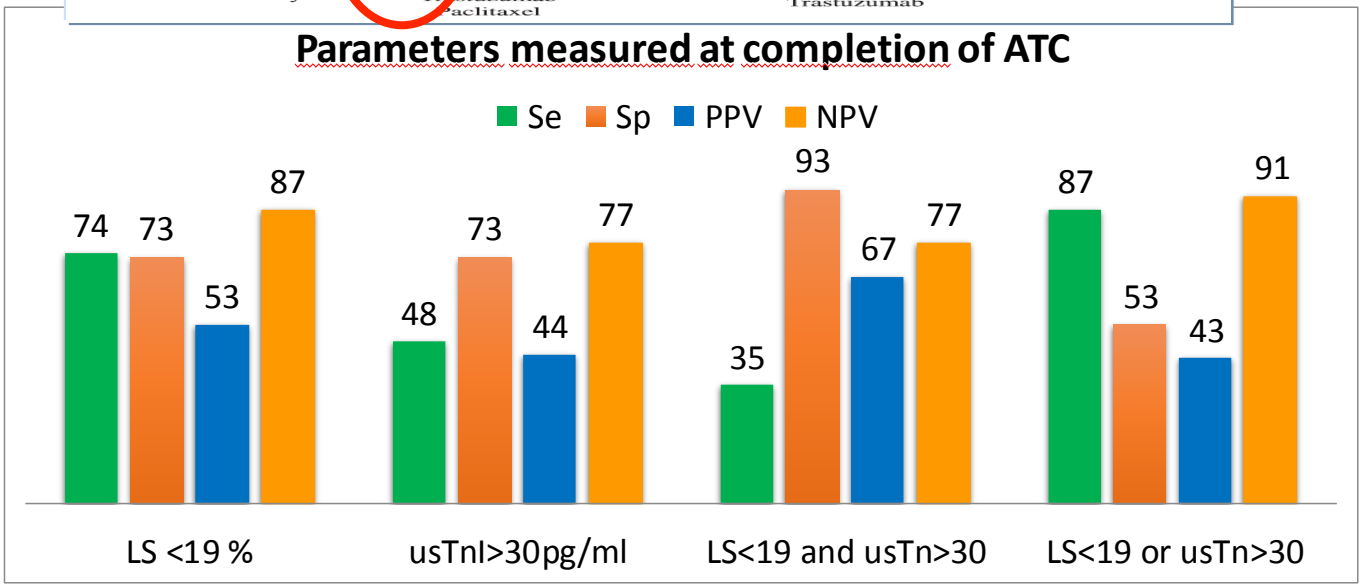
	All cancer	ATC + TZM	ATC	TZM	Other Chemotherapy	None
1 year	7.5 %	22 %	9.8 %	16.7 %	8.4 %	7 %
2 years	13.3 %	33.2 %	15.3 %	23.2 %	13.7 %	12.8 %
3 years	18.7 %	41.9 %	20.2 %	32.1 %	19.2 %	18.1 %

HF or CM are common complications after trastuzumab therapy for older women, with higher rates than those reported from clinical trials.

Chen J Am Coll Cardiol 2012 ; 60 : 2504 - 12

How to prevent LV systolic dysfunction secundary to chemotherapy?





Longitudinal strain < 19 % remained the only independent predictor of cardiotoxicity in multivariate analysis

Peak systolic longitudinal strain was calculated by averaging the values of peak systolic strain in the basal and midventricular segments of the 4- and 2-chamber views

Sawaya Circ Cardiovasc Imaging. 2012;5:596-603