Un survol des dernières lignes directrices sur la cardio-oncologie

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CONFLITS D'INTÉRÊTS

- Aucun

OBJECTIF

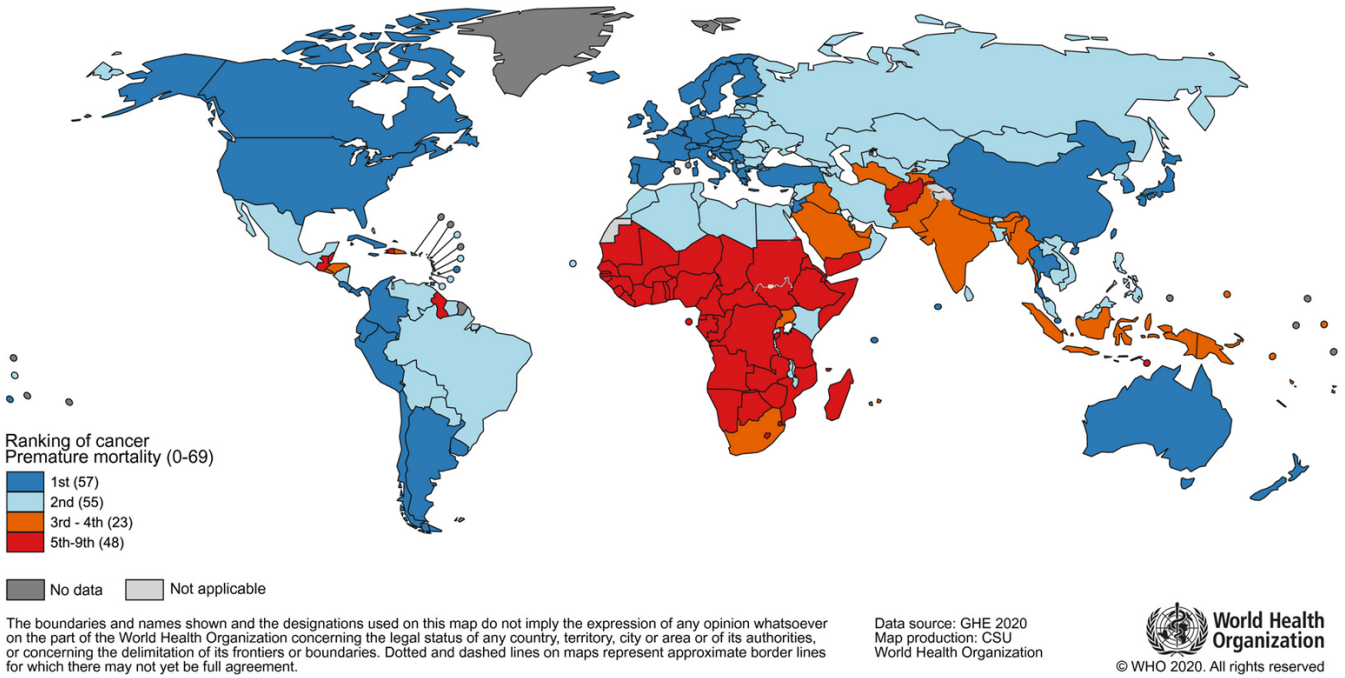
Établir qui devrait être suivi en cardio-oncologie et comment

Définir la cardio-toxicité

Prise en charge initiale d'une cardio-toxicité pour les chimiothérapies les plus courantes (anthracycline et HER2)

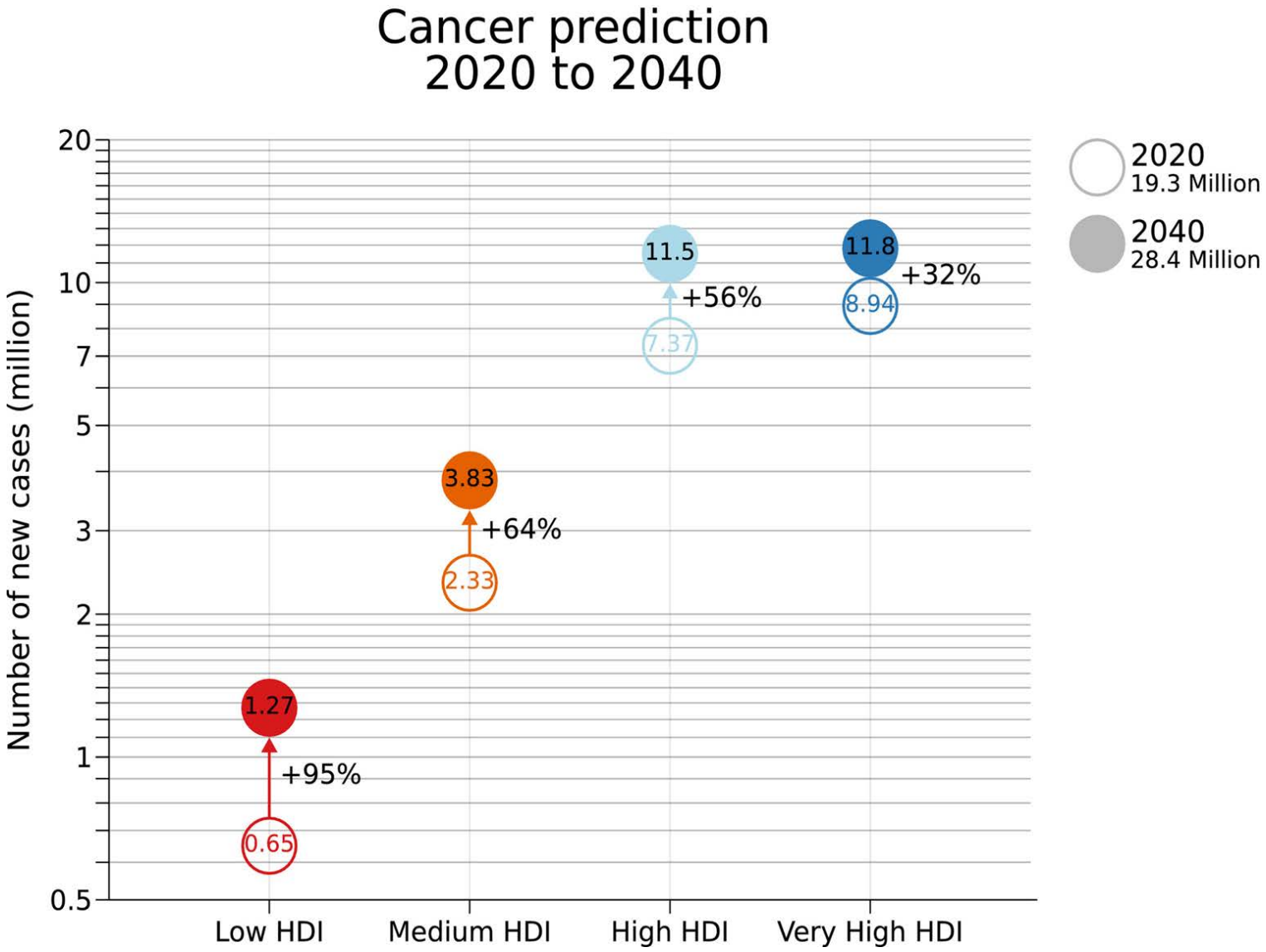
Inhibiteurs du point de contrôle immunitaire et myocardite

LA PROBLÉMATIQUE



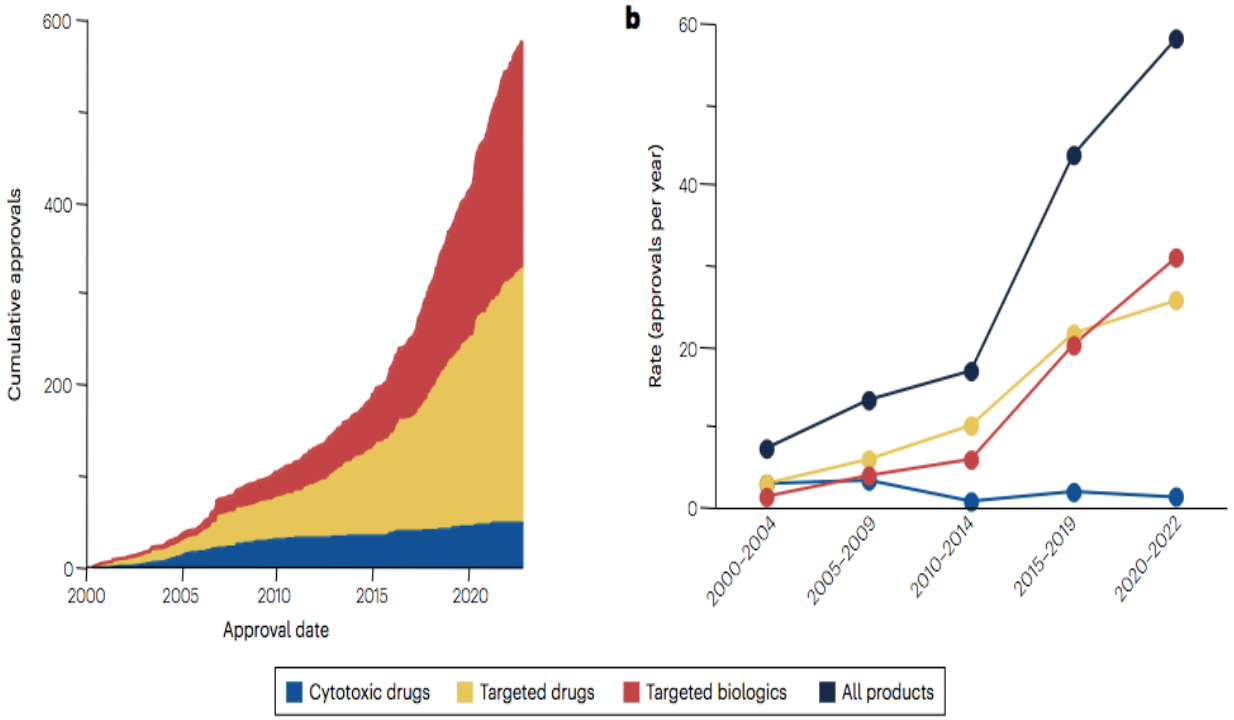
CA A Cancer J Clinicians, Volume: 71, Issue: 3, Pages: 209-249,

Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries



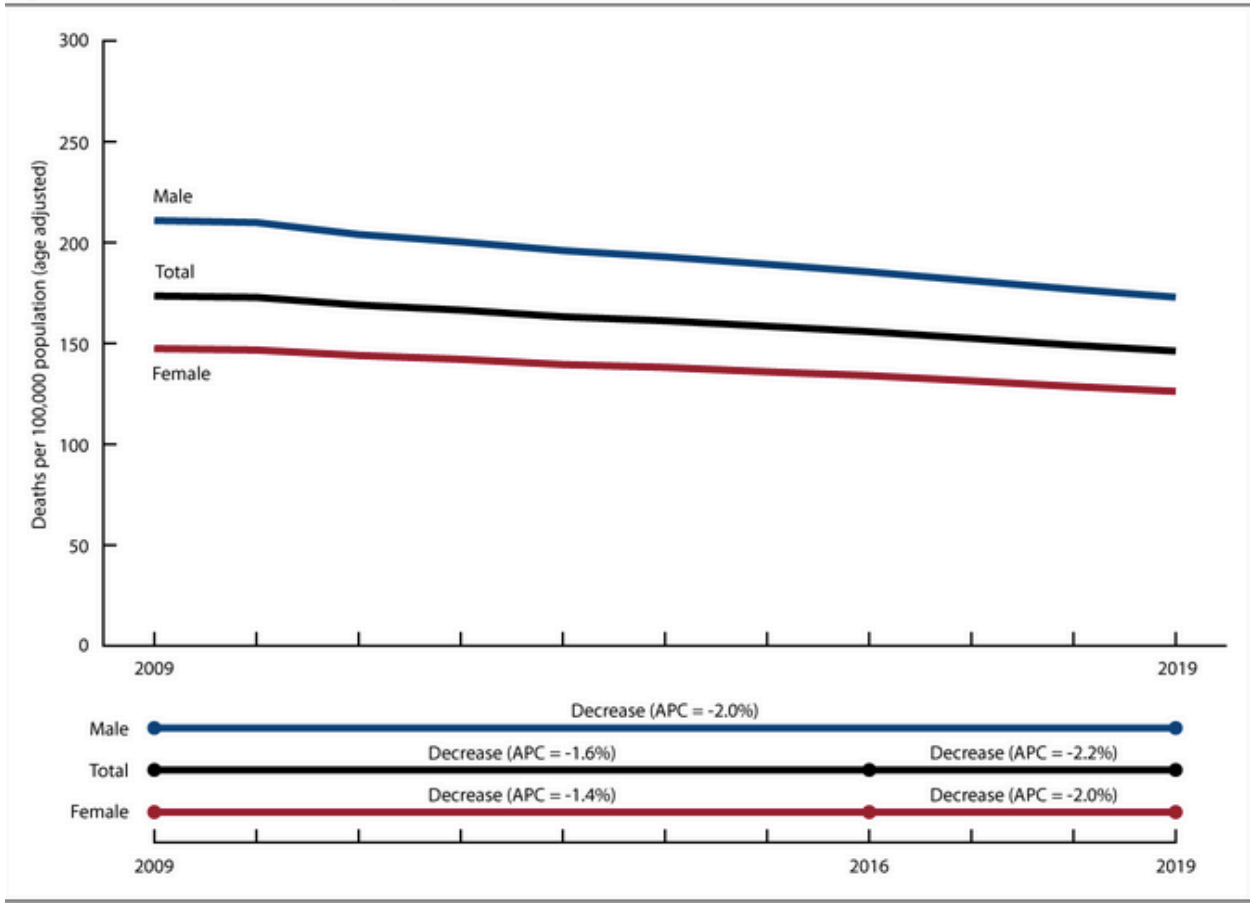
CA A Cancer J Clinicians, Volume: 71, Issue: 3, Pages: 209-249,

INTRODUCTION



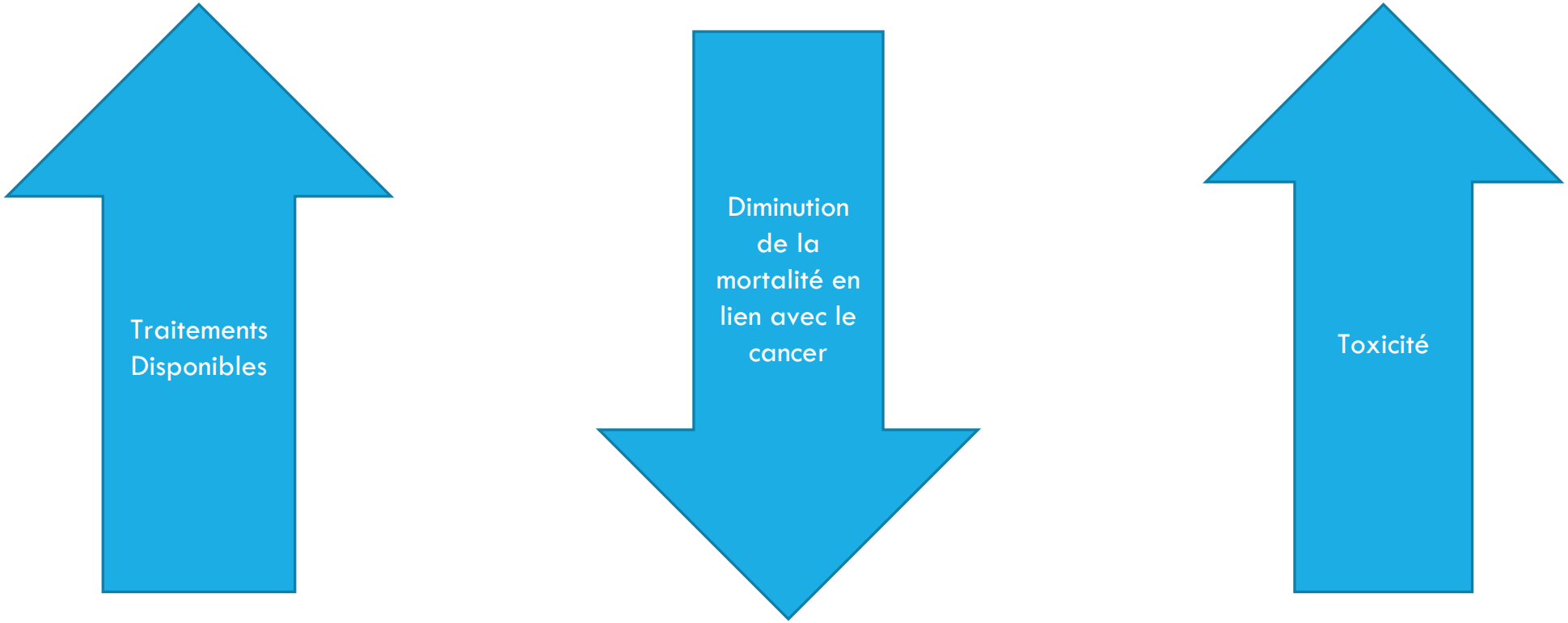
Nature Reviews Drug Discovery, Volume 22. August 2023:625–640

Figure 1. Cancer death rates, by sex: United States, 2009–2019



National Center for Health Statistics, National Vital Statistics System, Mortality and *Health, United States, 2020–2021*

INTRODUCTION



CLINIQUE DE CARDIO-ONCOLOGIE

- **Éviter l'interruption du traitement oncologique tout en empêchant les manifestations toxiques sur le système cardiovasculaire**
- Traiter la cardio-toxicité

PRÉVENTION CARDIOVASCULAIRE

Traiter les facteurs de risques agressivement

Éviter bolus ou doses élevée anthracycline

Formulation spécial de doxorubicin liposomal

Dexrazoxane

BB/IECA ?

EFFET PROTECTEUR BB/IECA

Echocardiography Imaging Measures and Study Drug Hemodynamic Effect[a]

	No.	Baseline unadjusted	Adjusted 3 Mo	6 Mo	EOT	vs Baseline
3D-LVEF, %						
Placebo	42	67.3 (66.0 to 68.5)	64.1 (63.3 to 64.9)	63.0 (62.0 to 64.0)	63.5 (62.5 to 64.5)	−4.4
Ramipril	44	65.7 (64.7 to 66.7)	65.4 (64.6 to 66.2)	65.0 (64.0 to 65.9)[b]	64.4 (63.4 to 65.5)	−3.0
Bisoprolol	45	66.5 (65.2 to 67.7)	65.5 (64.7 to 66.3)	65.1 (64.2 to 66.1)[b]	65.2 (64.2 to 66.2)	−1.9
Ramipril plus bisoprolol	43	66.4 (65.5 to 67.4)	65.9 (65.1 to 66.7)[b]	64.9 (64.0 to 65.9)[b]	65.6 (64.6 to 66.6)[b]	−1.3
All	174	66.5 (65.9 to 67.0)	NA	NA	NA	NA

JACC: CARDIOONCOLOGY, VOL. 4, NO. 1, 2022

EFFET PROTECTEUR BB/IECA

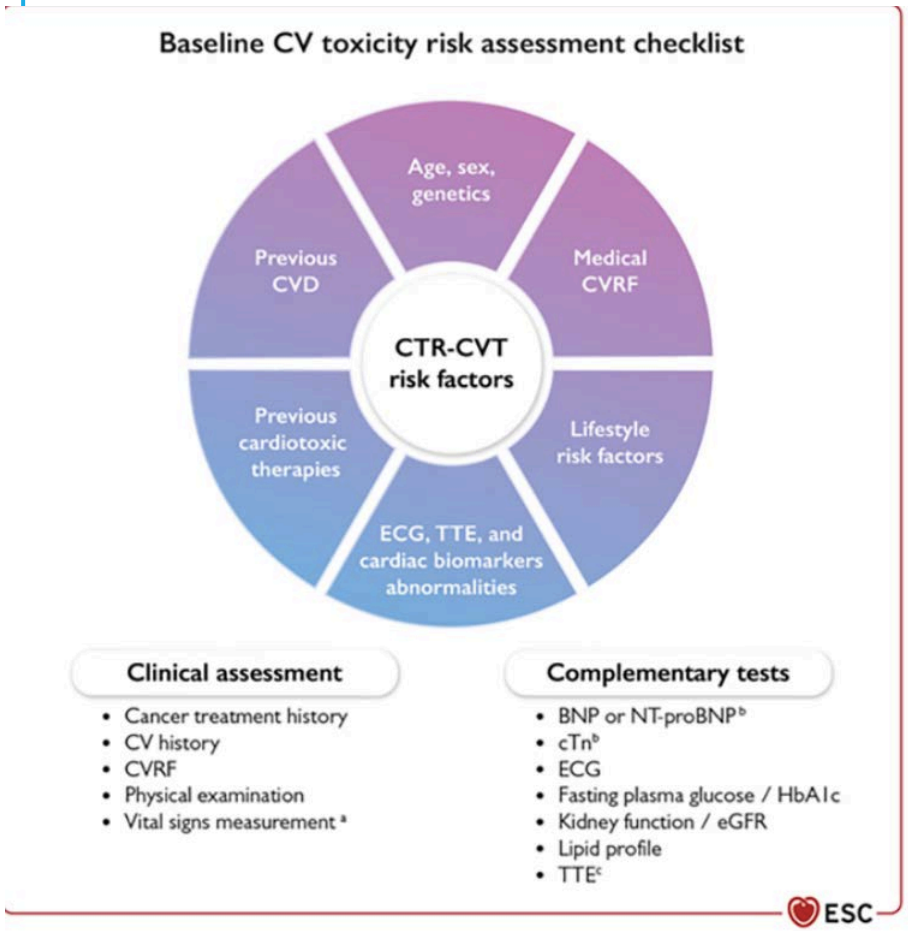
TABLE 2 Recent Randomized Controlled Trials on Cardioprotection During Trastuzumab Therapy

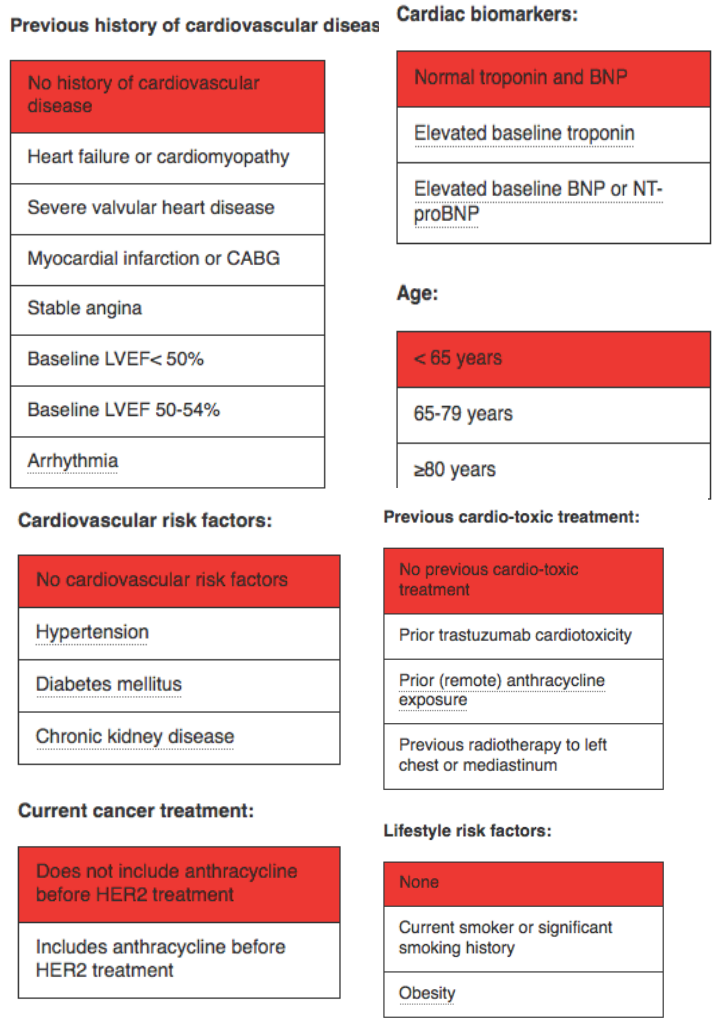
Trial	Trial Design	Trial Intervention	Imaging Method	N	Result of Primary Endpoint	Result of Key Secondary Endpoints
Pharmacologic intervention						
MANTICORE 101-Breast[44]	Randomized Placebo-controlled Double-blind Few were treated with anthracyclines	Bisoprolol/ perindopril/placebo	CMR	99	No between-group difference in LVEDVi	• Bisoprolol attenuated the decline in LVEF • Perindopril attenuated the decline in LVEF
Boekhout et al[45]	Randomized Multicenter Placebo-controlled Double-blind All were treated with anthracycline in advance	Candesartan/placebo	MUGA	210	No between-group difference in incidence of cardiotoxicity, defined as decline in LVEF of ≥15% or ≤15% to an absolute value < 45%	No between-group differences in changes in LVEF, troponin T, or NT-proBNP
Guglin et al[46]	Randomized Multicenter Placebo-controlled 189 were treated with anthracyclines	Lisinopril/carvedilol/ placebo	Echocardiography MUGA	468	No between-group difference in incidence of cardiotoxicity, defined as a reduction in LVEF of ≥10% or a decrease of ≥5% to a value <50%	• Reduction in the incidence of cardiotoxicity if patients treated with sequential anthracyclines in both lisinopril and carvedilol arms • No between-group difference if no anthracycline exposure

LVEDVi = left ventricular end-diastolic indexed volume; MANTICORE 101-Breast = Multidisciplinary Approach to Novel Therapies in Cardio-Oncology Research; MUGA = multigated acquisition; NT-proBNP = N-terminal pro-B-type natriuretic peptide; other abbreviations as in Table 1.

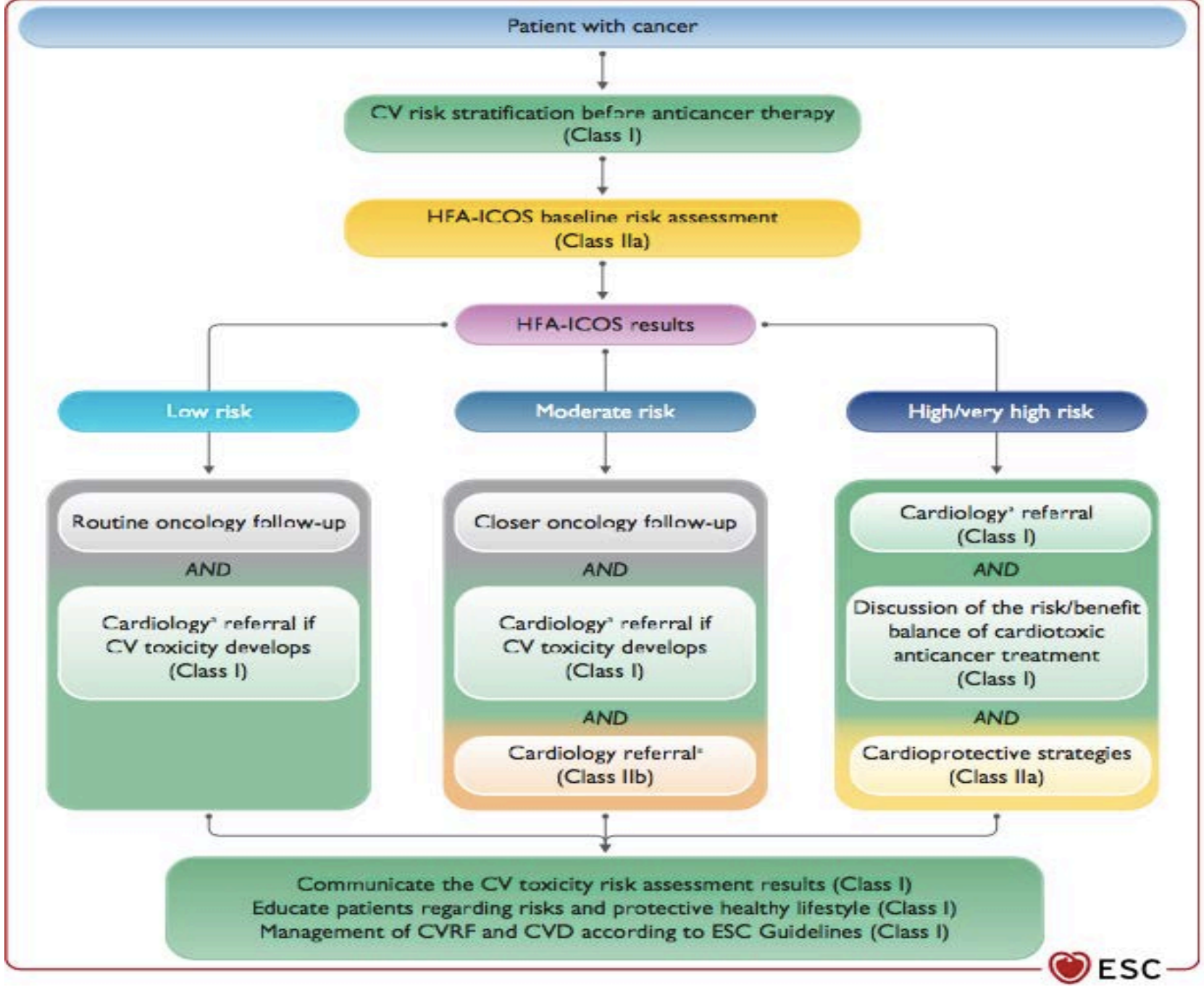
JACC: CARDIOONCOLOGY, VOL. 4, NO. 1, 2022

ÉVALUATION DU RISQUE DE TOXICITÉ CARDIAQUE





Eur Heart J. 2022;43:4229-361.

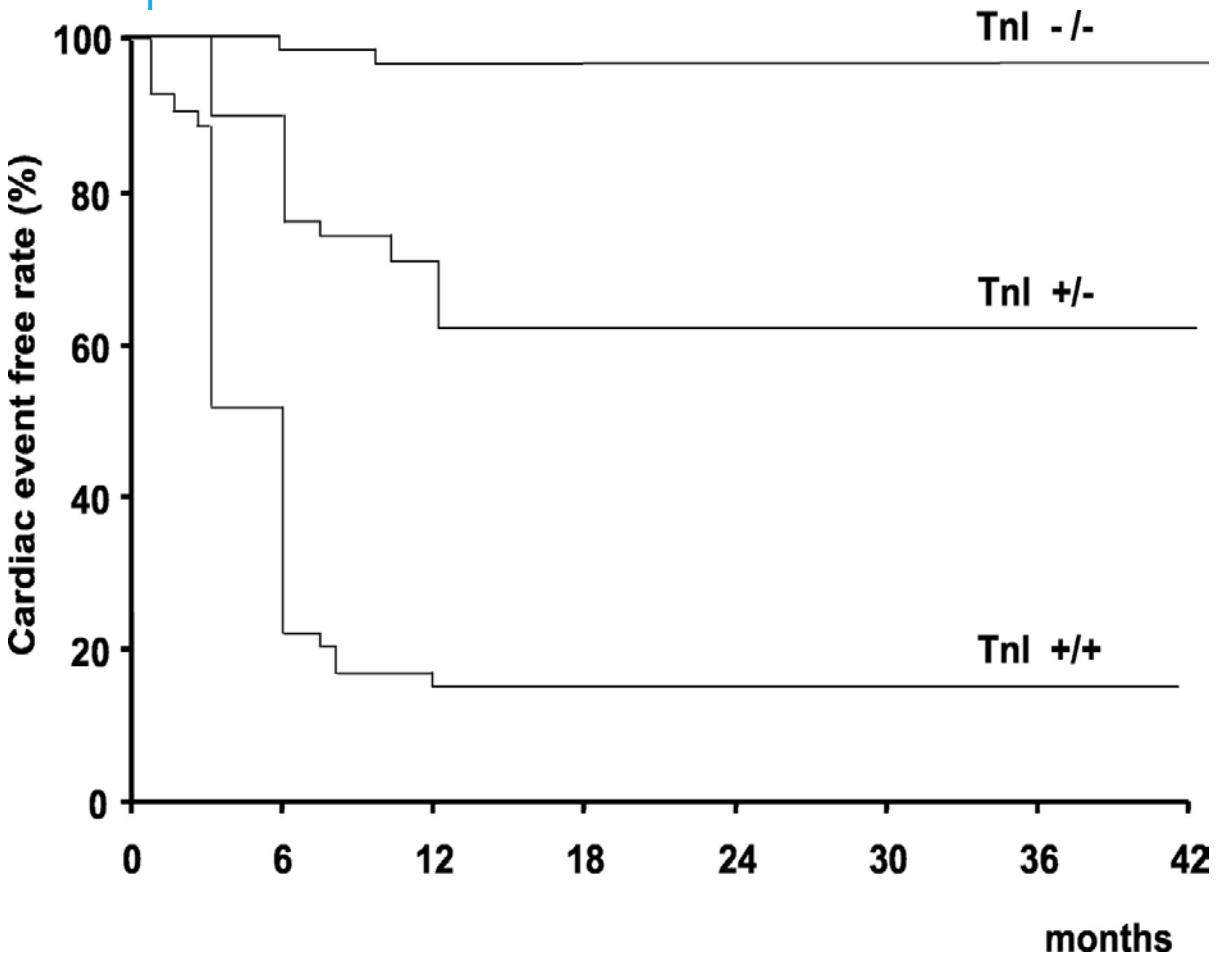


EUR HEART J, VOLUME 43, ISSUE 41, 1 NOVEMBER 2022, PAGES 4229–43

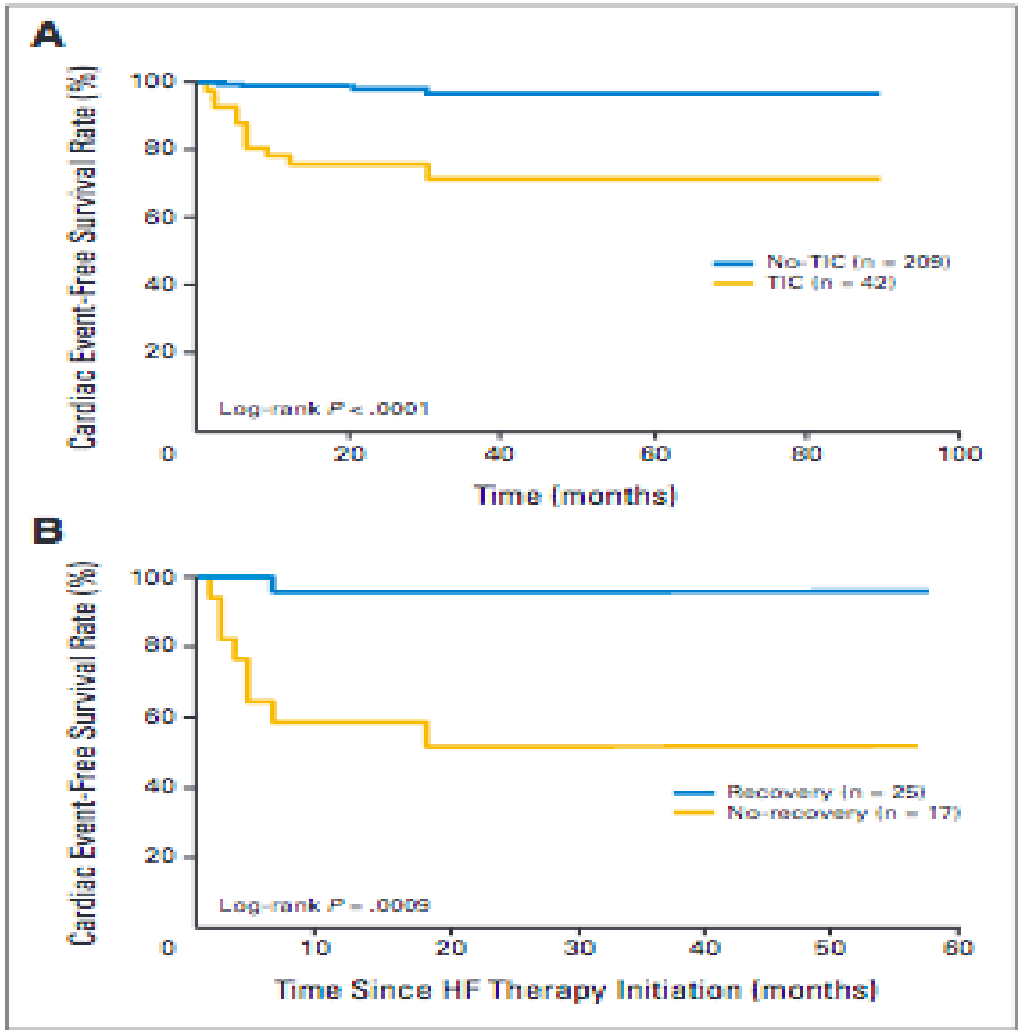
OUTILS DE TRAVAIL

- ECG
- Troponine
- NT-ProBNP
- Imagerie
  - ETT (3D/strain)
  - IRM
  - Ventriculographie isotopique

TROPONINE



Circulation 2004;109:2749–2754.



J Clin Oncol 28:3910-3916

BNP

Effect	HR (95% CI)	*P*
Carfilzomib *v* bortezomib	3.0 (1.1 to 8.4)	.04
Elevated baseline natriuretic peptide levels *v* normal levels	4.1 (2.1 to 8.1)	< .001
Normal baseline natriuretic peptide levels that became elevated mid–first cycle of treatment *v* normal levels	9.5 (4.3 to 20.7)	< .001
≤ 1 traditional CV risk factor *v* ≥ 2	0.5 (0.3 to 0.9)	.02
Time from myeloma diagnosis to enrollment in PROTECT	0.98 (0.6 to 1.5)	.9

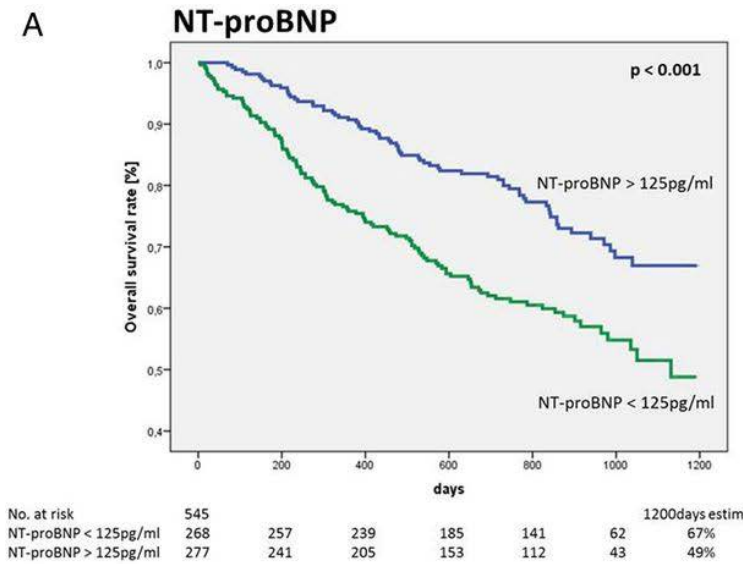
Abbreviations: CV, cardiovascular; CVAE, cardiovascular adverse event; HR, hazard ratio; PROTECT, Prospective Observation of Cardiac Safety With Proteasome Inhibitor.

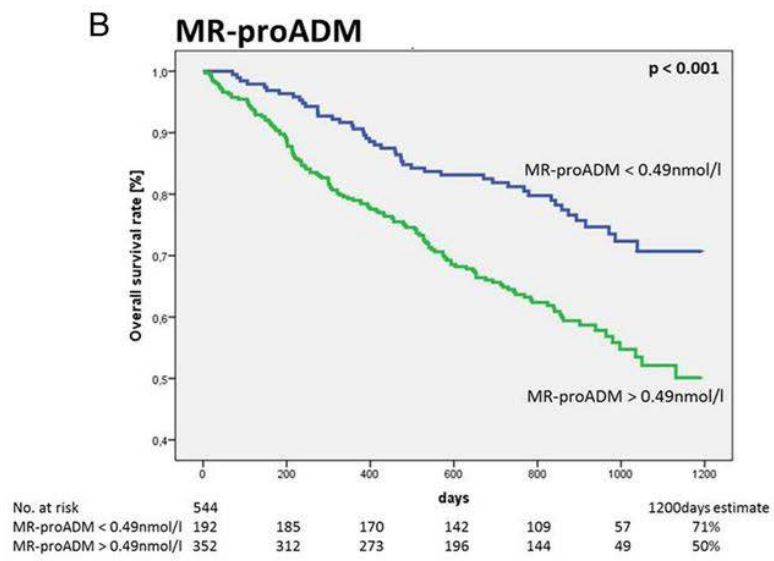
J Clin Oncol. 2019 Aug 1; 37(22): 1946–1955

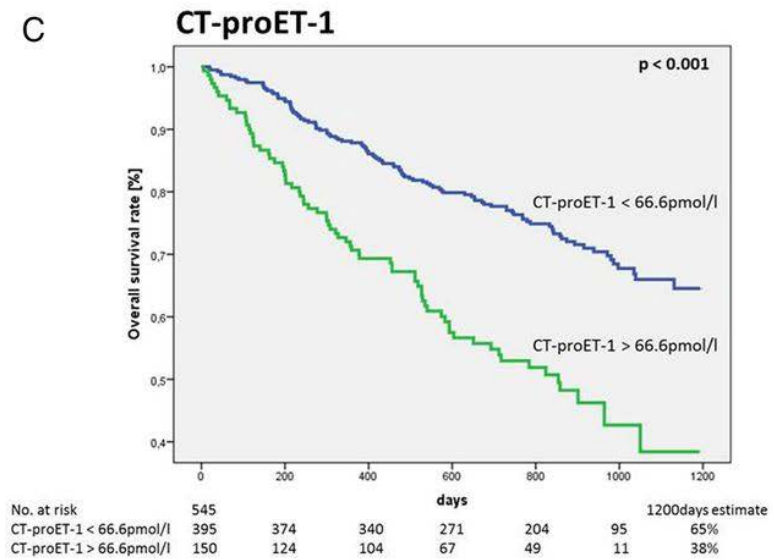
Table 2 Tumour entities and staging for patients with confirmed cancer (n=555)

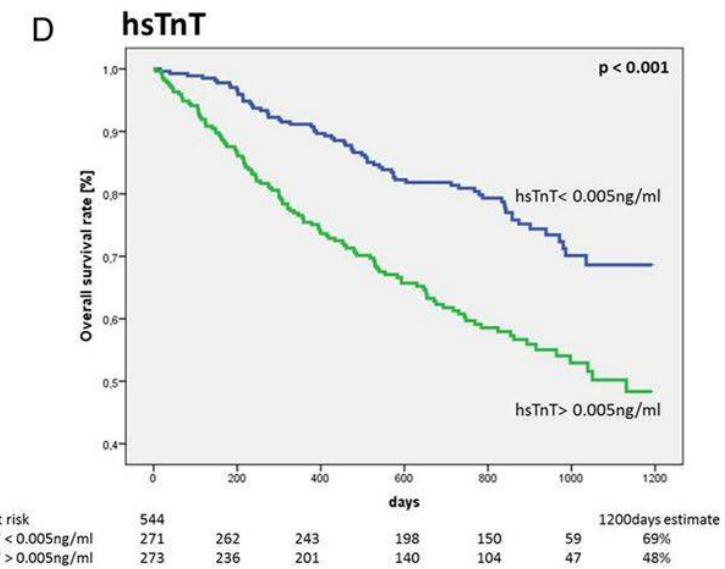
	Patients with cancer (n=555)
Tumour entity	
Lung cancer, n (%)	61 (11.0%)
Breast cancer, n (%)	146 (26.3%)
Brain tumour, n (%)	23 (4.1%)
ENT tumour, n (%)	33 (5.9%)
Gastrointestinal tumours, n (%)	67 (12.1%)
Myelodysplastic malignancies, n (%)	68 (12.3%)
Myeloproliferative neoplasias, n (%)	99 (17.8%)
Oesophageal cancer, n (%)	11 (2.0%)
Testicular cancer, n (%)	2 (0.4%)
Neuroendocrine tumour, n (%)	11 (2.0%)
Sarcoma, n (%)	9 (1.6%)
Mesothelioma, n (%)	3 (0.6%)
Prostate cancer, n (%)	2 (0.4%)
Renal cell carcinoma, n (%)	4 (0.7%)
Thymoma, n (%)	1 (0.2%)
Skin cancer, n (%)	2 (0.4%)
Urogenital tumours, n (%)	2 (0.4%)
Oral cancer, n (%)	1 (0.2%)
Other, n (%)	10 (1.8%)
Tumour stage	
Stage 1, n (%)	93 (16.7%)
Stage 2, n (%)	49 (8.8%)
Stage 3, n (%)	108 (19.5%)
Stage 4, n (%)	177 (31.9%)
No staging, n (%)	128 (23.1%)

Counts are given as numbers and percentages.
Myelodysplastic malignancies: haematological malignancies with abnormal differentiation of myeloid or lymphoid cell lines (eg, AML, acute myeloid leukemia; ALL, acute lymphoid leukemia; lymphomas, multiple myeloma); myeloproliferative neoplasias: haematological neoplasias with normal cell differentiation (eg, essential thrombocytosis, polycythaemia vera, myelofibrosis).
ENT, ear, nose, throat.









Heart 2015;101:1874–1880.

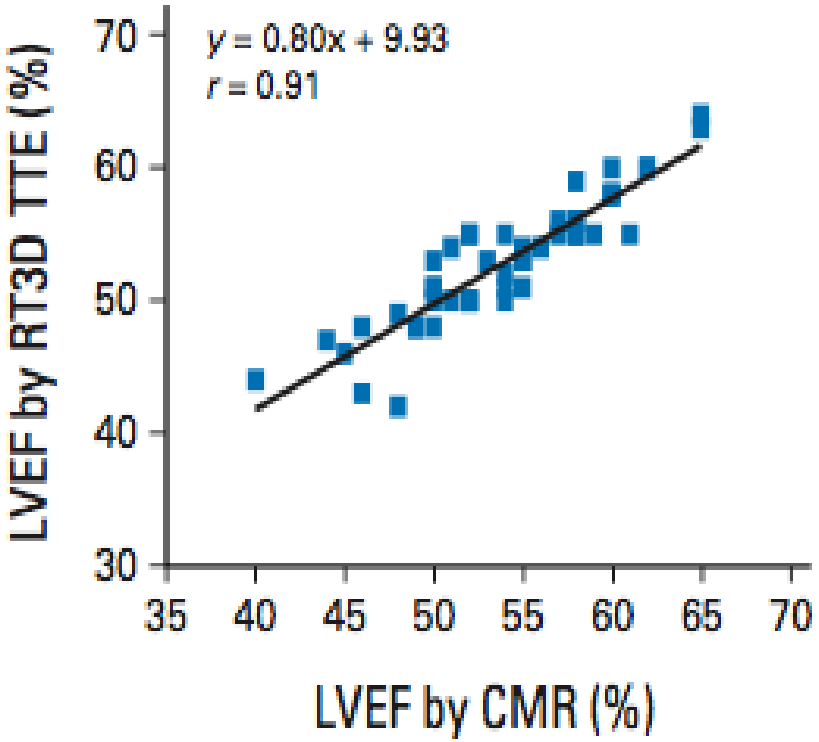
TROPONINE/NT-PROBNP

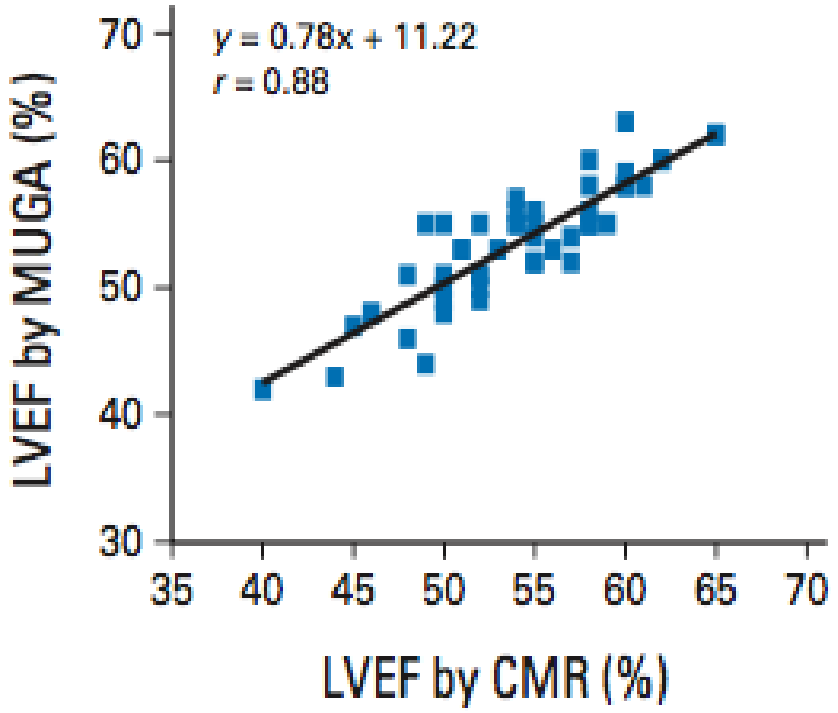
- Utile pour valeur de base
- Facteur de mauvais pronostic
- Moins de récupération de la FEVG si troponine de base augmentée
- Démontre possiblement une atteinte directe de la tumeur sur le système cardiovasculaire

IMAGERIE

- Règles
    1. Toujours utiliser le même type d'examen pour comparer la fonction ventriculaire

IMAGERIE



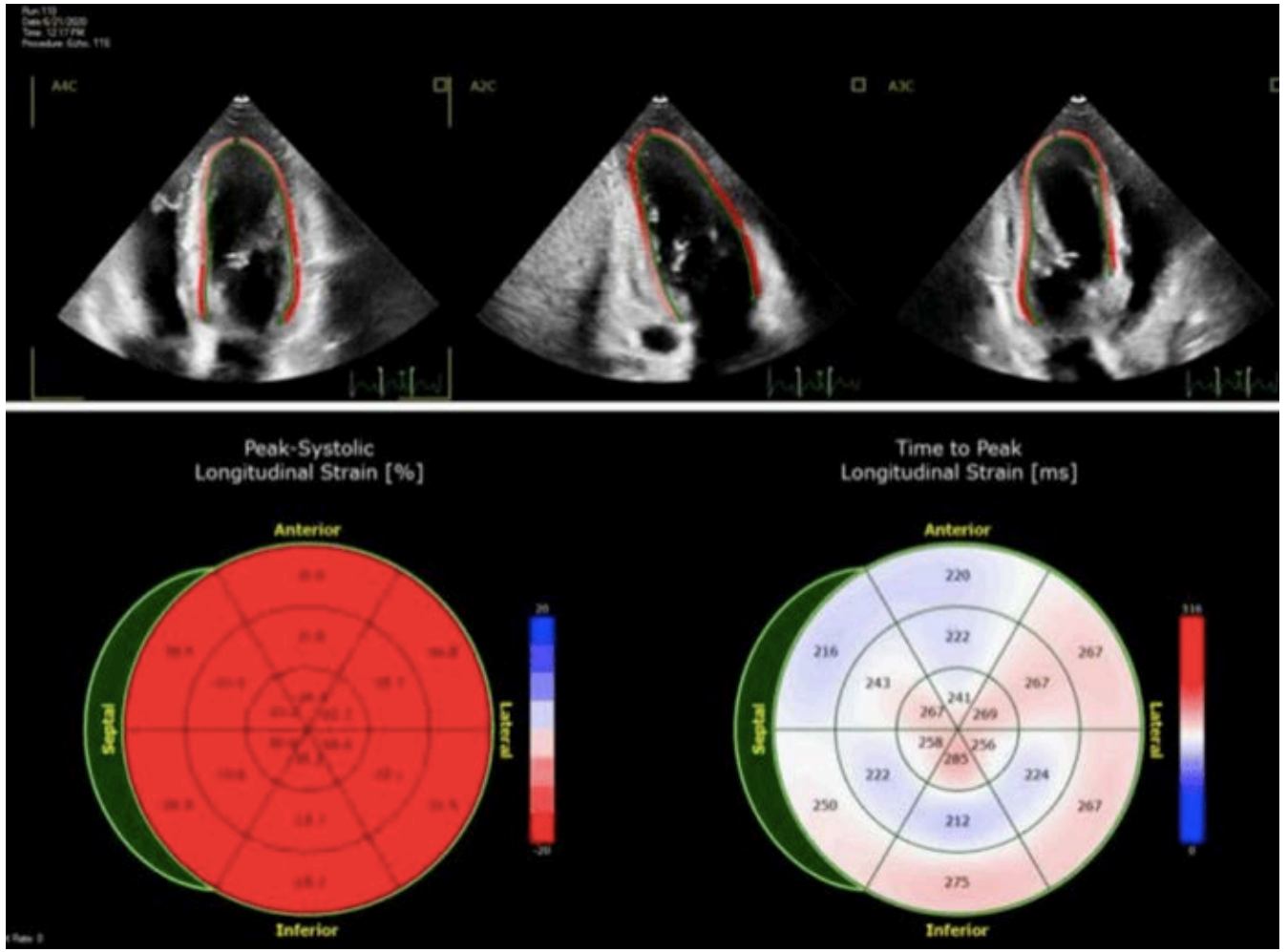


J Clin Oncol 28:3429-3436

IMAGERIE

- Toujours utiliser le même type d'examen pour comparer la fonction ventriculaire
- En ordre de priorité
  - ETT
  - IRM
  - Ventriculographie isotopique
- Utiliser le 3D pour la FEVG
- Agent de contraste au besoin

STRAIN


A4C
A2C
A3C
Peak-Systolic
Longitudinal Strain [%]
Anterior
Septal
Lateral
Inferior
Time to Peak
Longitudinal Strain [ms]
Anterior
220
222
216
267
243
267
241
267
269
258
256
285
222
224
250
267
212
275
Septal
Lateral
Inferior

Myocardial Strain Is Associated with Adverse Clinical Cardiac Events in Patients Treated with Anthracyclines

Mohammed T. Ali, MD, Evin Yucel, MD, Souhila Bouras, MD, Lin Wang, MD, Hong-wen Fei, MD, Elkan F. Halpern, PhD, and Marielle Scherrer-Crosbie, MD, PhD. *Boston, Massachusetts*

Table 2 Echocardiographic variables in patients who did or did not develop CEs

Variable	Total (n = 450)	No CEs (n = 422)	CEs (n = 28)	P
Baseline LVEF (%)	62 ± 8	62 ± 7	58 ± 10	.005
LV EDV (mL)	114 ± 32	114 ± 33	111 ± 32	.640
LV EDVI (mL/m^2)	59 ± 14	59 ± 14	60 ± 12	.890
LV ESV (mL)	45 ± 16	45 ± 16	48 ± 20	.340
LV ESVI (mL/m^2)	24 ± 7	23 ± 7	26 ± 13	.072
GLS (%)	−19.4 ± 2.9	−19.7 ± 2.7	−15.0 ± 2.8	.000
Average segmental longitudinal strain (%)	−19.9 ± 3.1	−20.3 ± 2.4	−13.2 ± 2.3	.000

EDV, End-diastolic volume; *EDVI*, end-diastolic volume indexed to body surface area; *ESV*, end-systolic volume; *ESVI*, end-systolic volume indexed to body surface area.
Data are expressed as mean ± SD.

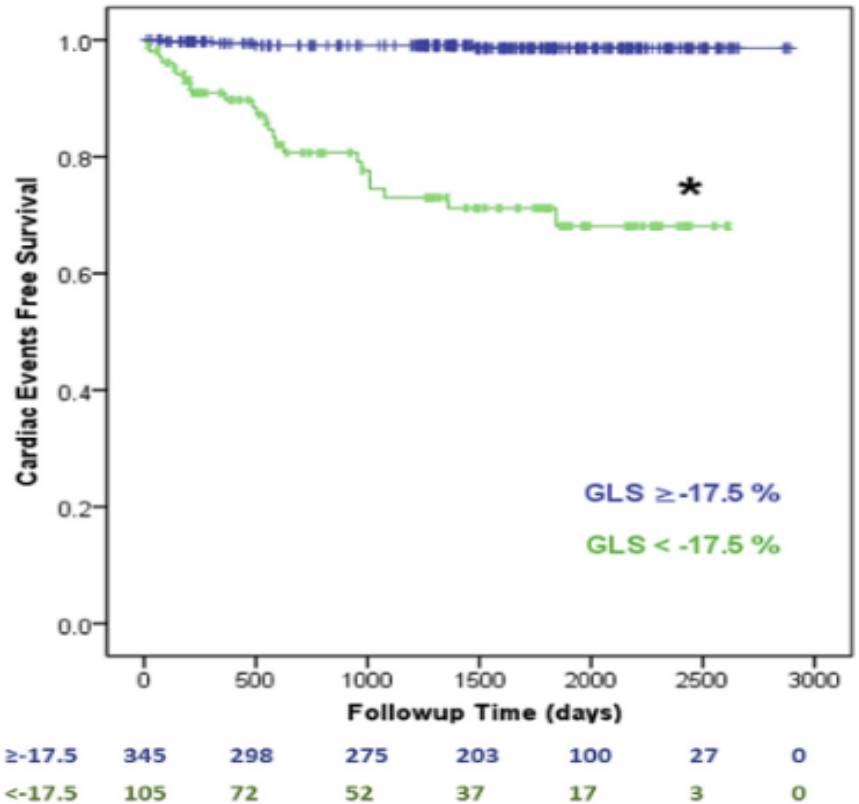


Figure 2 CE-free survival according to GLS. Kaplan-Meier curves depicting event-free survival in patients with GLS above or below the absolute value of −17. %. *Pts*, Patients. *P < .0001.

European Heart Journal – Cardiovascular Ima
doi:10.1093/ehjci/jev113

Echocardiographic p … ar size and function as … heart failure in patie… ejection fraction of 5… anthracyclines

Negareh Mousavi[1], Timothy C. Ta… ng[1], and Marielle Scherrer-Crosbie[1]*

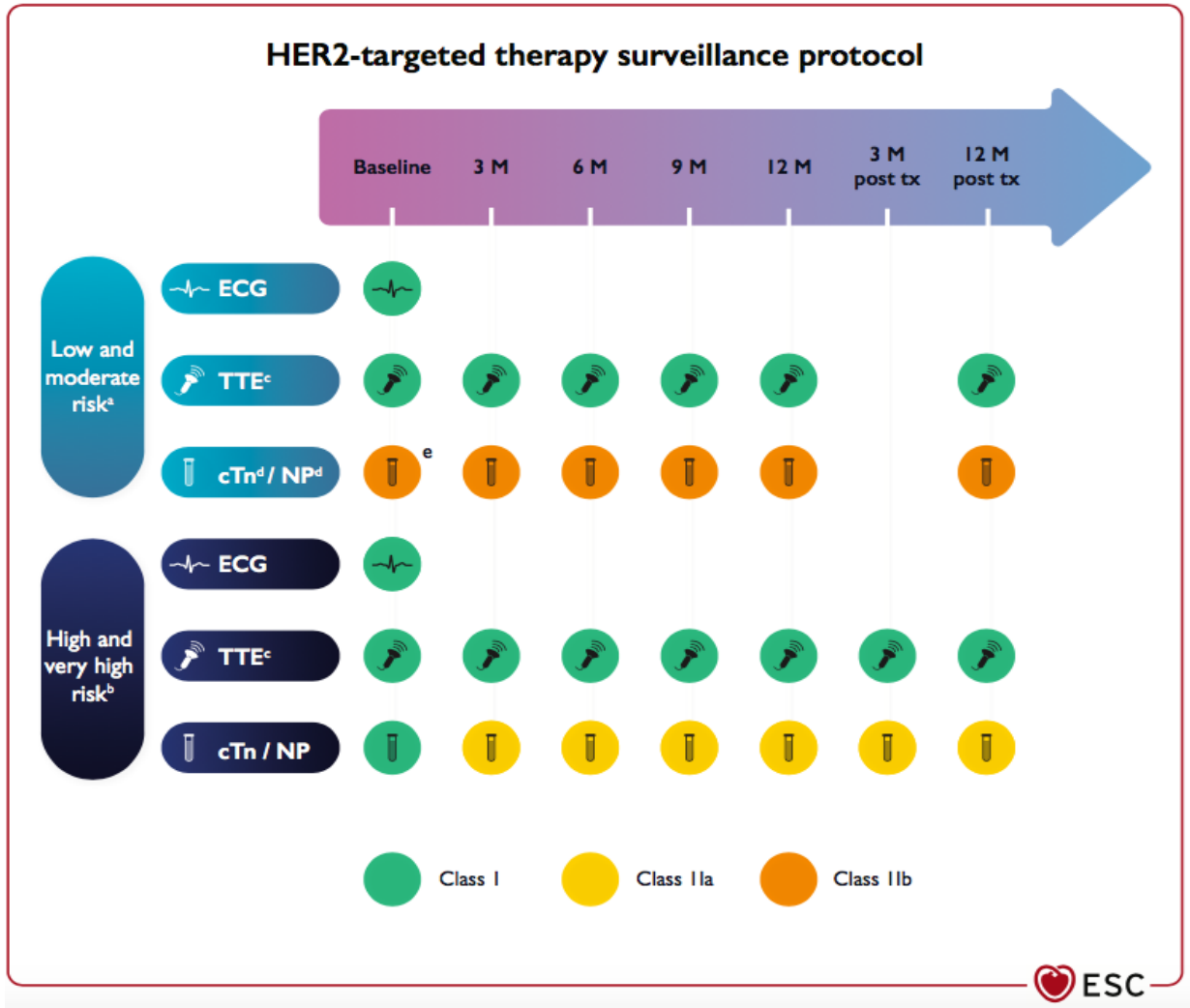
Un détérioration de plus que 15% du GLS initial prédit une chute de FEVG d'au moins 10% dans 65% à 93% des cas

Table 5 Univariable clinical and echocardiographic predictors of overall mortality in patients with an LVEF of 50–59% treated with anthracyclines

Variable	Hazard ratio	95% CI	*P*-value
Age (per year increase)	1.03	1.01–1.05	<0.0001
Gender (Male)	1.34	0.80–2.29	0.267
Cancer type			
Other vs. breast	3.75	1.75–8.53	0.0006
Other vs. blood	2.23	1.21–3.98	0.0105
Baseline LVEF (per % increase)	0.90	0.82–0.98	0.018
LVEDV (per mL increase)	0.99	0.98–1.00	0.26
LVEDVI (per mL/m^2 increase)	0.98	0.96–1.01	0.123
LVESV (per mL increase)	0.988	0.961–1.014	0.35
LVESVI (per mL/m^2 increase)	0.99	0.95–1.04	0.715
GLS (per % decrease)	1.13	1.03–1.25	0.0105

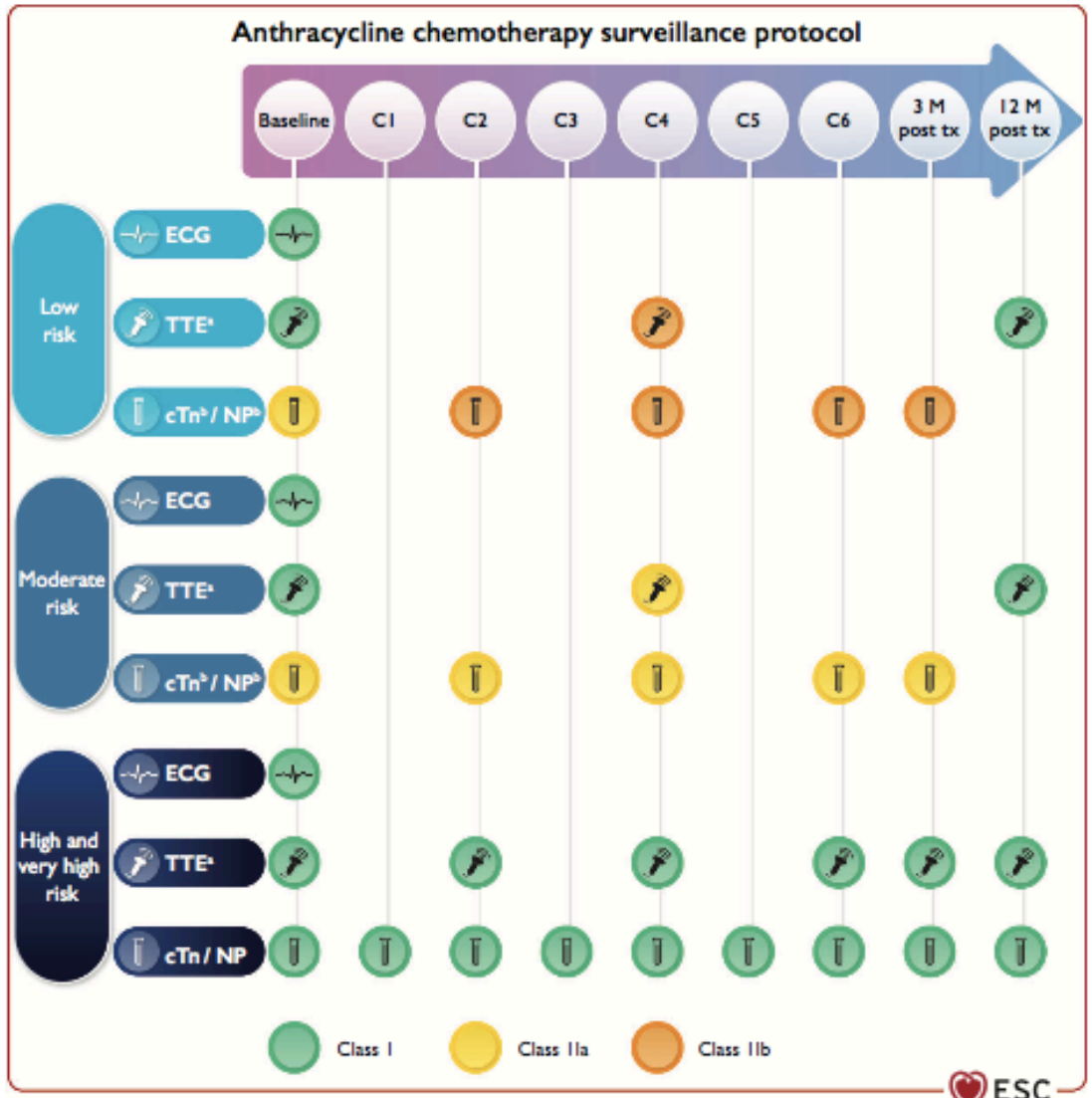
LVEF, left ventricular systolic function; LV, left ventricle; LVEDV, left ventricular end-diastolic volume; LVEDVI, left ventricular end-diastolic volume indexed to BSA; LVESV, left ventricular end-systolic volume; LVESVI, left ventricular end-systolic volume indexed to BSA; LVEF, left ventricular function, GLS, global longitudinal strain.

SUIVIT: THÉRAPIE CIBLÉ HER2



European Heart Journal (2022) 00, 1–133

SUVIT: ANTHRACYCLINE



European Heart Journal (2022) 00, 1–133

TOXICITÉ CARDIAQUE

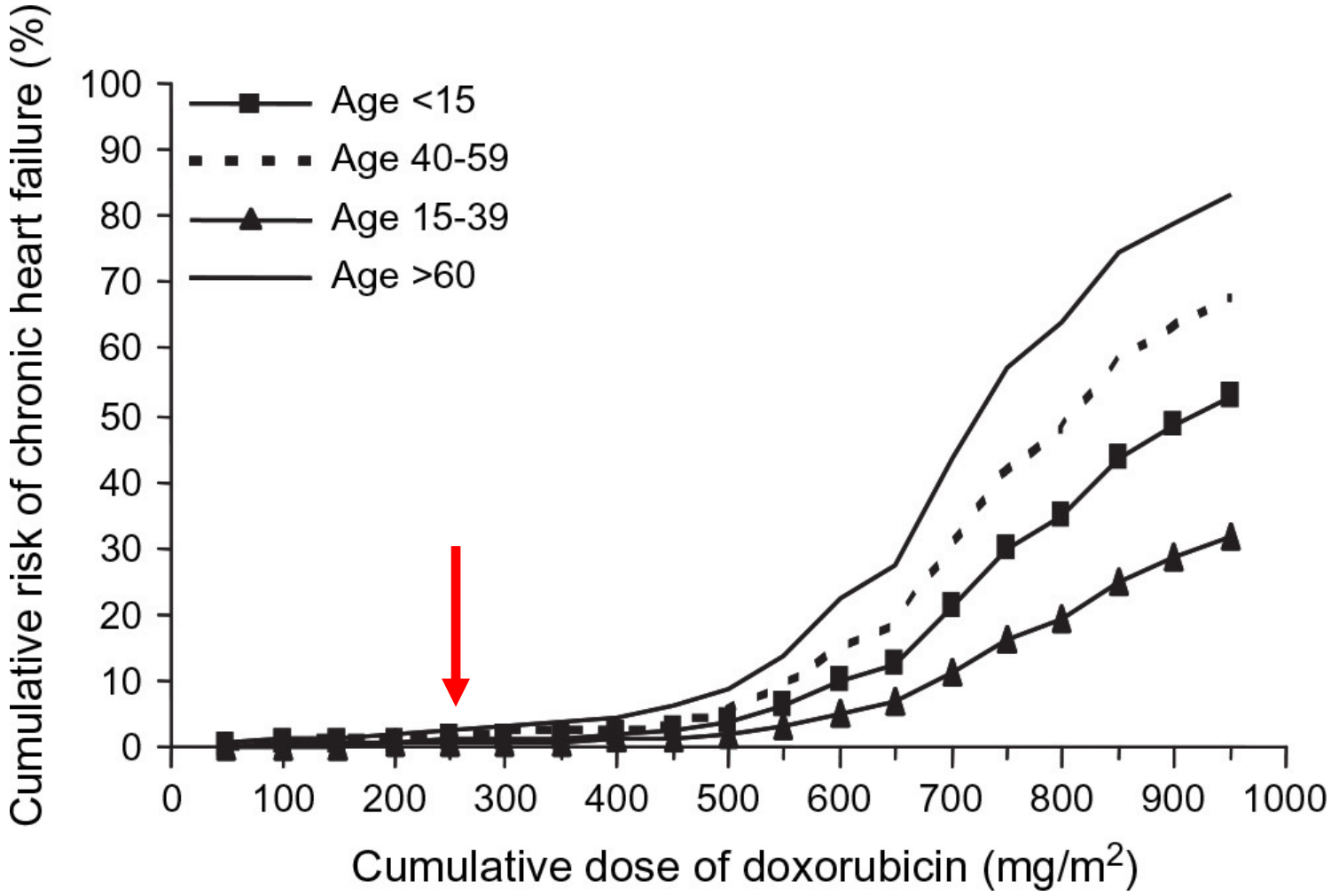
Asymptomatique

- Sévère:
  - diminution de FEVG en dessous de 40%
- Modérée:
  - Diminution de FEVG > 10% pour une FEVG entre 40-49% ou
  - Diminution de FEVG <10% pour FEVG entre 40-49% **ET**
    - Baisse de GLS de plus que 15% de valeur de base ou augmentation des biomarqueurs
- Légère:
  - FEVG plus que 50% **ET**
    - Baisse de GLS de plus que 15% de valeur de base ou augmentation des biomarqueurs

Symptomatique

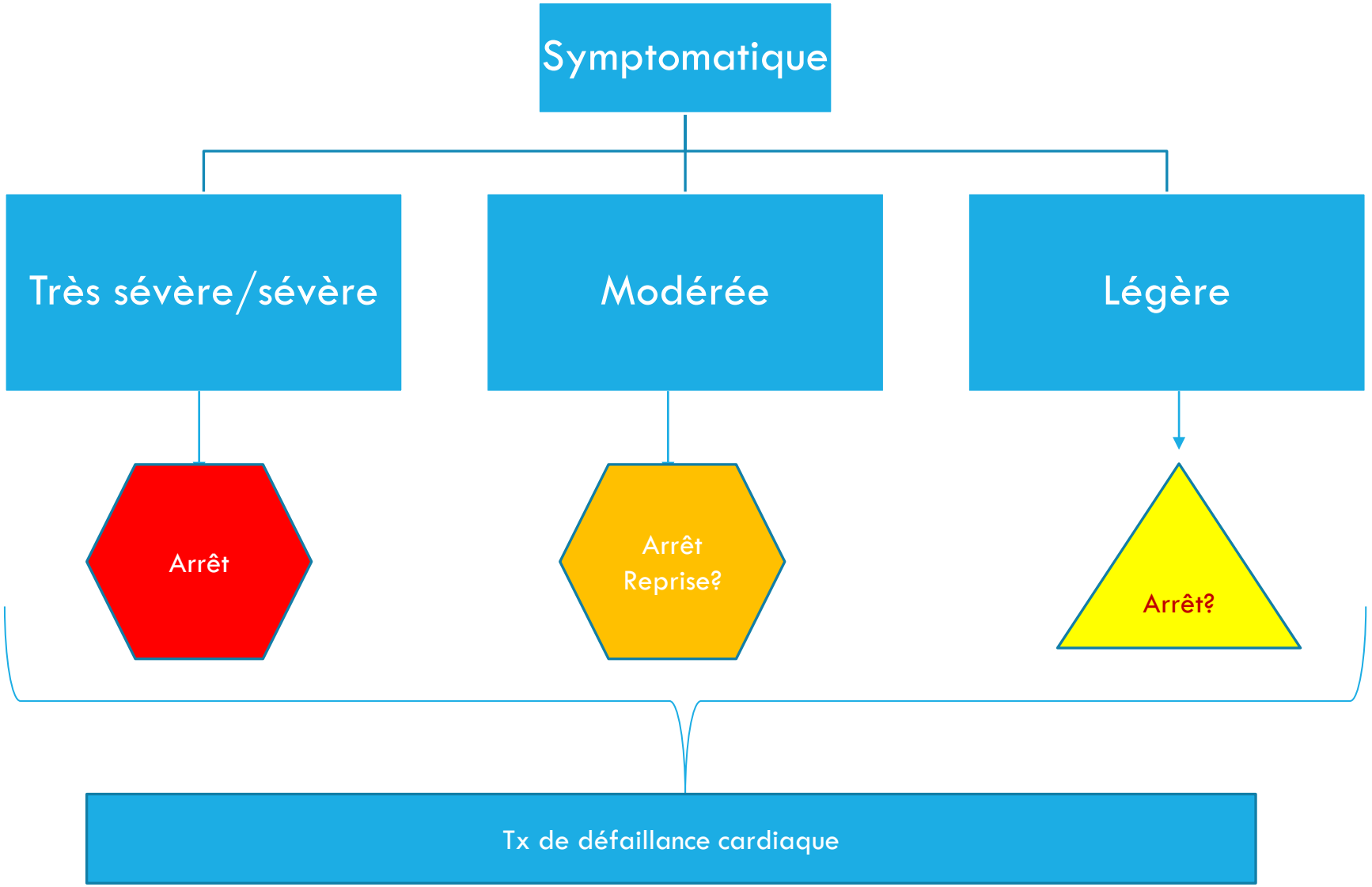
- Très sévère:
  - Support inotrope ou mécanique
- Sévère:
  - Nécessitant hospitalisation
- Modérée:
  - Nécessitant intensification du traitement de la défaillance cardiaque
- Légère:
  - symptômes de défaillance cardiaque léger ne nécessitant pas d'intensification du traitement

TOXICITÉ ANTHRACYCLINE

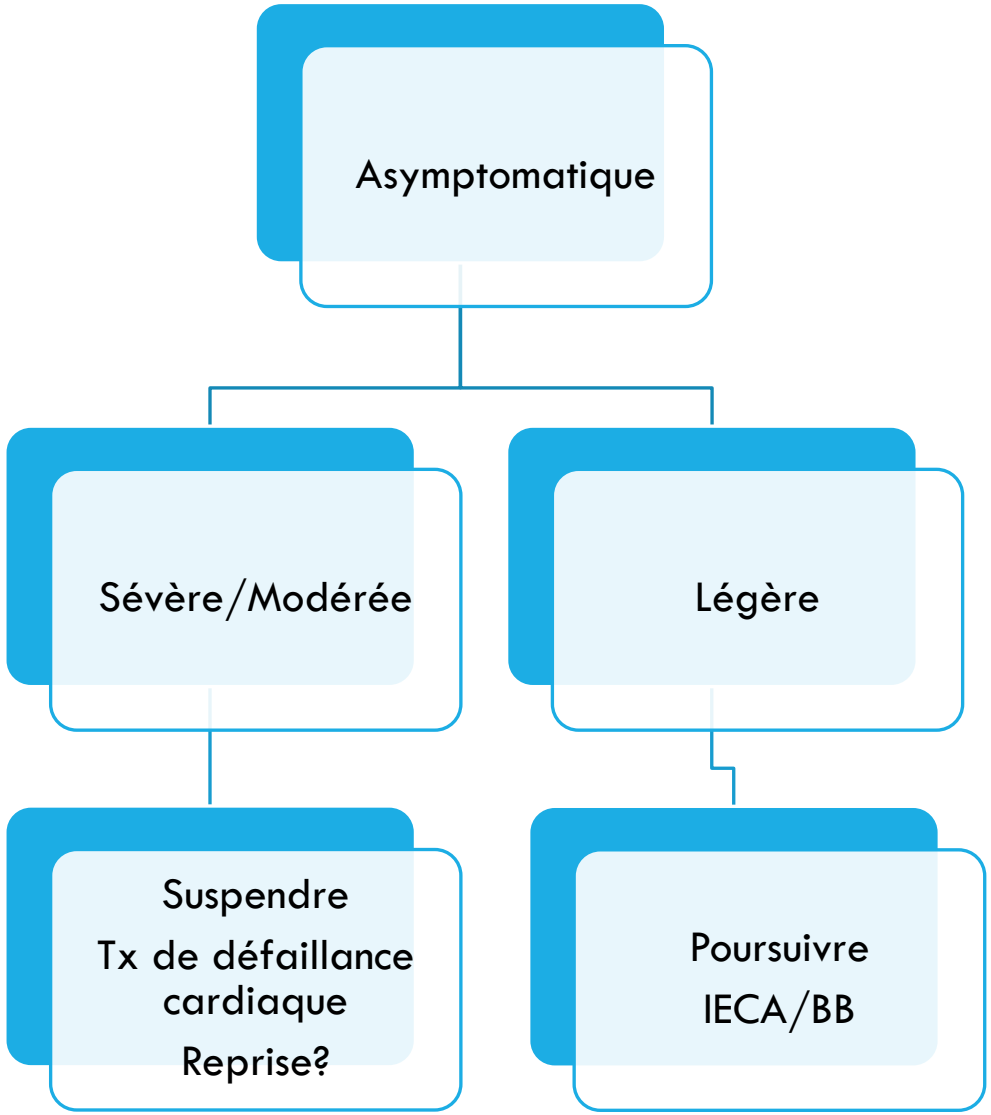


Annals of Oncology 20: 816–827, 2009

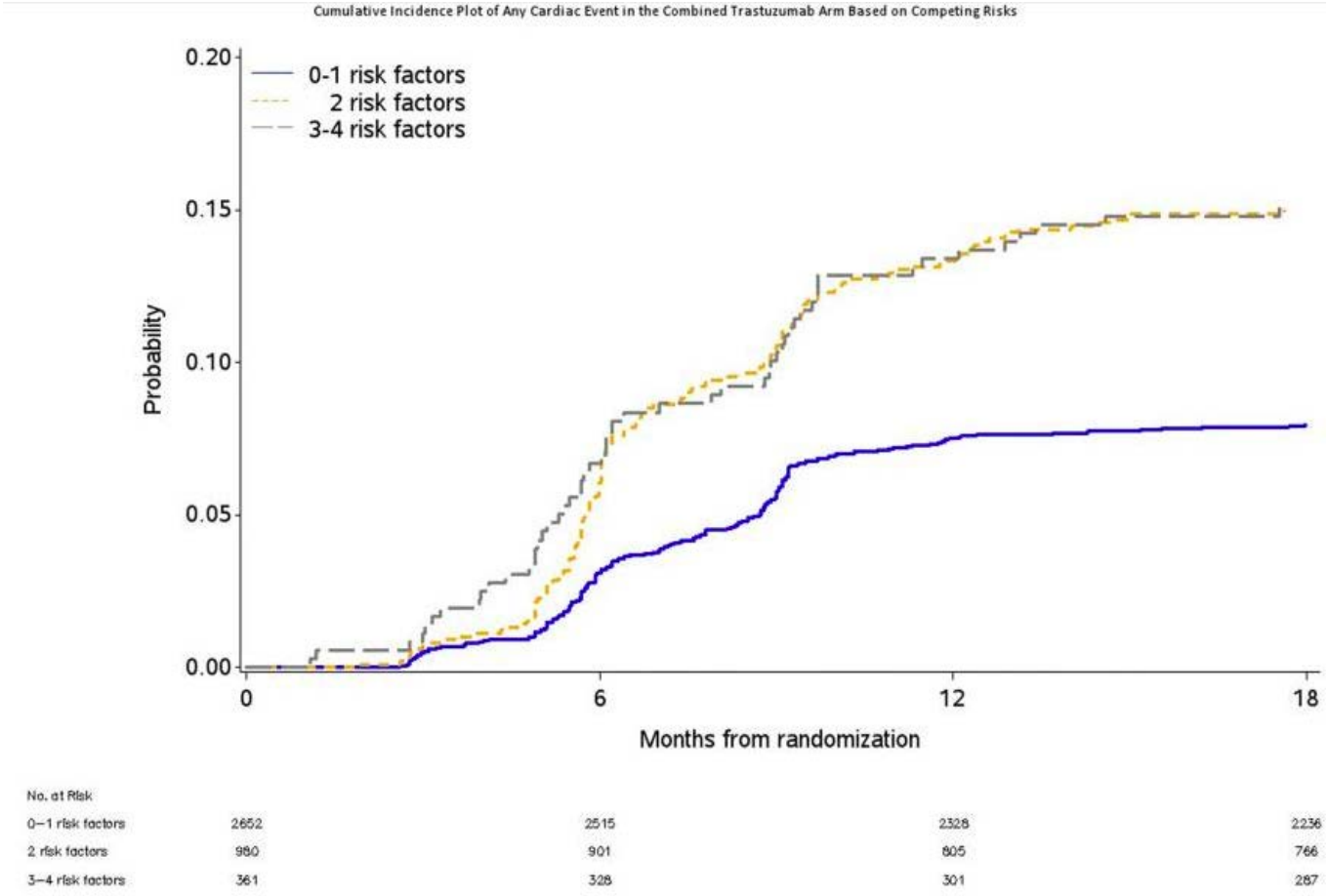
TOXICITÉ ANTHRACYCLINE PRISE EN CHARGE-SYMPTOMATIQUE



TOXICITÉ ANTHRACYCLINE : PRISE EN CHARGE- ASYMPTOMATIQUE



TOXICITÉ HER-2



- Dysfonction du VG jusqu'à 15-20%
- Dysfonction de Type II
- Lien avec:
  - ⬅Facteurs de risques
  - ⬅Utilisation concomitante d'anthracycline

Breast Cancer Res Treat. 2020 January ; 179(1): 161–171

TOXICITÉ HER-2

Symptomatique

Modérée/Sévère

- Interruption du traitement
- Tx de l'insuffisance cardiaque
- ?Reprise du traitement (discussion avec EMD)

Légère

- Tx de défaillance cardiaque
- Interruption du traitement selon discussion EMD

Asymptomatique

Sévère

- Interruption du traitement
- Tx de insuffisance cardiaque
- ?Reprise du traitement (discussion avec EMD)

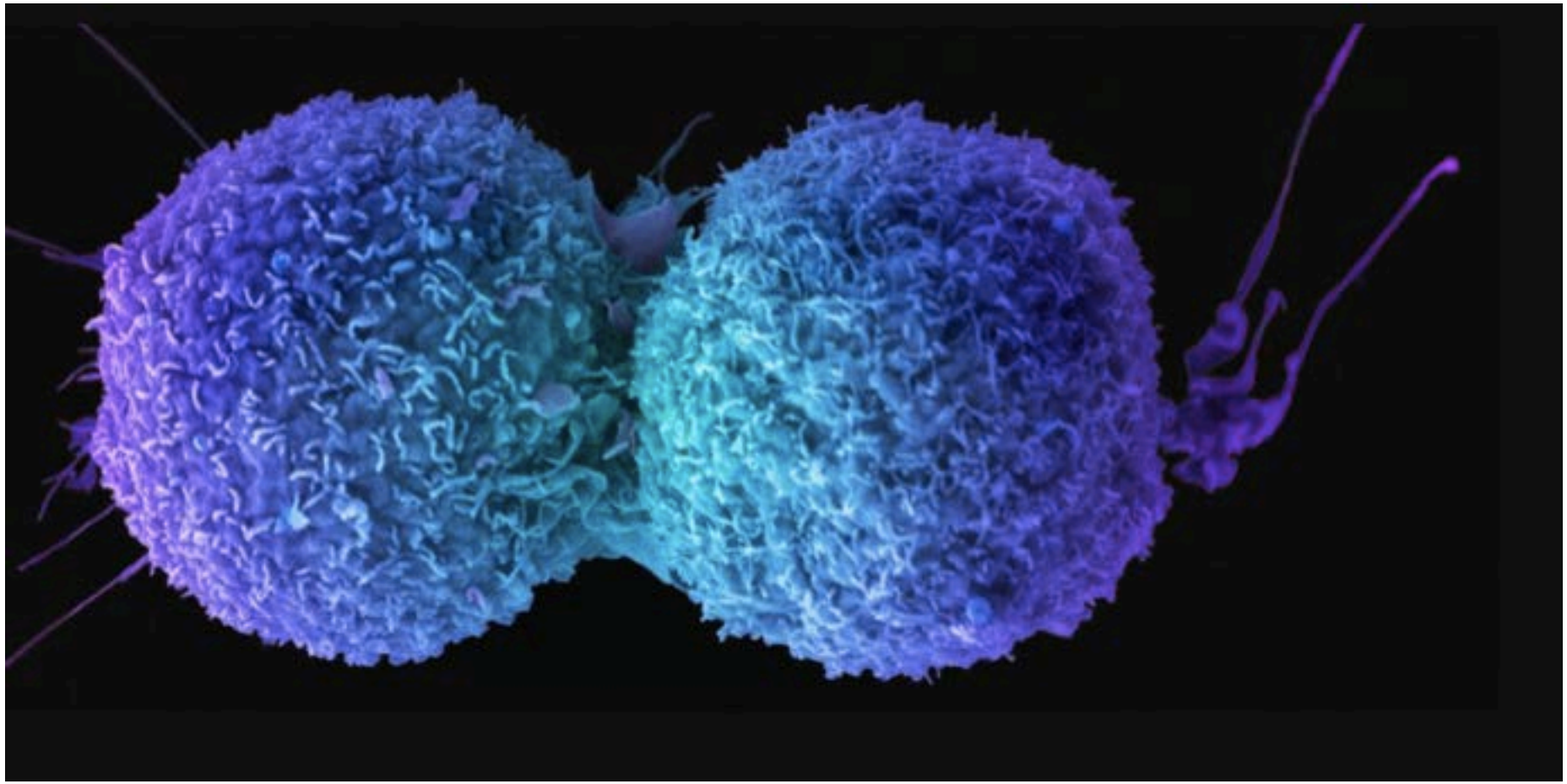
Modérée

- Tx de insuffisance cardiaque
- Poursuivre TX (Classe IIa)

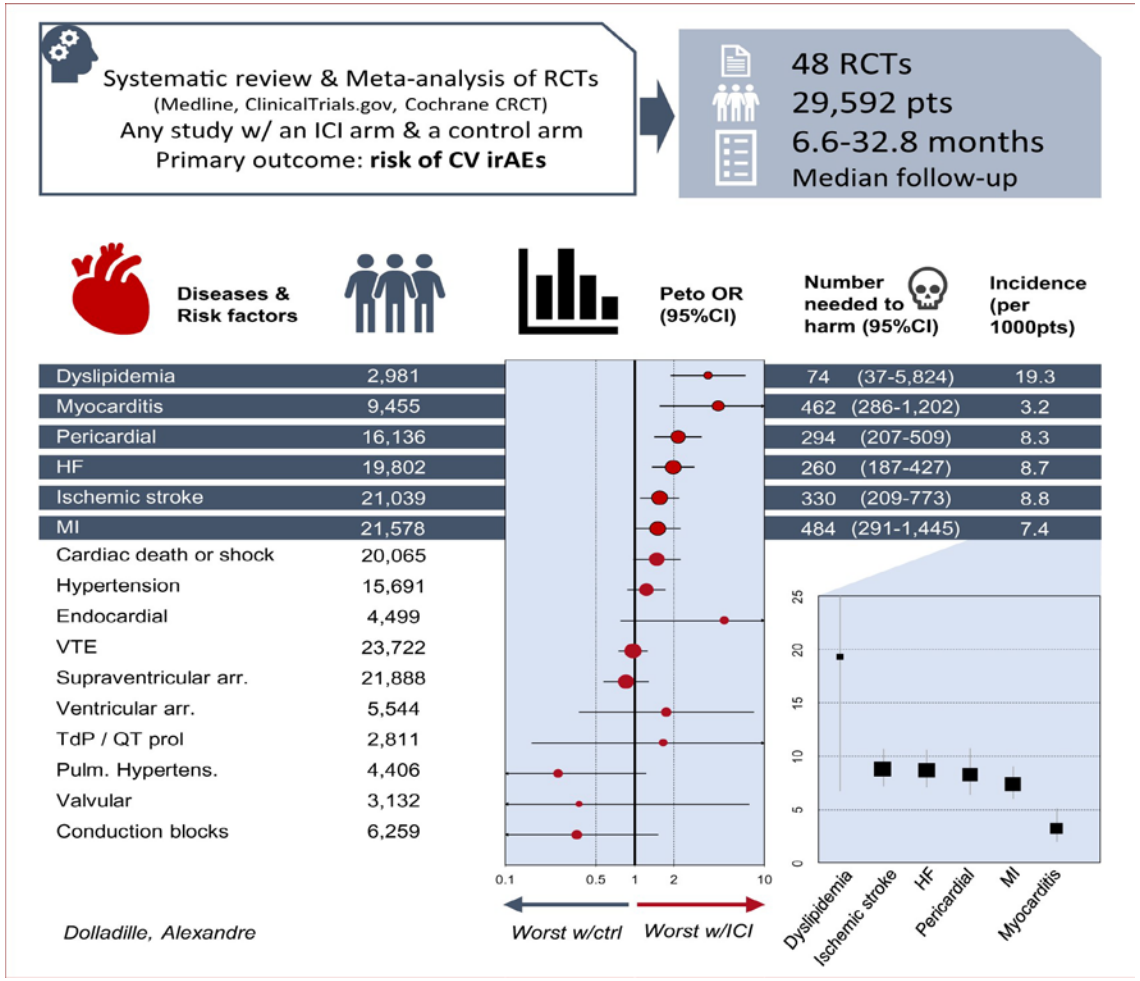
Légère

- Poursuivre tx
- IECA/BB? (Classe IIa)

INHIBITEURS DU POINT DE CONTRÔLE IMMUNITAIRE



CARDIOVASCULAR IMMUNOTOXICITIES (RISK AND INCIDENCE) OF IMMUNE CHECKPOINT INHIBITORS FROM RANDOMIZED …



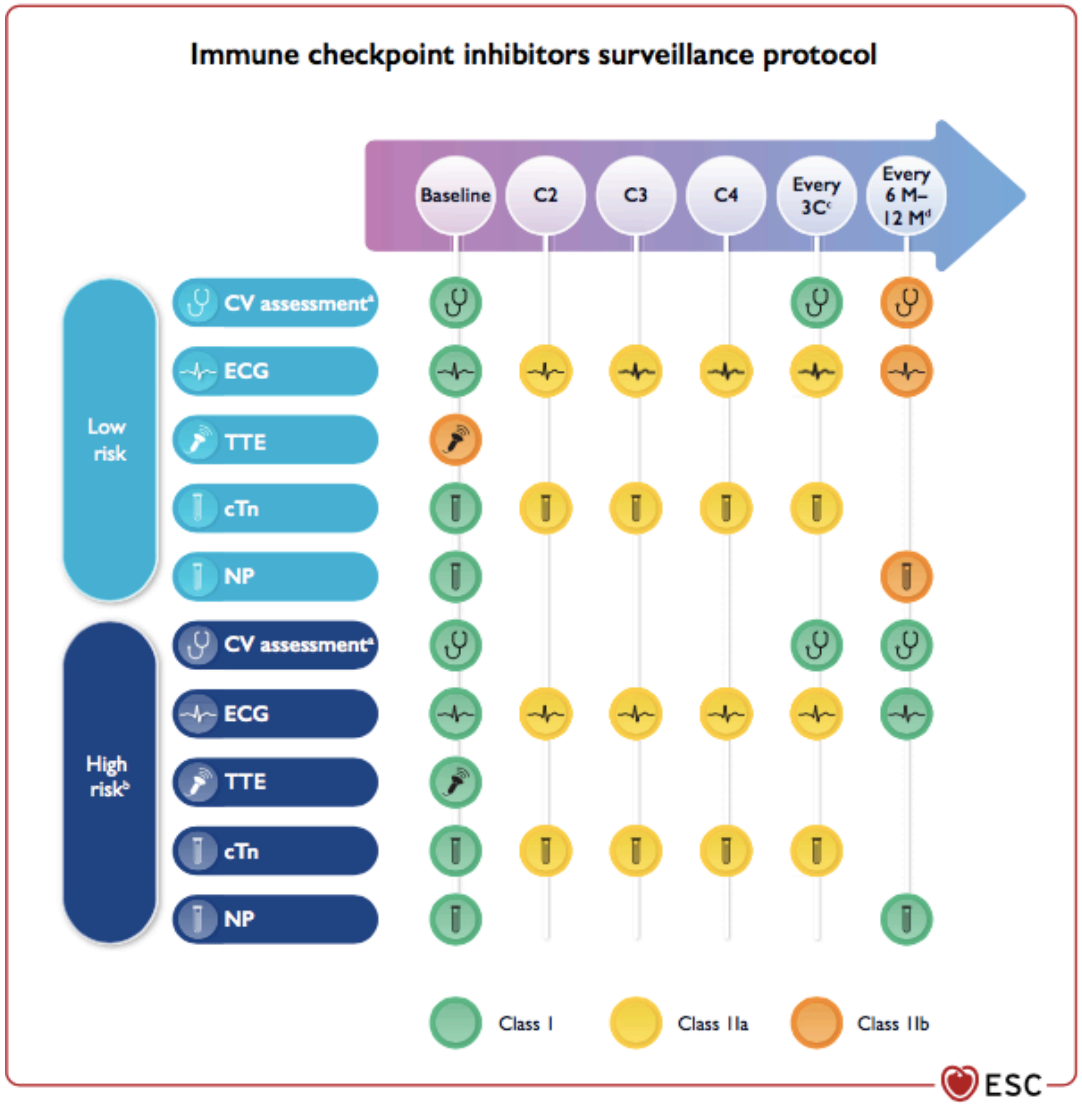
-taux de myocardite est faible avec une incidence de 0.04% à 1.14%
-Mais taux de mortalité est élevé (25 à 50%)
-Premier 3 mois de traitement dans la majorité des cas

Eur Heart J, Volume 42, Issue 48, 21 December 2021, Pages 4964–4977

MYOCARDITE-DIAGNOSTIC

1. Augmentation des troponines+
   a) Images compatibles de myocardite à l'IRM cardiaque ou
   b) 2 des critères suivants
      a) Symptômes cliniques
      b) Arythmie ventriculaire
      c) Diminution de la FEVG
      d) Autres manifestation immunitaires (myosite, myopathie, myasthénie grave)

SURVEILLANCE



Eur Heart J. 2022;43:4229-361

MYOCARDITE-SÉVÉRITÉ

Fulminante

- Instabilité hémodynamique
- Arythmie ventriculaire importante
- Bloc AV

Non Fulminate

- Pas d'instabilité hémodynamique, arythmie ventriculaire importante ou bloc AV
- Avec ou sans chute de la FEVG

Réfractaire au Stéroïde

- État clinique qui ne s'améliore pas malgré methylprednisolone

MYOCARDITE- RÉCUPÉRATION

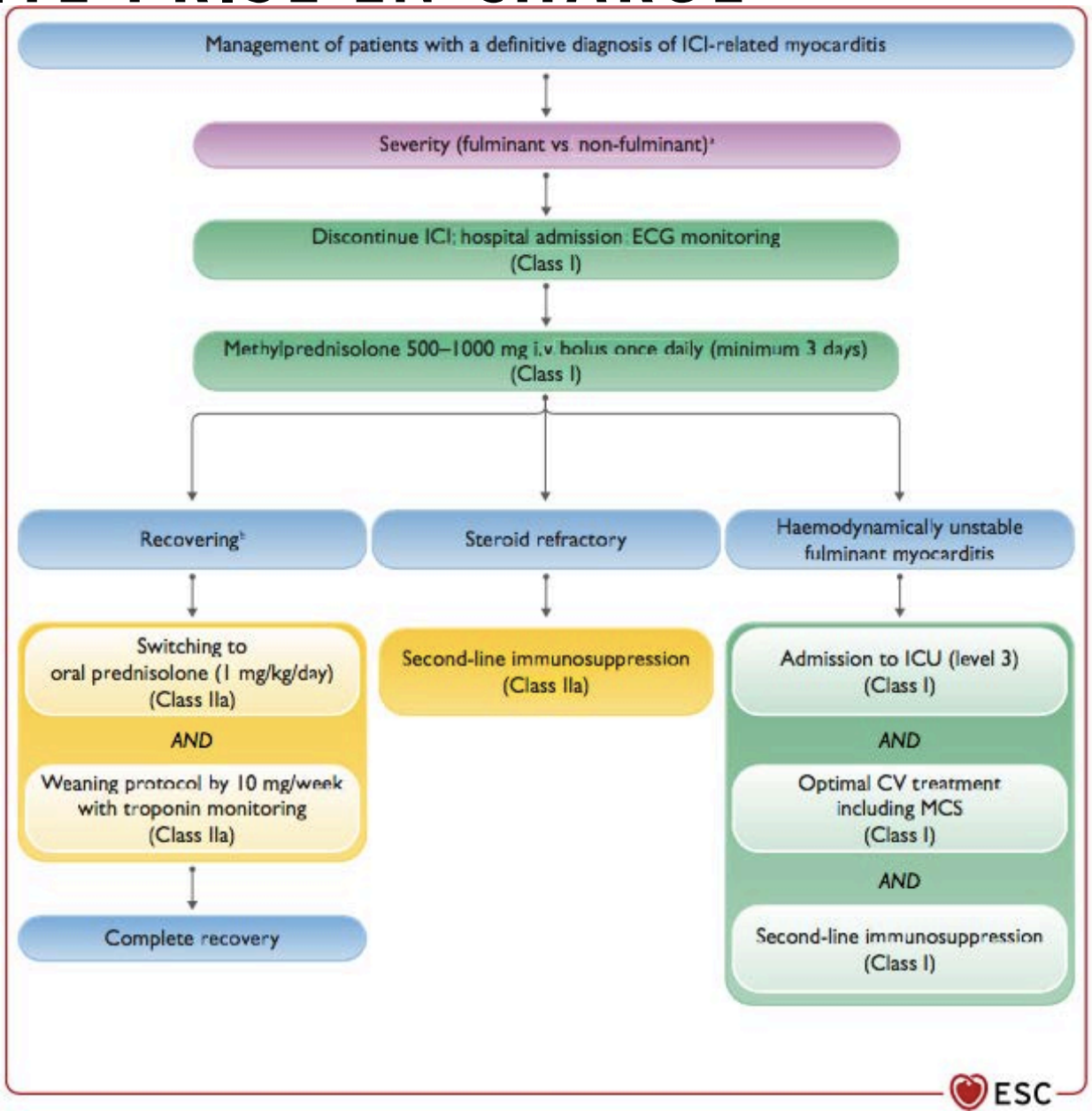
Complète

- Tx sevré
- Plus de symptômes, FEVG normal, biomarqueurs normaux

En Récupération

- Amélioration de l'état clinique, biomarqueurs et imagerie avec traitement en sevrage

MYOCARDITE-PRISE EN CHARGE



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CONCLUSION

Premier objectif est de prévenir la cardiotoxicité

- Adresser les facteurs de risque
- Rôle BB/IECA pas certain
- Évaluer le niveau de risque individuel

Type et fréquence des suivis vas dépendre du risque ainsi que du type de traitement

Patient haut risque- suivit étroit en cardiologie avec tropo/NTproBNP/imagerie

L'arrêt du traitement de chimio est le dernier recours et implique une discussion entre EMD

Si myocardite suspecté, cesser immédiatement le tx. La reprise vas dépendre de la sévérité de la myocardite et du bénéfice du traitement

Le traitement de la défaillance cardiaque est celui recommandé pas les lignes directrices

MERCI!