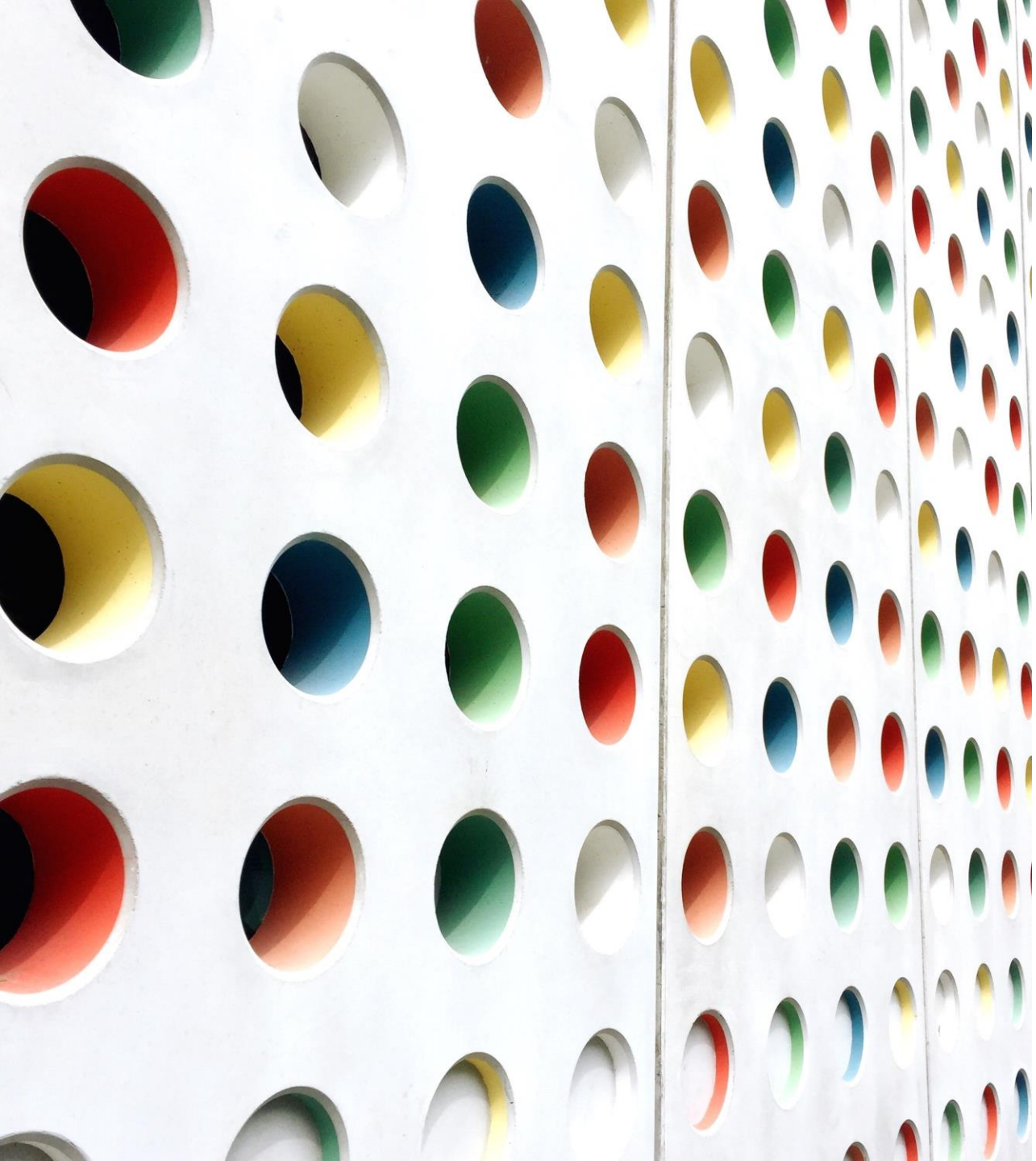


Πρωτόκολλα καρδιολογικής παρακολούθησης κατά τη διάρκεια της αντικαρκινικής θεραπείας

ΚΟΥΛΑΟΥΖΙΔΗΣ ΓΕΩΡΓΙΟΣ

ΚΑΡΔΙΟΛΟΓΟΣ

Γ.Ν.Θ. Γ.ΠΑΠΑΝΙΚΟΛΑΟΥ

2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS): Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC)

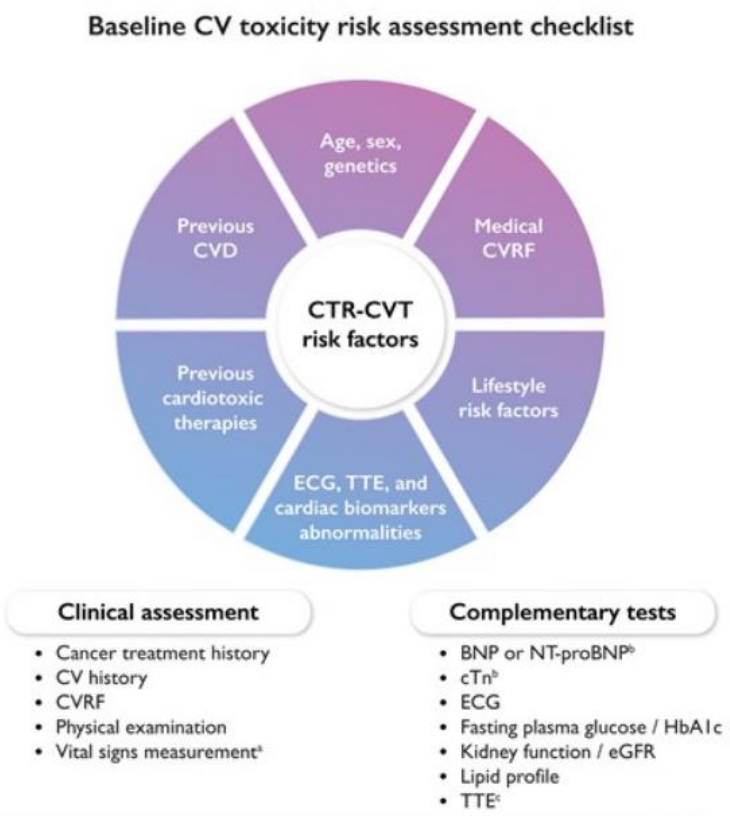
- 30 international experts from 13 countries collaborated to put together a 133-page document (plus an additional 45-page supplement) with 837 references.
- 82 tables and 48 figures.

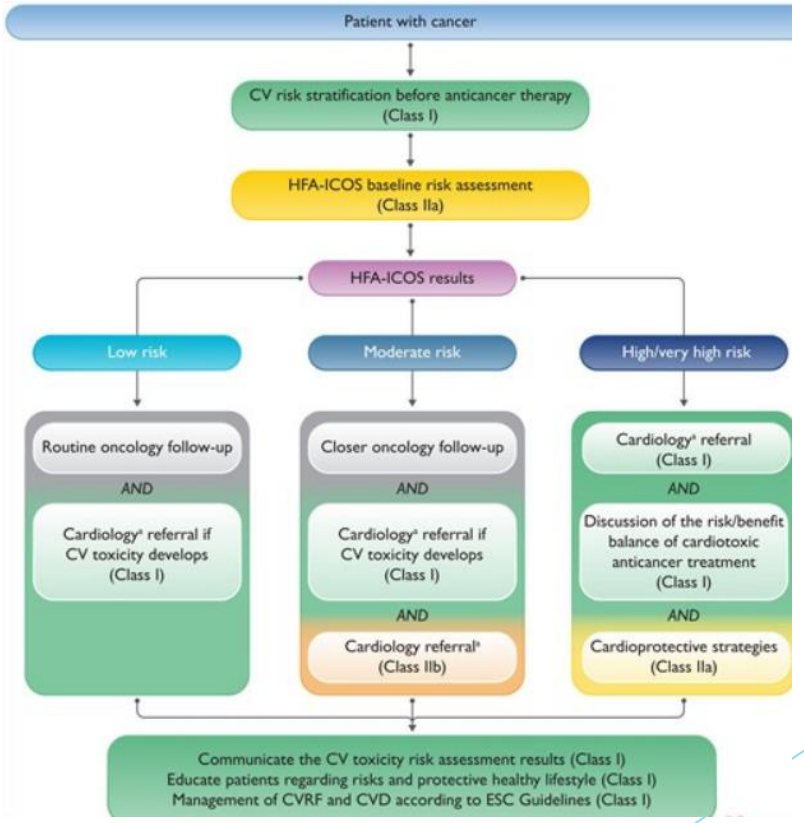
Cancer drug-specific proformas

1. Anthracyclines
2. HER2 inhibitors
3. VEGF inhibitors
4. Bcr-Abl TKI
5. Proteasome inhibitors
6. RAF/MEK inhibitors
7. Androgen deprivation therapy

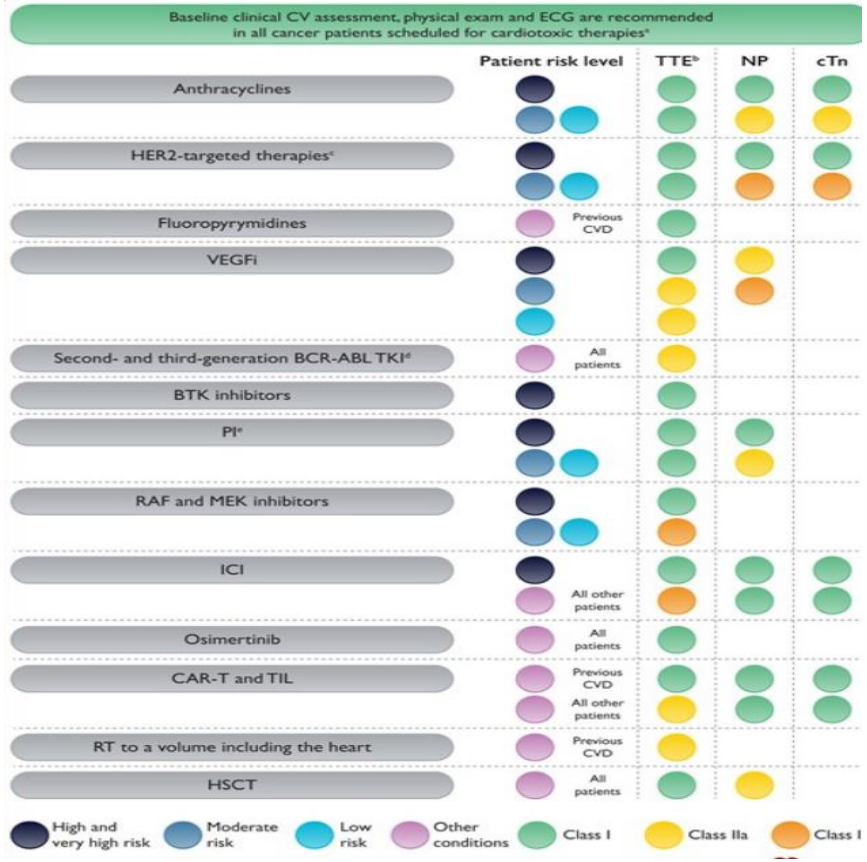
Lyon AR, Lopez-Fernadez T, Cough LS et al. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS): Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC). Eur Heart J 2022;43(41): 4229-4361.

Baseline cardiovascular toxicity risk assessment





Baseline screening recommendations for patients with cancer treated with potentially cardiotoxic drugs



Recommendations for ECG baseline assessment

Recommendations	Class	Level
An ECG is recommended in all patients starting cancer therapy as part of their baseline CV risk assessment.	I	C
In patients with an abnormal baseline ECG, referral to a cardiologist is recommended.	I	C

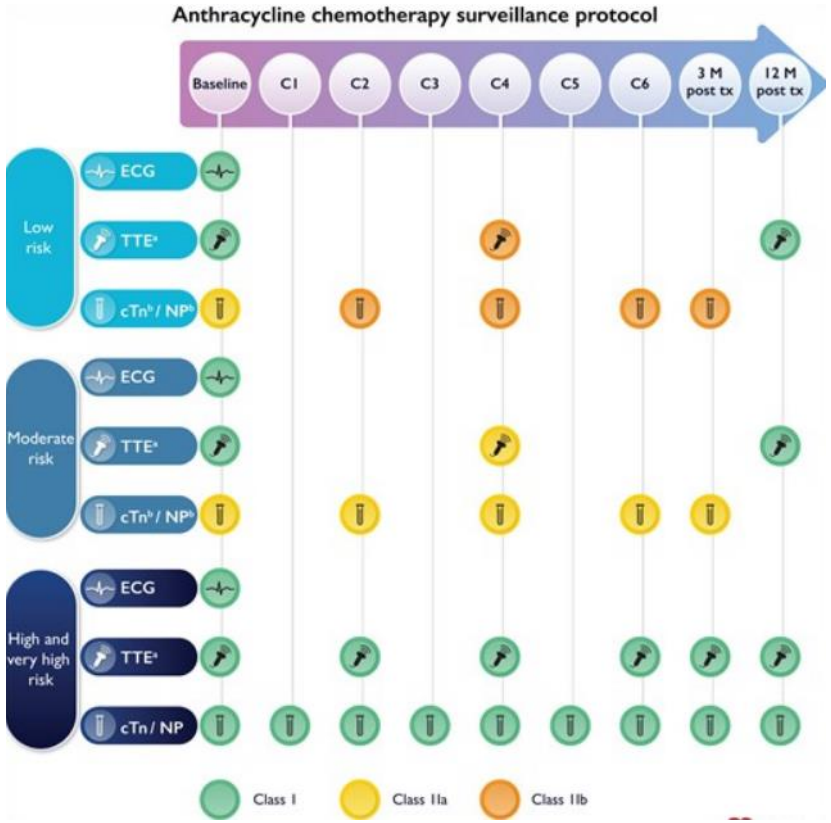
Recommendations for cardiac biomarker assessment prior to potentially cardiotoxic therapies

Recommendation	Class	Level
Baseline measurement of NP and/or cTn is recommended in all patients with cancer at risk of CTRCD if these biomarkers are going to be measured during treatment to detect CTRCD.	**I**	**C**

Recommendations for cardiac imaging modalities in patients with cancer

General	Class	Level
Echocardiography is recommended as the first-line modality for the assessment of cardiac function in patients with cancer.	I	C
3D echocardiography is recommended as the preferred echocardiographic modality to measure LVEF.	I	B
GLS is recommended in all patients with cancer having echocardiography, if available.	I	C
CMR should be considered for the assessment of cardiac function when echocardiography is unavailable or non-diagnostic.	IIa	C
MUGA may be considered when TTE is not diagnostic and CMR is not available.	IIb	C
Baseline cardiac imaging prior to potentially cardiotoxic therapies		
Baseline comprehensive TTE is recommended in all patients with cancer at high risk and very high risk of CV toxicity before starting anticancer therapy.	I	C

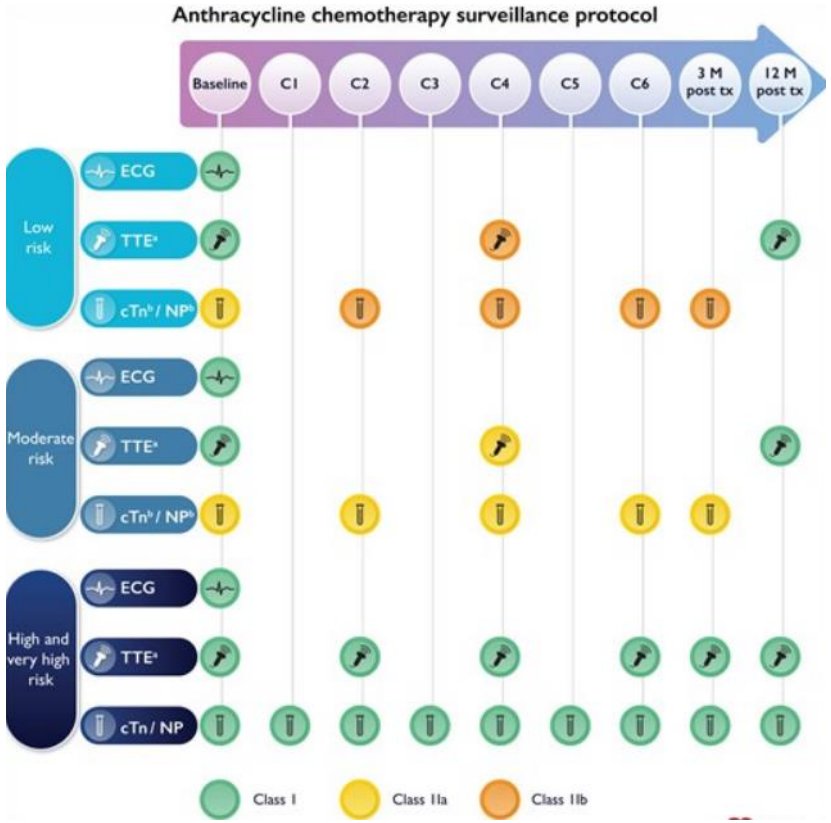
Cardiovascular toxicity monitoring in patients receiving anthracyclines (1)



TTE:

- Baseline,12M post treatment in all patients (Class I, Level B)
- Every other cycle, 3M and 12M post treatment in **high/very high** risk patients(Class I, Level B)
- In **moderate-risk** patients should be considered after a cumulative dose of ≥250 mg/m^2 of doxorubicin or equivalent(Class IIa, Level C)
- In **low-risk** patients, may be considered after a cumulative dose of ≥250 mg/m^2 of doxorubicin or equivalent (Class IIb, Level C).

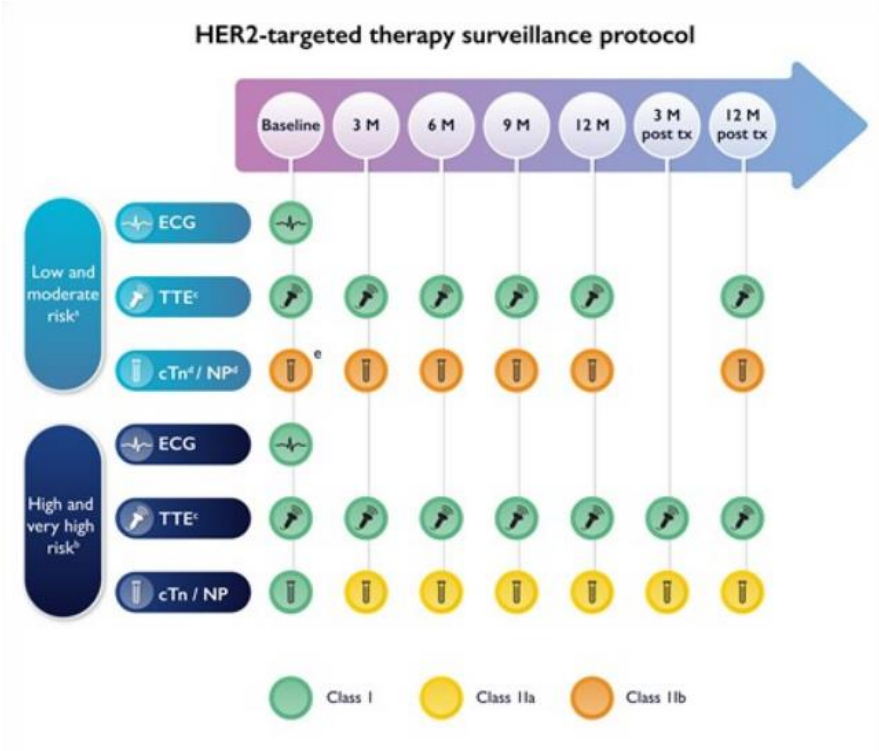
Cardiovascular toxicity monitoring in patients receiving anthracyclines (1)



Cardiac serum biomarkers:

- Baseline, before every cycle, EOT, 3M and 12 M post treatment in **high/very high risk** patients (Class I, Level B)
- Every two cycles and within 3 M after EOT should be considered in **moderate-risk** patients and in **low-risk** patients receiving a cumulative dose of ≥250 mg/m2 of doxorubicin or equivalent (Class IIa, Level C)
- Every two cycles and within 3M after EOT may be considered in **low-risk** patients (Class IIb, Level C).

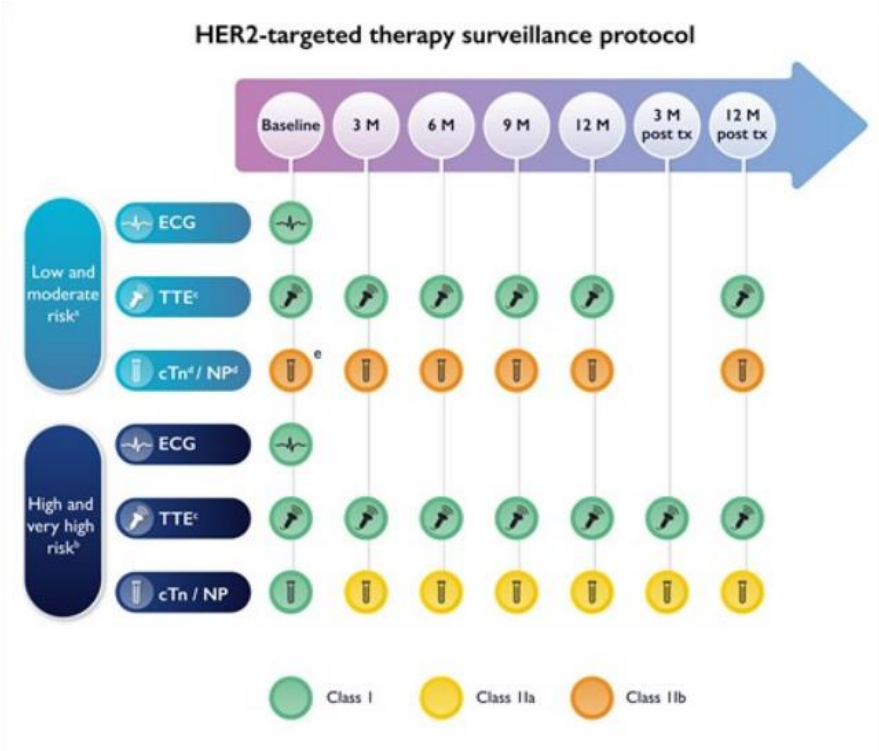
HER2-targeted therapies (1)



TTE:

- Should be performed in week 2 or 3 of a 3-weekly trastuzumab cycle.
- After the first year, in **low-** and **moderate-risk** metastatic HER2+ disease who are asymptomatic with normal TTE , monitoring can be reduced to every 6 months(Class I, Level C).
- After 3 months, in **low-risk** HER2+ EBC patients who are asymptomatic with normal TTE, monitoring may be considered to reduce to every 4 months (Class IIb, Level C).
- In **high-** and **very high-risk** metastatic HER2+ disease, may be considered every 2–3 cycles depending on the absolute risk and local availability.

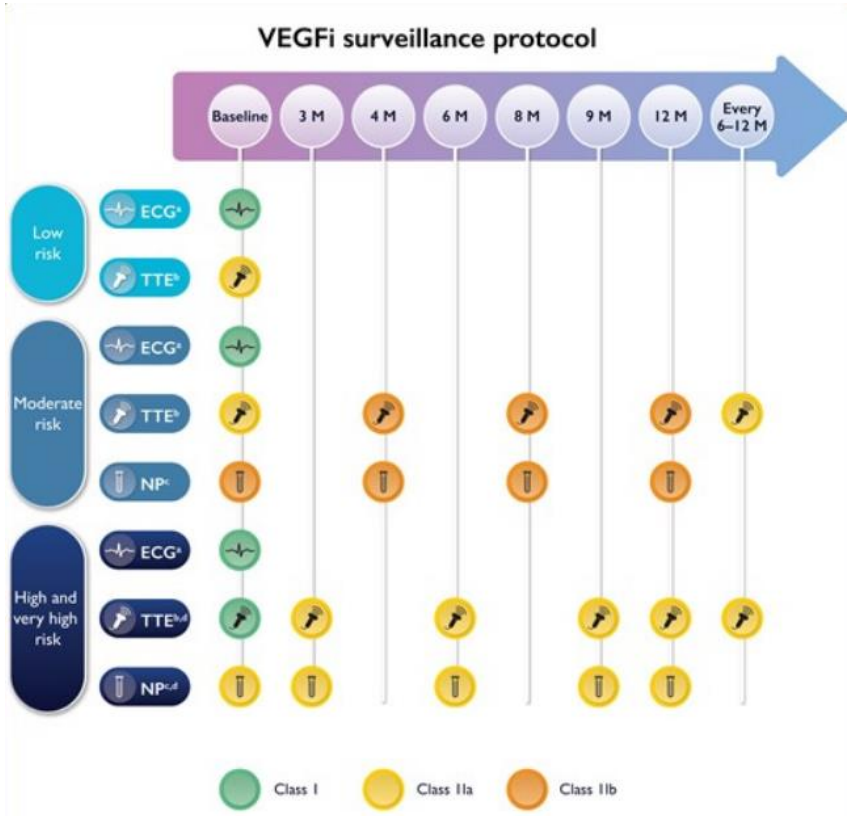
HER2-targeted therapies (2)



Cardiac serum biomarkers:

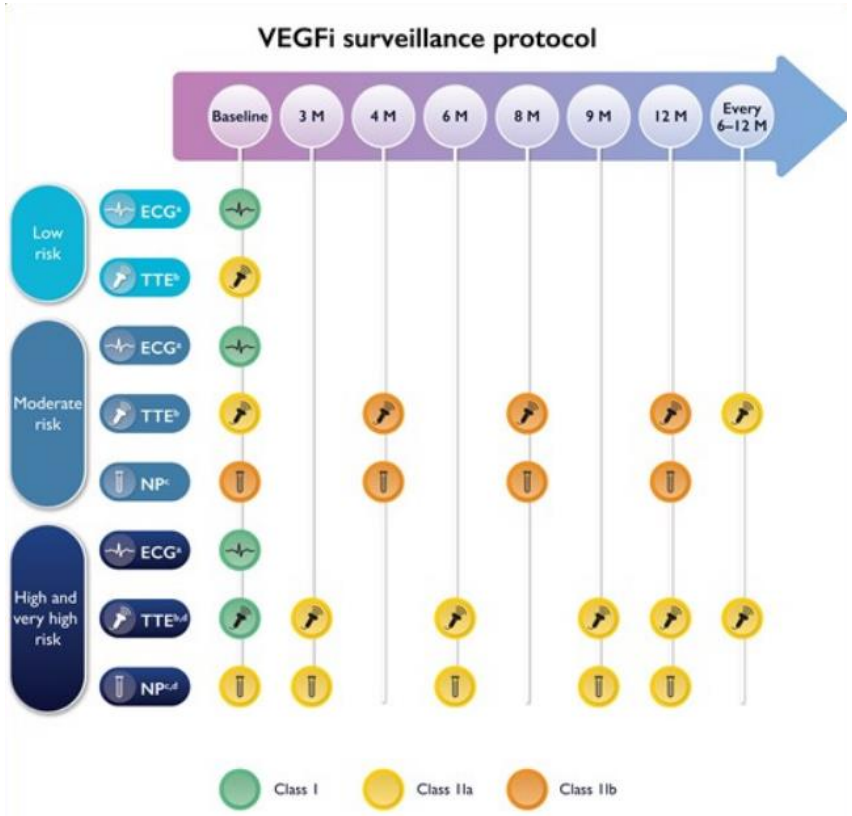
- In **high-** and very **high-risk** patients prior to anti-HER2-targeted therapies (Class I, Level C)
- Every 2–3 cycles during therapy and 3 and 12M after the end of therapy should be considered in **high-** and **very high-risk** HER2+ EBC patients(Class IIa, Level C)
- Should be considered in **low-** and **moderate-risk** patients post-anthracycline chemotherapy but prior to starting anti-HER2-targeted therapies(Class IIa, Level A)
- At baseline, every 3 M, and 12 M after therapy may be considered in **low-** and **moderate-risk** HER2+ EBC patients(Class IIb, Level C)

Vascular endothelial growth factor inhibitors (1)



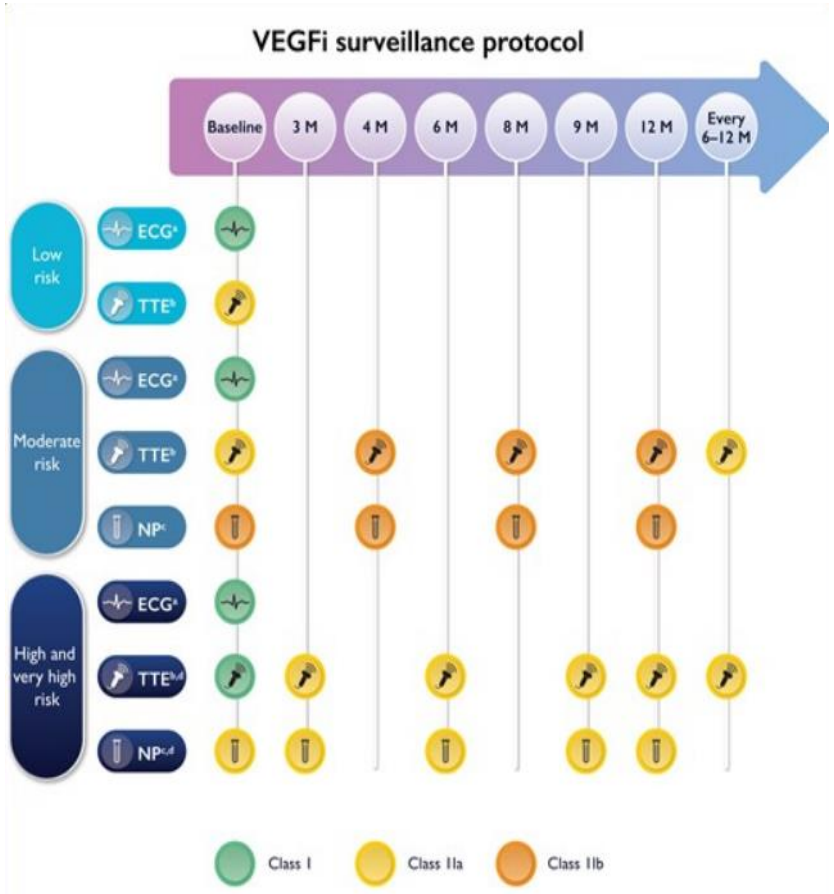
- BP measurement is recommended for patients treated with VEGFi, bevacizumab, or ramucirumab at every clinical visit (Class I, Level C).
- Daily home monitoring of during the first cycle, after each increase of VEGFi dose, and every 2–3 weeks thereafter is recommended.
- In patients at **moderate-** or **high-risk** of QTc prolongation, ECG is recommended monthly during the first 3 months and every 3–6 months thereafter. (Class I, Level C)

Vascular endothelial growth factor inhibitors (2)



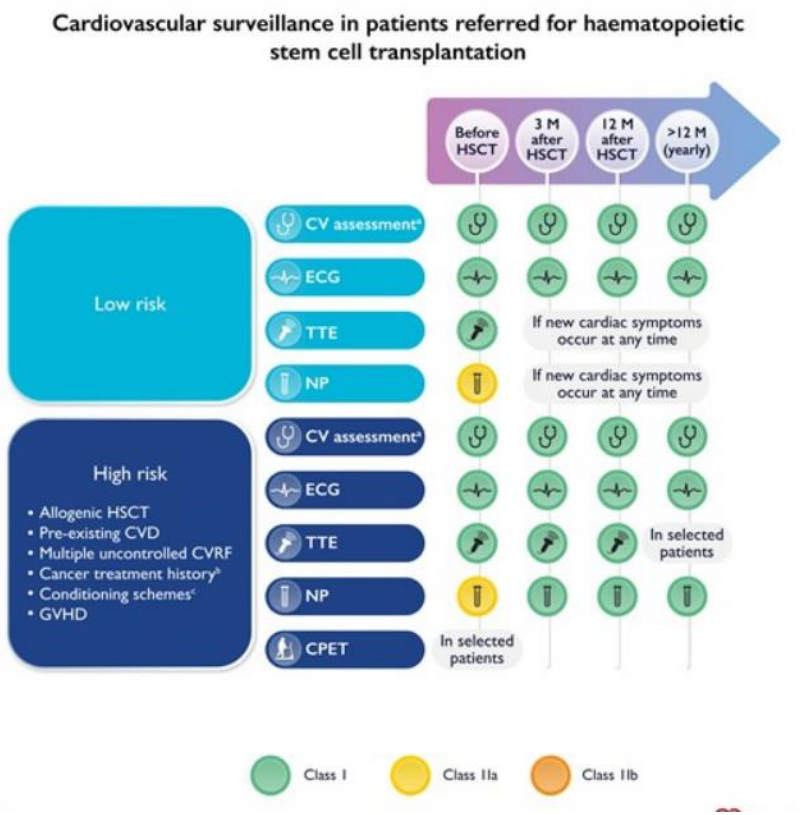
- NP may be considered at baseline and then every 4 months during the first year **in moderate-risk** patients (Class IIb, Level C)
- NP should be considered at baseline, 4 weeks after starting treatment, and them every 3 months during the first year in **high-** and **very high-risk** patients (Class IIa, Level C)

Vascular endothelial growth factor inhibitors (3)



Echocardiography		
Baseline TTE is recommended in **high-** and **very high-**risk patients treated with VEGFi or bevacizumab.	**I**	**C**
Baseline TTE should be considered in **low-** and **moderate-**risk patients	**IIa**	**C**
TTE may be considered every 4 months during the first year in **moderate-**risk patients	**IIb**	**C**
TTE should be considered every 3 months during the first year in **high-** and **very high-**risk patients	**IIa**	**C**
TTE every 6–12 months should be considered in **moderate-** and **high-risk** patients with cancer who require long-term treatment.	**IIa**	**C**

Haematopoietic stem cell transplantation



- *TTE:*

At 3M and 12M post HSCT in **high-** and **very high-risk** patients

- *Cardiac serum biomarkers:*

At 3M and 12M post HSCT in **high-** and **very high-risk** patients

- *ECG*

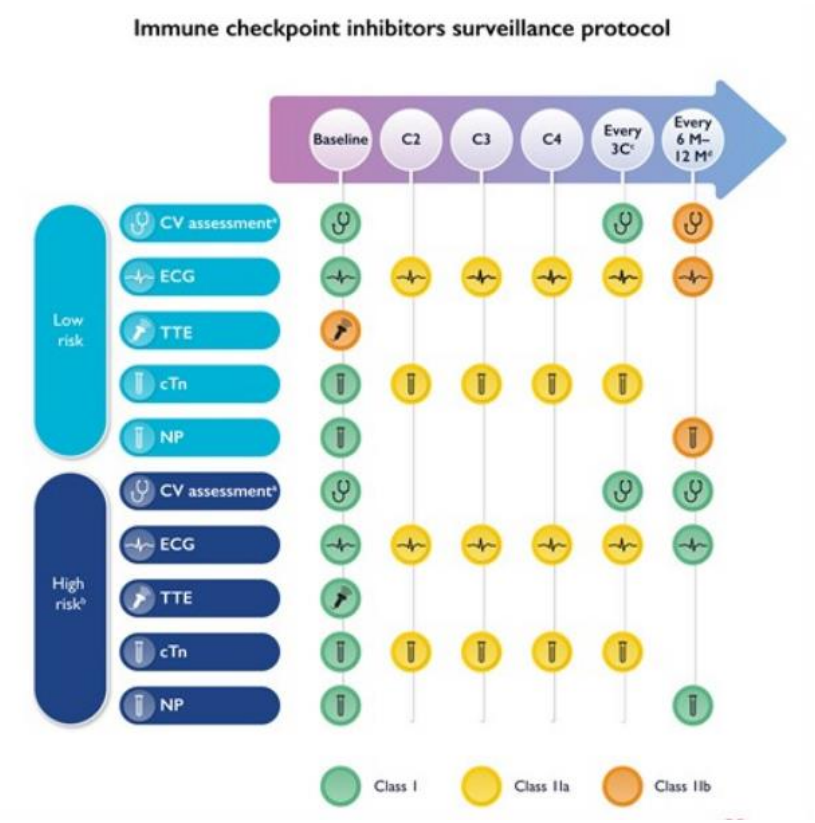
At 3M and 12M post HSCT in **ALL** patients

Bruton tyrosine kinase inhibitors

Recommendations	Class[a]	Level[b]
BP monitoring and management		
BP measurement is recommended for patients treated with BTK inhibitors at every clinical visit.[264]	I	B
Weekly home monitoring of BP during the first 3 months and every month thereafter should be considered for patients treated with BTK inhibitors.	IIa	C
Echocardiography		
Baseline echocardiography is recommended in high-risk patients[c] scheduled to receive BTK inhibitors.[267,268]	I	C
TTE is recommended in all patients who develop AF during BTK inhibitor therapy.	I	C
AF		
Opportunistic screening for AF by pulse-taking or ECG rhythm strip is recommended at every clinical visit during BTK inhibitor therapy.[273]	I	C

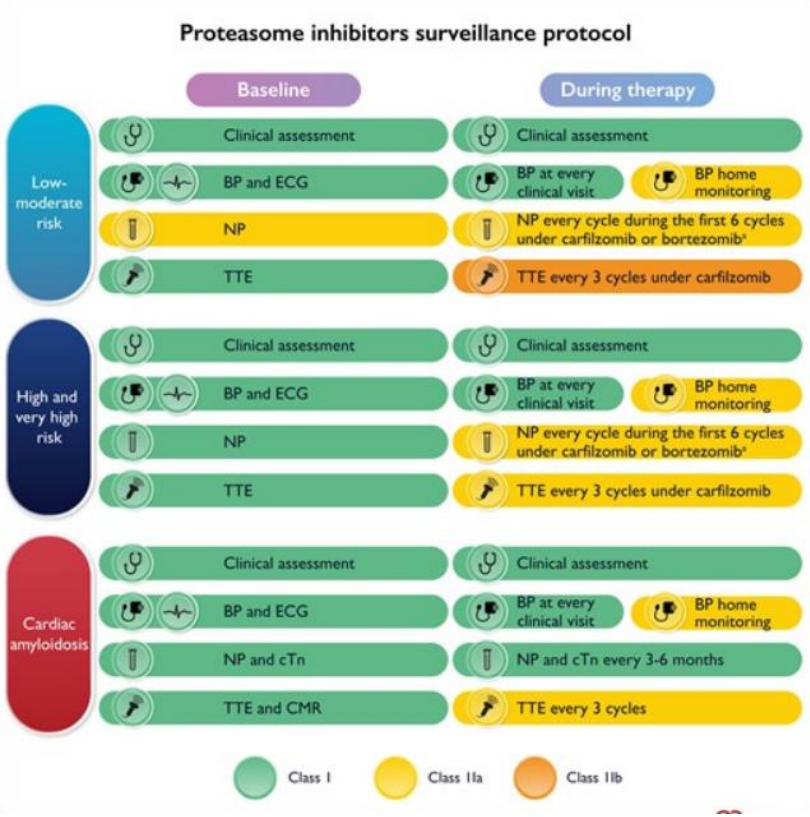
- Male, age ≥ 65 years, previous history of hypertension, DM, QTc ≥ 480 ms, AF, HF, cardiomyopathy, or severe VHD

Immune checkpoint inhibitors



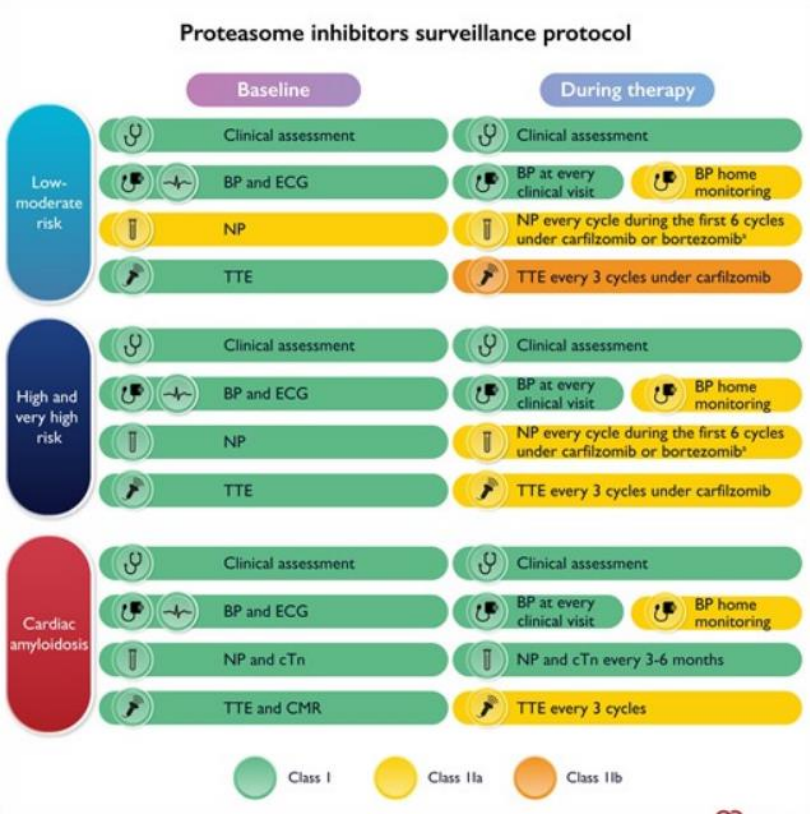
Recommendations	Class[a]	Level[b]
ECG, NP, and cTn measurements are recommended in all patients before starting ICI therapy.[333]	I	B
Baseline echocardiography is recommended in high-risk patients[c] before starting ICI therapy.[333]	I	B
Baseline echocardiography may be considered in all patients before starting ICI therapy.	IIb	C
Serial ECG and cTn measurements should be considered before ICI doses 2, 3, and 4, and if normal, reduce to every three doses until completion of therapy to detect subclinical ICI-related CV toxicity.[333]	IIa	B
CV assessment[d] is recommended every 6–12 months in high-risk patients[c] who require long-term (>12 months) ICI treatment.[321–323,335,336]	I	C
CV assessment[d] may be considered every 6–12 months in all patients who require long-term (>12 months) ICI treatment.	IIb	C

Multiple myeloma therapies



BP monitoring		
BP measurement is recommended for patients treated with PI at every clinical visit.	**I**	**C**
Home monitoring of BP weekly during the first 3 months and monthly thereafter should be considered for patients treated with PI.	**IIa**	**C**
Cardiac serum biomarkers		
Measurement of NP is recommended prior to PI in high- and very high-risk patients.[66,303]	**I**	**C**
Measurement of NP should be considered prior to PI in low- and moderate-risk patients.[66]	**IIa**	**C**
In patients receiving carfilzomib or bortezomib, measurement of NP should be considered at baseline and every cycle during the first 6 cycles.[c,66]	**IIa**	**B**
NP and cTn measurements are recommended at baseline and every 3–6 months in patients with AL-CA.[d,290]	**I**	**B**

Multiple myeloma therapies

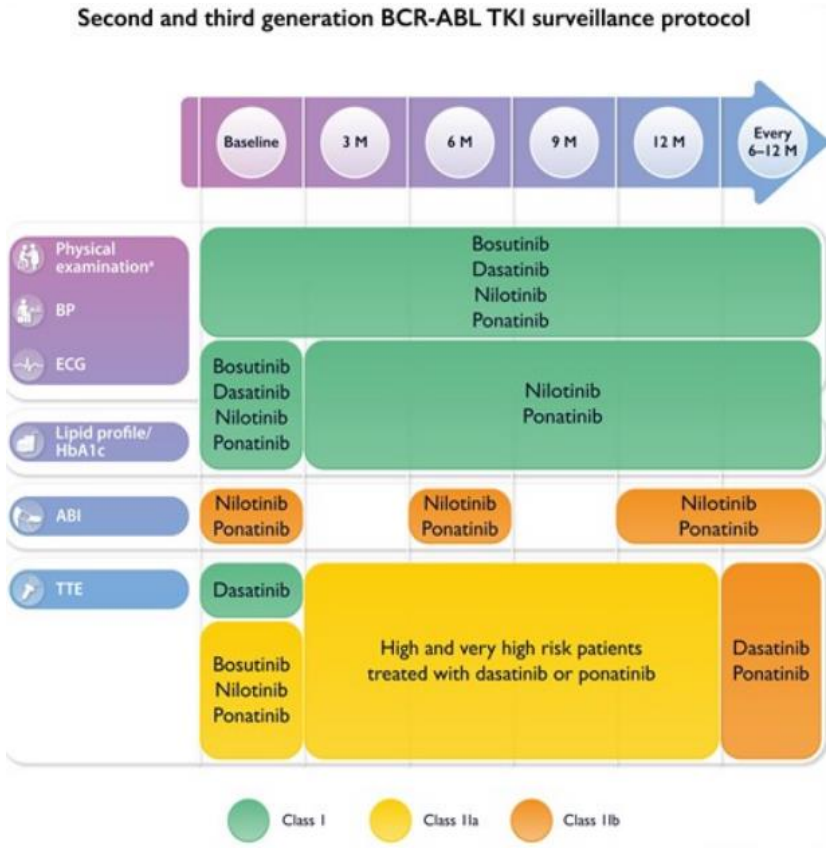


TTE		
Baseline echocardiography, including assessment for AL-CA, is recommended in all patients with MM scheduled to receive PI.	I	C
Echocardiography surveillance every 3 cycles should be considered in high- and very high-risk patients receiving carfilzomib.[280]	IIa	B
Echocardiography surveillance every 3 cycles may be considered in low- and moderate-risk patients receiving carfilzomib.	IIb	C
Echocardiography surveillance should be considered every 3–6 months in patients with AL-CA treated with PI.[d,290]	IIa	C

Rapidly accelerated fibrosarcoma (RAF) and mitogen-activated extracellular signal-regulated kinase(MEK) inhibitors

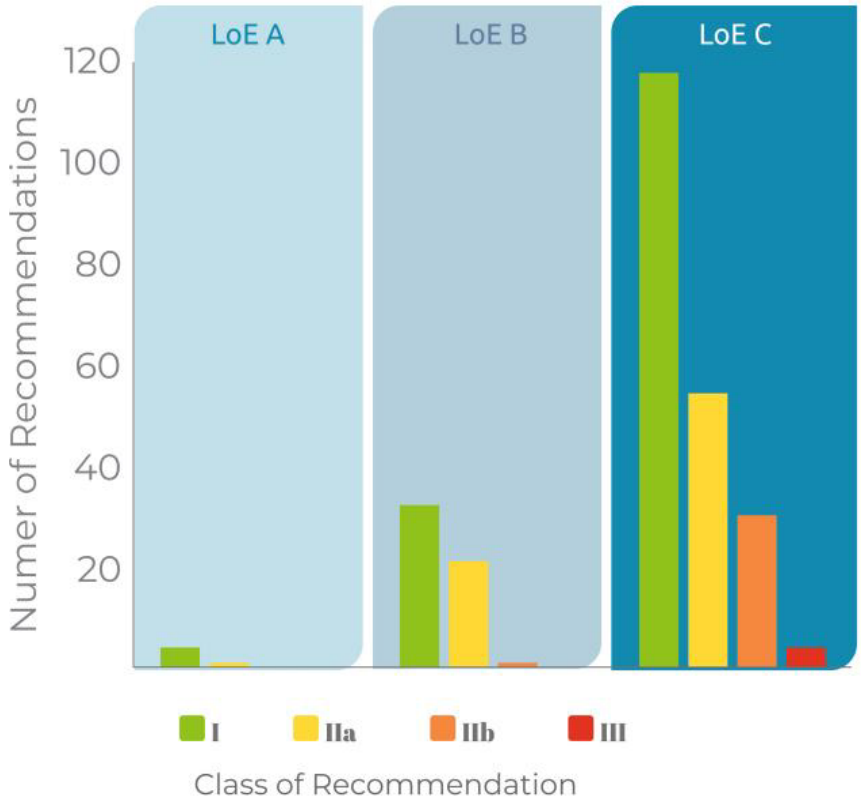
Recommendations	Class[a]	Level[b]
BP monitoring at each clinical visit and weekly outpatient monitoring during the first 3 months of treatment and monthly thereafter is recommended.	I	C
In patients treated with cobimetinib/vemurafenib, an ECG is recommended at 2 and 4 weeks after initiation of treatment and every 3 months thereafter.[c]	I	C
Baseline echocardiography is recommended in all high- and very high-risk patients scheduled to receive combined RAF and MEK inhibitors.	I	C
Baseline echocardiography may be considered in low- and moderate-risk patients scheduled to receive combined RAF and MEK inhibitors.	IIb	C
Echocardiography should be considered every 4 months during the first year in high- and very high-risk patients receiving combined RAF and MEK inhibitors.	IIa	C

Second- and third-generation BCR-ABL tyrosine kinase inhibitors



Recommendations	Class[a]	Level[b]
Baseline CV risk assessment[c] is recommended in patients who require second- or third-generation BCR-ABL TKI.[256,261]	I	C
In patients treated with nilotinib or ponatinib, CV risk assessment[c] is recommended every 3 months during the first year and every 6–12 months thereafter.[256,261]	I	C
QTc[d] measurement should be considered at baseline, at 2 and 4 weeks after starting nilotinib, and 2 weeks after any dose increase.[259]	IIa	C
Baseline echocardiography should be considered in all patients before starting second- and third-generation BCR-ABL TKI.	IIa	C
Baseline echocardiography is recommended in patients scheduled to receive dasatinib.	I	C
Echocardiography should be considered every 3 months during the first year in high- and very high-risk patients receiving dasatinib or ponatinib.	IIa	C
Echocardiography may be considered every 6–12 months in patients who require long-term (>12 months) ponatinib or dasatinib.	IIb	C
Serial assessment of ankle brachial index may be considered to detect subclinical peripheral vascular disease.	IIb	C

Teske AJ. The ESC cardio-oncology 2022 guidelines; the ball is in our court. European Heart Journal-Cardiovascular Imaging 2023;24:e45-46



- 272 recommendations. 208 (76%) were supported by Level of Evidence: C evidence.
- 156 (57%) Class I recommendations, indicating that these strategies are indicated and should be implemented in clinical practice. However, of the Class I recommendations, 5 (3%) were supported by Level of Evidence: A evidence; 33 (21%) by Level of Evidence: B evidence; and 118 (76%) by Level of Evidence: C evidence.

'This will help translate initial enthusiasm into a well-functioning cardio-oncology unit where cancer patients' short- and long-term cardiovascular health is tailored to their individual needs, improving long-term outcomes and reducing cardiovascular morbidity. But then again, this is of course another level of evidence C.'

The European Society of Cardiology Cardio-Oncology Guidelines: Evidence Base, Actionability, and Relevance to Clinical Practice

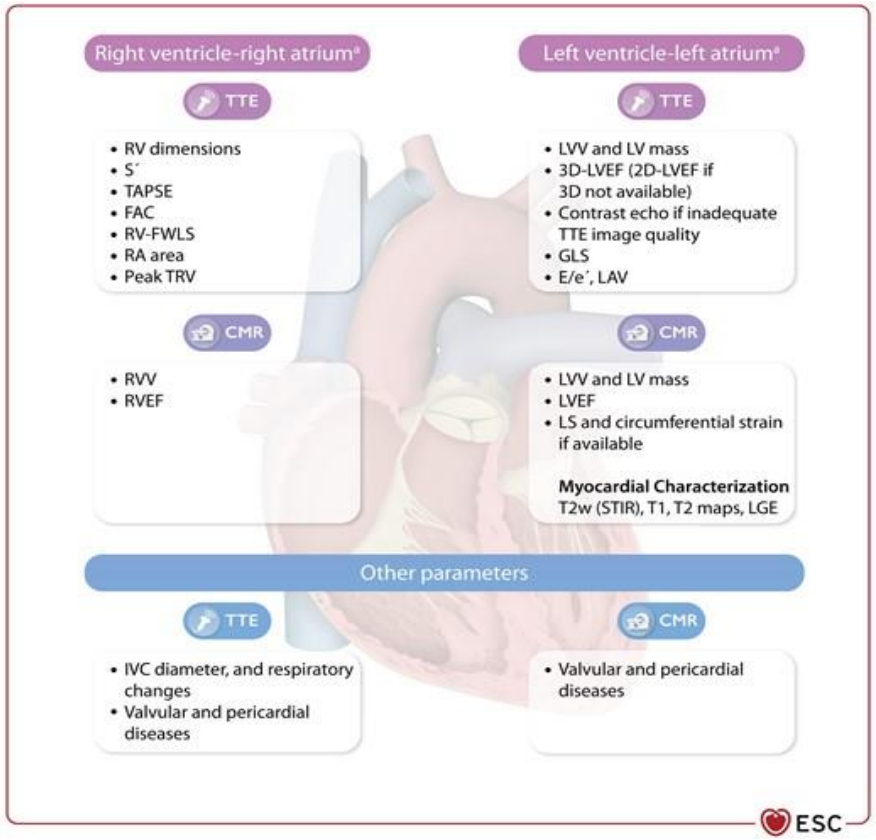
Darryl P Leong [1], Som D Mukherjee [2]

- Many centers in Canada do not have dedicated cardio-oncology clinics, so many patients with cardio-oncology issues are currently being managed by general cardiologists, especially in the community setting.
- It is unclear whether oncologists have the capacity or familiarity needed to complete a cardiovascular risk assessment.
- Access to cardiac magnetic resonance may be limited in some centers in Canada as well.

❖ Leong DP, Mukherjee SD. The European society of cardiology cardio-oncology guidelines: evidence base, actionability, and relevance to clinical practice. JACC CardioOncol 2022; 5(1): 137-140.

ESC Cardio-Oncology Guidelines: A Triumph-But Are We Overscreening?

Ronald M Witteles [1], Sunil A Reddy [2]



- Seventeen different metrics are recommended for every cancer patient having an TTE, including such unvalidated assessments as right ventricular free wall longitudinal strain.
- Considering the number of patients who receive cancer therapies and the number of assessments recommended for each study, echocardiogram labs would be overwhelmed.

❖ Witteles RM, Reddy SA.ESC cardio-oncology guidelines. A triumph-But are we over screening. JACC CardioOncol 2022 Dec 6;5(1):133-136.

The Potential Impact of the 2022 ESC Cardio-Oncology Guidelines on Clinical Practice in China

Gary Tse [1] [2], Qun Shao [3], Jiwei Liu [4], Yuhui Zhang [5]

- Reference values of CV biomarkers for Chinese patients need to be validated.
- Global longitudinal strain is not routinely obtained in China, especially in nontertiary hospitals and cancer hospitals.
- The accessibility of CMR throughout all of China is limited.
- Lack of collaborations and cooperation between oncologists and cardiologists.

Tse G, Shao Q , Liu J , Zhang Y. The Potential Impact of the 2022 ESC Cardio-Oncology Guidelines on Clinical Practice in China. JACC CardioOncol 2023 Feb 21;5(1):153-155.

Conclusions

- The new guidelines are a major milestone in the field.
- There will be an extremely valuable resource as a reference to the clinicians.
- The first time the world cardio-oncology appeared in PubMed was in 2008. Until today, there are 1,295 papers.
- **Rome wasn't built in a day.**

Ευχαριστώ