X SESSIONE

Rischio coronarico e terapia antineoplastica

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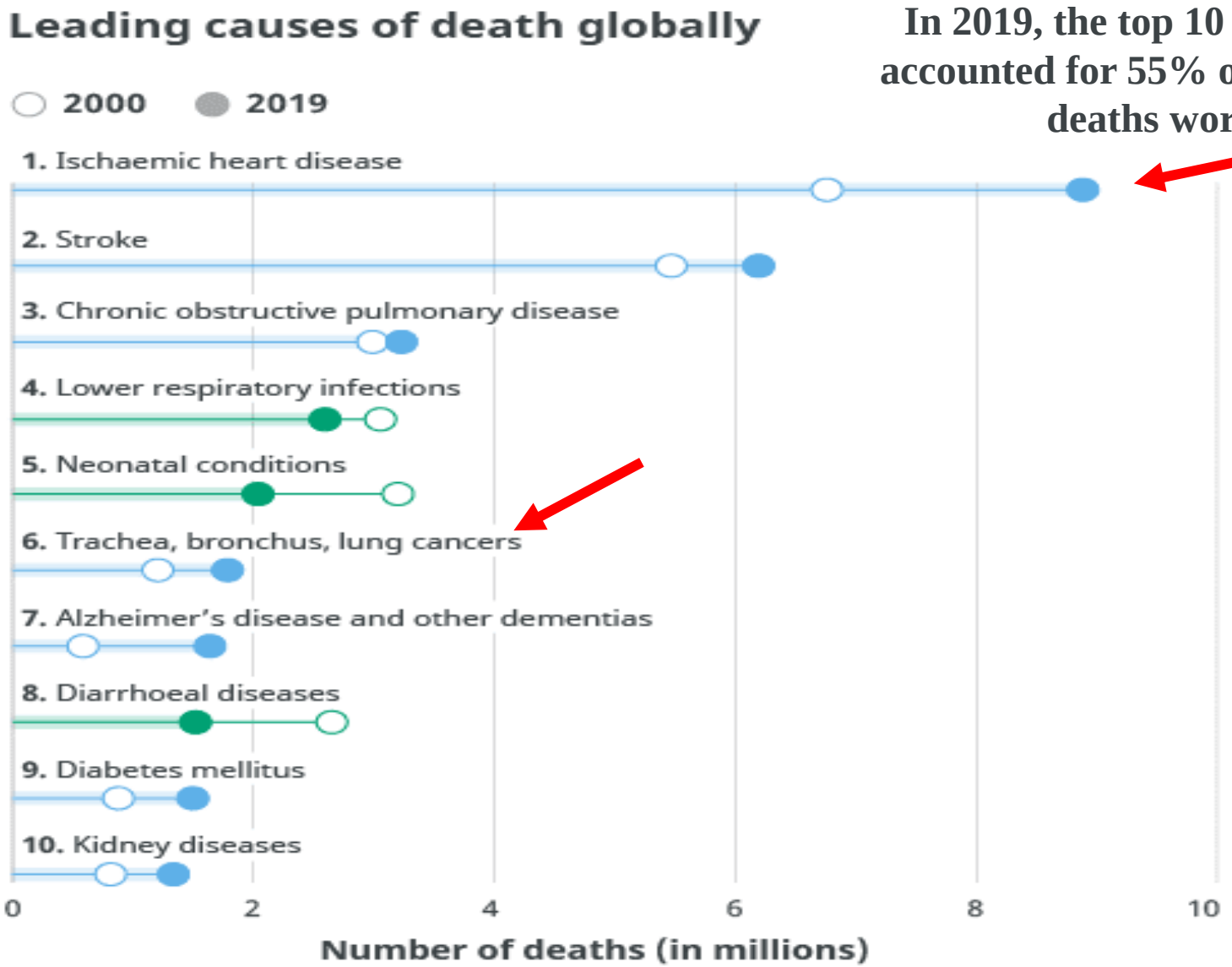
The top 10 causes of death

World Health Organization

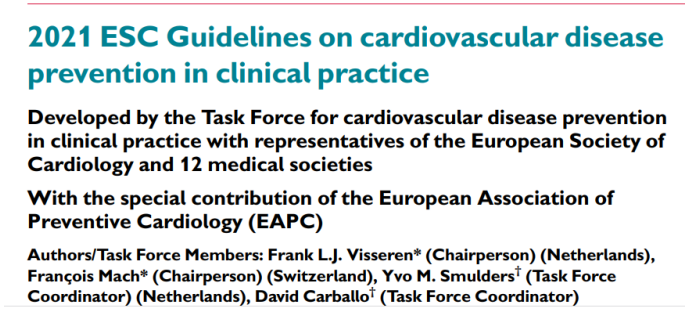


In 2019, the top 10 causes of death accounted for 55% of the 55.4 million deaths worldwide.

Epidemiological Data

- In the last decades, oncological therapy has changed **the natural history of many types of cancer**, which can now be considered curable or as chronic or slowly progressive diseases
- It is well known that **chemotherapy and radiotherapy may induce cardiotoxicity**
- **Anthracyclines** are among the most active antineoplastic agents and their **cardiac effects** have been known for a long time
- Patient treated with chemotherapy are at higher risk of cardiovascular events than the general population, so that **having undergone chemotherapy may be considered as a novel cardiovascular risk factor**

Cancer and ASCVD


2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

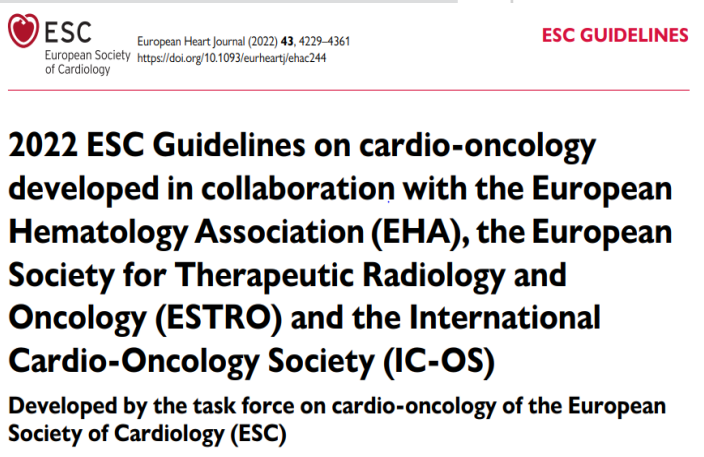
With the special contribution of the European Association of Preventive Cardiology (EAPC)

Authors/Task Force Members: Frank L.J. Visseren* (Chairperson) (Netherlands), François Mach* (Chairperson) (Switzerland), Yvo M. Smulders† (Task Force Coordinator) (Netherlands), David Carballo† (Task Force Coordinator)

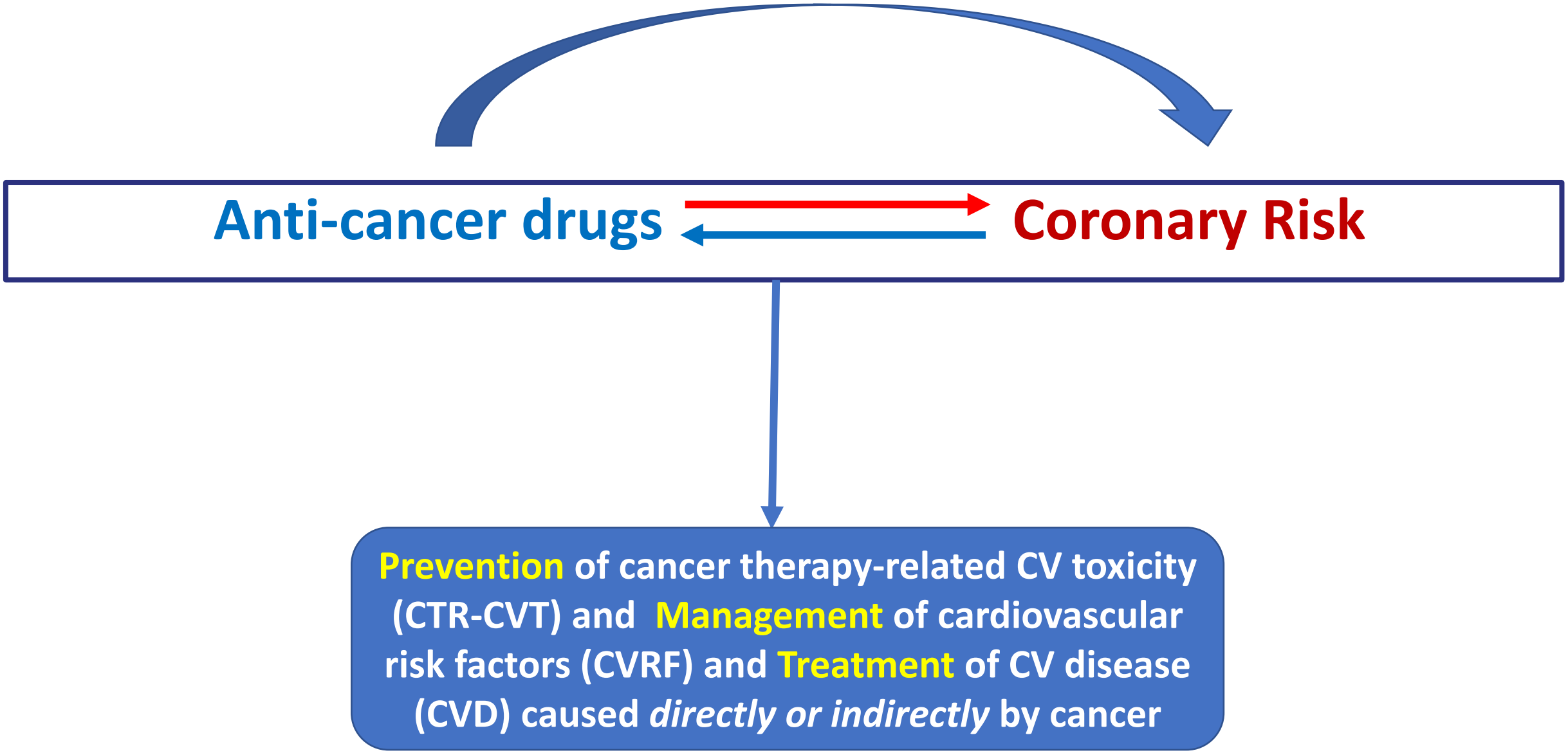
- In patients with cancer, there is an **overlap between cancer and ASCVD risk factors**,with shared biological mechanisms and genetic predispositions
- **Prevention and treatment** of these is therefore beneficial **in reducing both CVD as well as cancer risk**
- Moreover, the **rates of the extent of CVD risk** depend on both the **CVD toxicity of treatments and patient-related factors**
- Owing to **recent improvements in clinical outcomes** for many patients with cancer, **CVD mortality may ultimately exceed** those from **most forms of cancer recurrence**

Factors that could influence perioperative risk during cancer surgery and preventive strategies—Patient-related factors

Factors that could influence perioperative risk during cancer surgery	Preventive strategies
• Lifestyle risk factors: smoking, obesity, sedentary lifestyle • Poorly controlled CVRF: hypertension, DM • Pre-existing CVD including CTR-CVT • Cardiac medications that increase perioperative bleeding risk (e.g. antiplatelets and anticoagulants) • Historical primary malignancy • Current cancer type, stage and location	• Optimal management of CVRF and CVD • Optimize VTE and ATE preventive strategies



(*European Heart Jou*

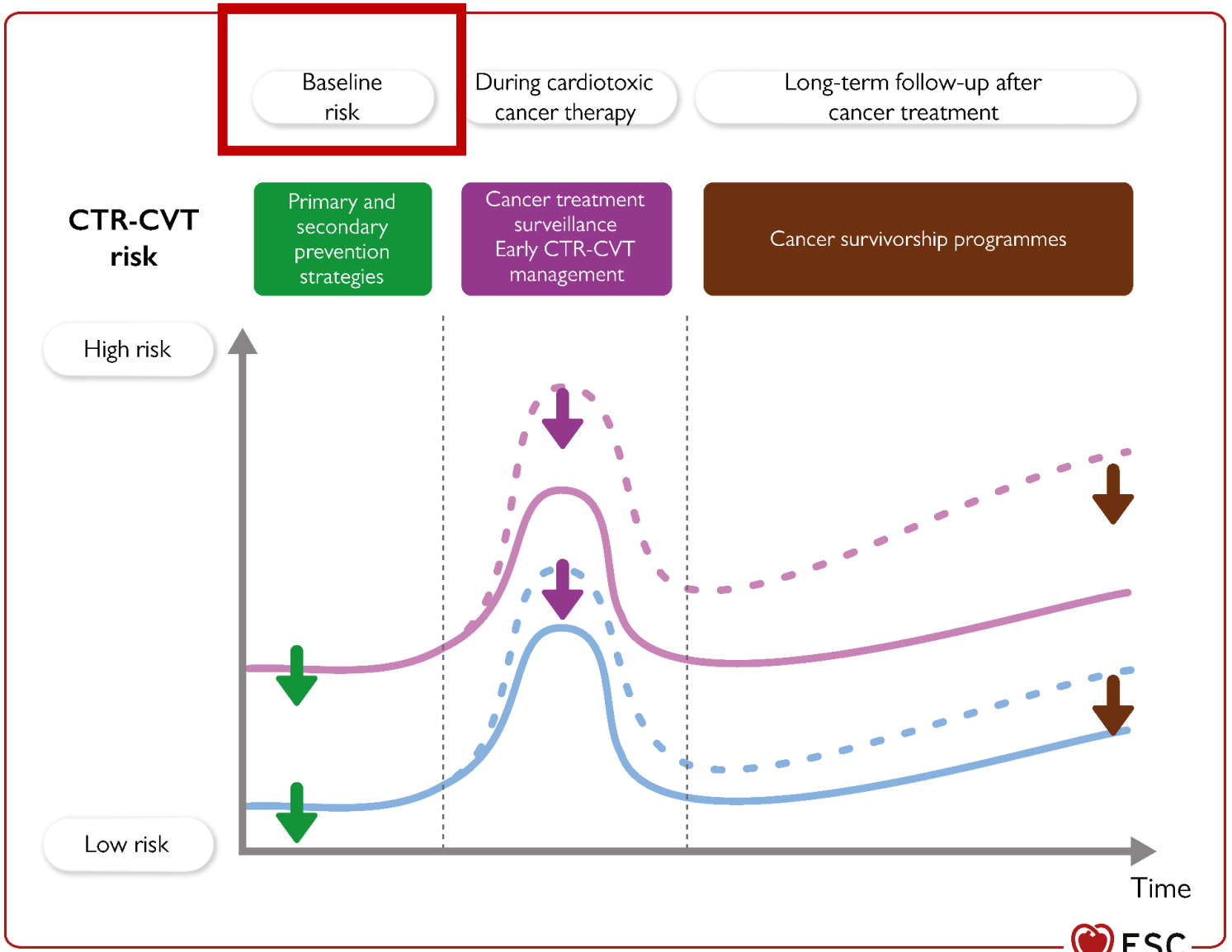

Anti-cancer drugs
Coronary Risk
Prevention of cancer therapy-related CV toxicity (CTR-CVT) and Management of cardiovascular risk factors (CVRF) and Treatment of CV disease (CVD) caused directly or indirectly by cancer

Tossicità dei farmaci antineoplastici

La tossicità da farmaci antineoplastici può essere distinta, a seconda del *timing* di insorgenza, in:

- **acuta**: quando si manifesta immediatamente dopo la somministrazione del farmaco
- **subacuta**: entro 2 settimane dal trattamento antineoplastico
- **cronica a insorgenza precoce:** (entro un anno)
- **cronica a insorgenza tardiva:** (oltre l'anno dall'inizio del trattamento)

Dynamics of cardiovascular toxicity risk of patients with cancer over their therapy continuum

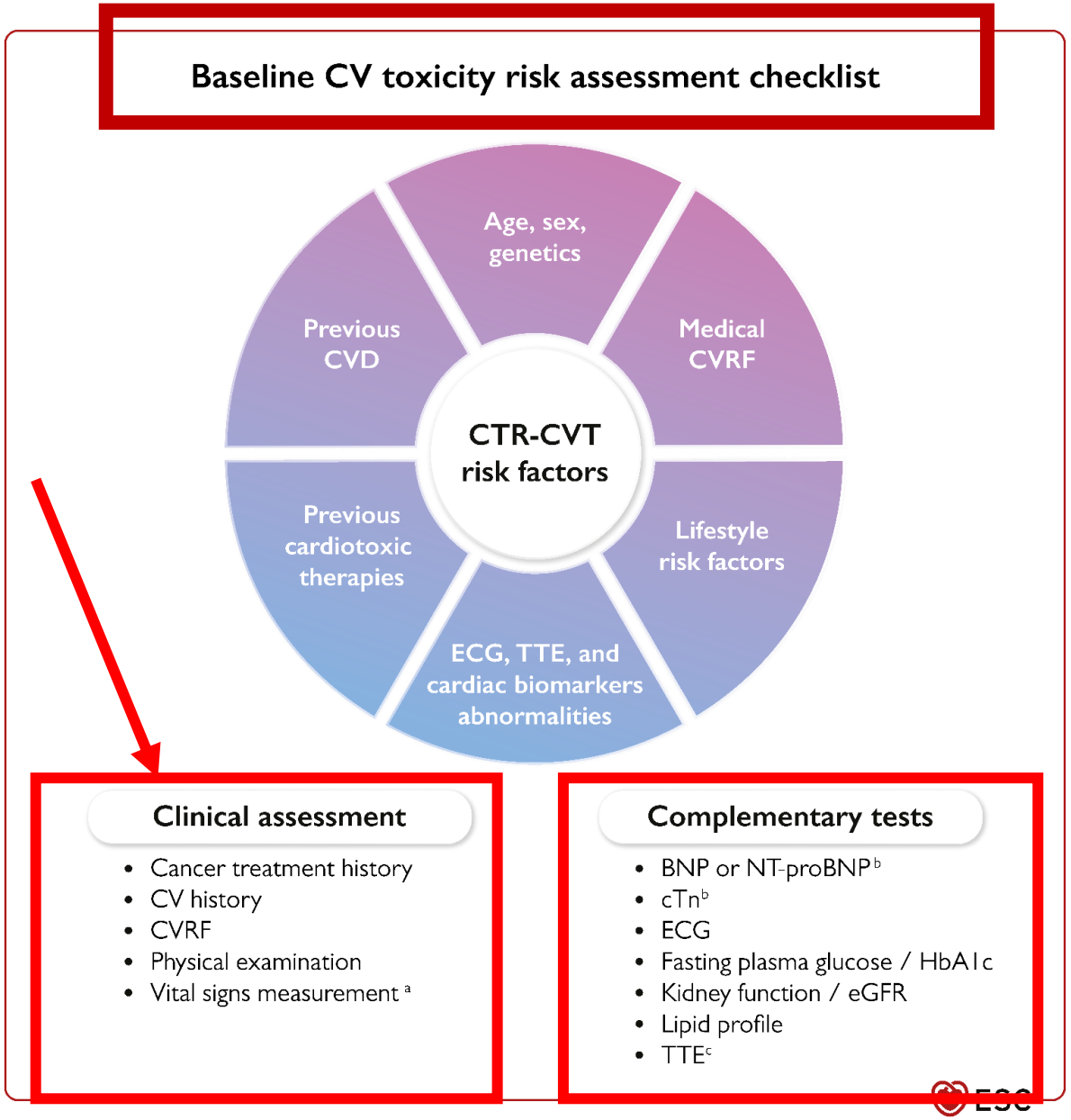


2022 ESC Guidelines on cardio-oncology
(*European Heart Journal*; 2022 – doi: 10.1093/eurheartj/ehac244)

Baseline cardiovascular toxicity risk assessment checklist

The principle underlying the dynamic course of CTR-CVT development in patients with cancer is that:

the absolute risk depends on their baseline risk and changes with exposure to cardiotoxic therapies over time



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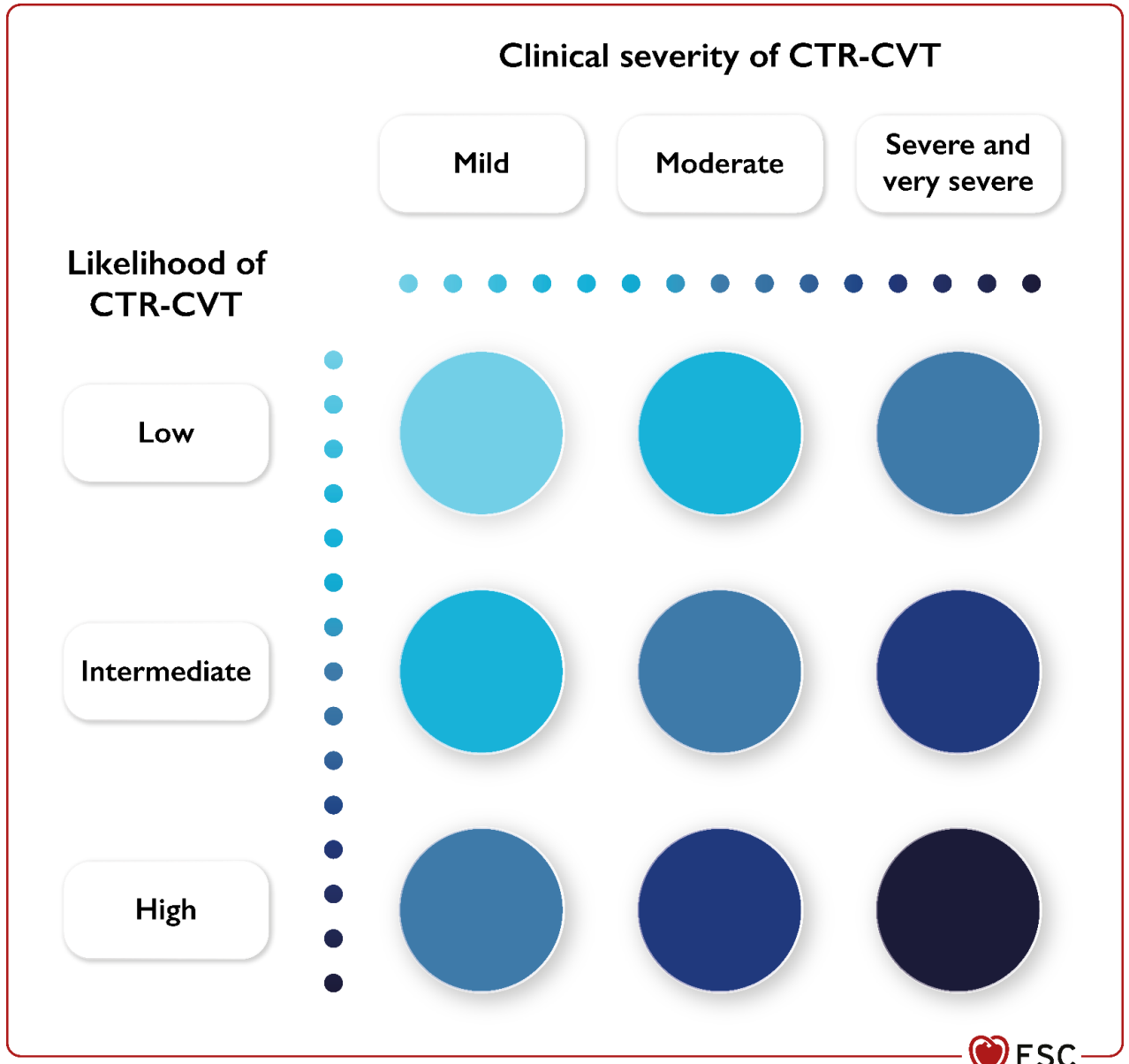
Dimensions of cancer therapy-related cardiovascular toxicity risk and disease severity

The risk itself can be understood in two ways:

(1) the likelihood of its occurrence

(2) the severity of the complication



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Cancer therapy-related cardiovascular toxicity definitions—vascular toxicity

Asymptomatic vascular toxicity	Symptomatic vascular toxicity
CAD	Stroke/Transient ischaemic attack
PAD	MI
Carotid artery disease	ACS
Venous thrombosis	CCS
Arterial thrombosis	PAD
Peripheral vasoreactivity	Vasospastic angina
Coronary epicardial vasoreactivity	Microvascular angina
Coronary microvascular vasoreactivity	Raynaud´s phenomenon

Heart Failure Association–International Cardio-Oncology Society baseline cardiovascular toxicity risk stratification

2022 ESC Guidelines on cardio-oncology
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Recommendations for a general approach to cardiovascular toxicity risk categorization

Recommendations	Class	Level
CV toxicity risk stratification before starting potentially cardiotoxic anticancer therapy is recommended in all patients with cancer.	I	B
Communicating the results of the CV toxicity risk assessment to the patient and other appropriate healthcare professionals is recommended.	I	C
The use of HFA-ICOS risk assessment should be considered to stratify CV toxicity risk in patients with cancer scheduled to receive cardiotoxic anticancer therapy.	IIa	C
It is recommended that patients categorized to be at low CV toxicity risk should proceed to anticancer therapy without delay.	I	C

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Recommendations for electrocardiogram 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

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(*European Heart Journal*; 2022 – doi: 10.1093/eurheartj/ehac244)

Recommendation for cardiac biomarker assessment prior to potentially cardiotoxic therapies

Recommendations	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

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Recommendations for cardiac imaging modalities in patients with cancer

Recommendations	Class	Level
General		
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

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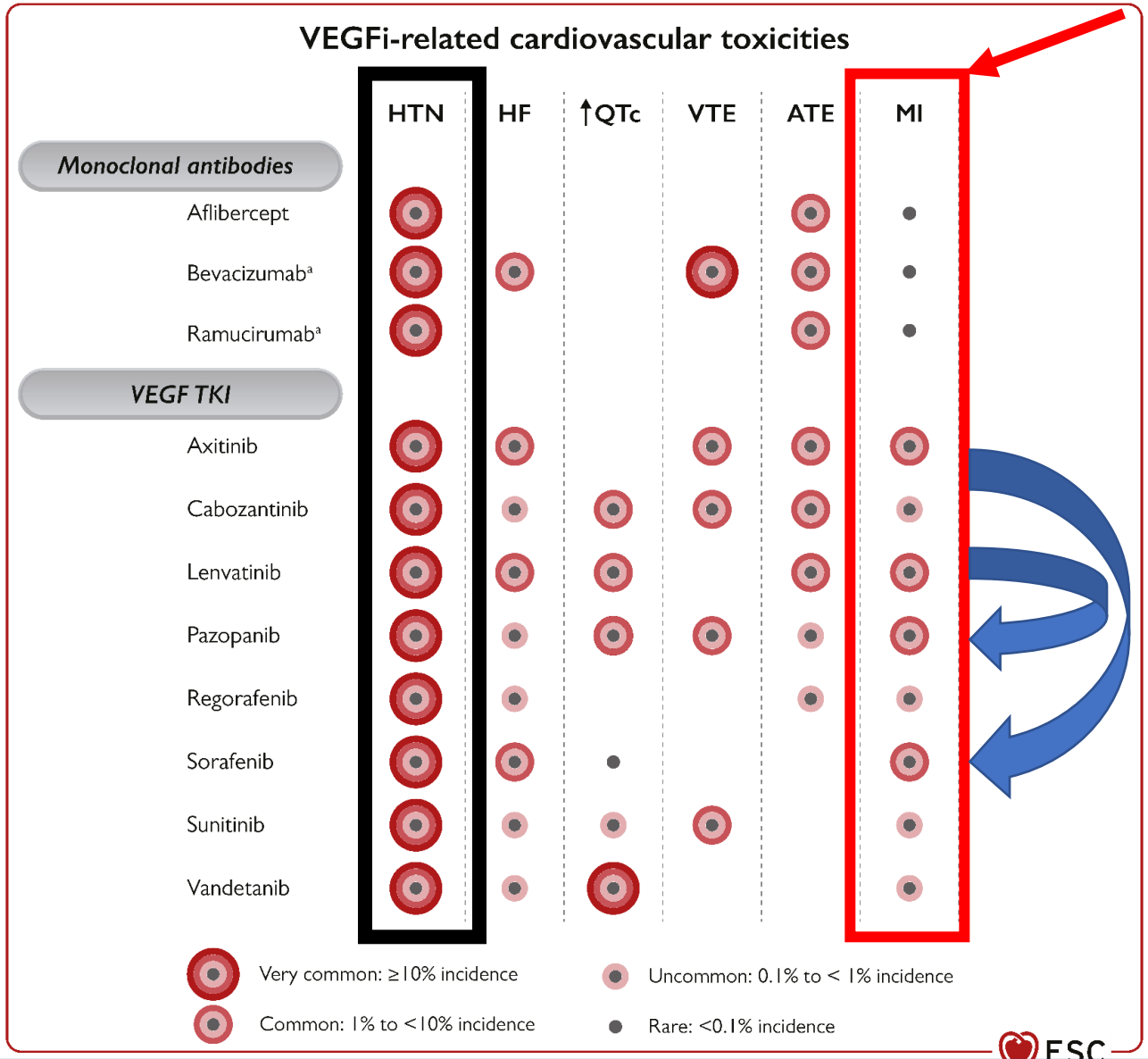
VEGFi-related cardiovascular toxicities

- **Monoclonal antibody**
- **Vascular endothelial growth factor tyrosine kinase inhibitors (VEGF TKI)**

2 principali meccanismi:

- **attraverso anticorpi monoclonali che agiscono a livello extracellulare sul recettore (es. bevacizumab e ramucirumab);**
- **attraverso l'inibizione della via intracellulare, tramite il blocco dell'attività tirosin-kinasica del recettore del fattore di crescita dell'endotelio vascolare -VEGF (es. sunitinib, sarafenib ed altri inibitori della tirosin-kinasi).**



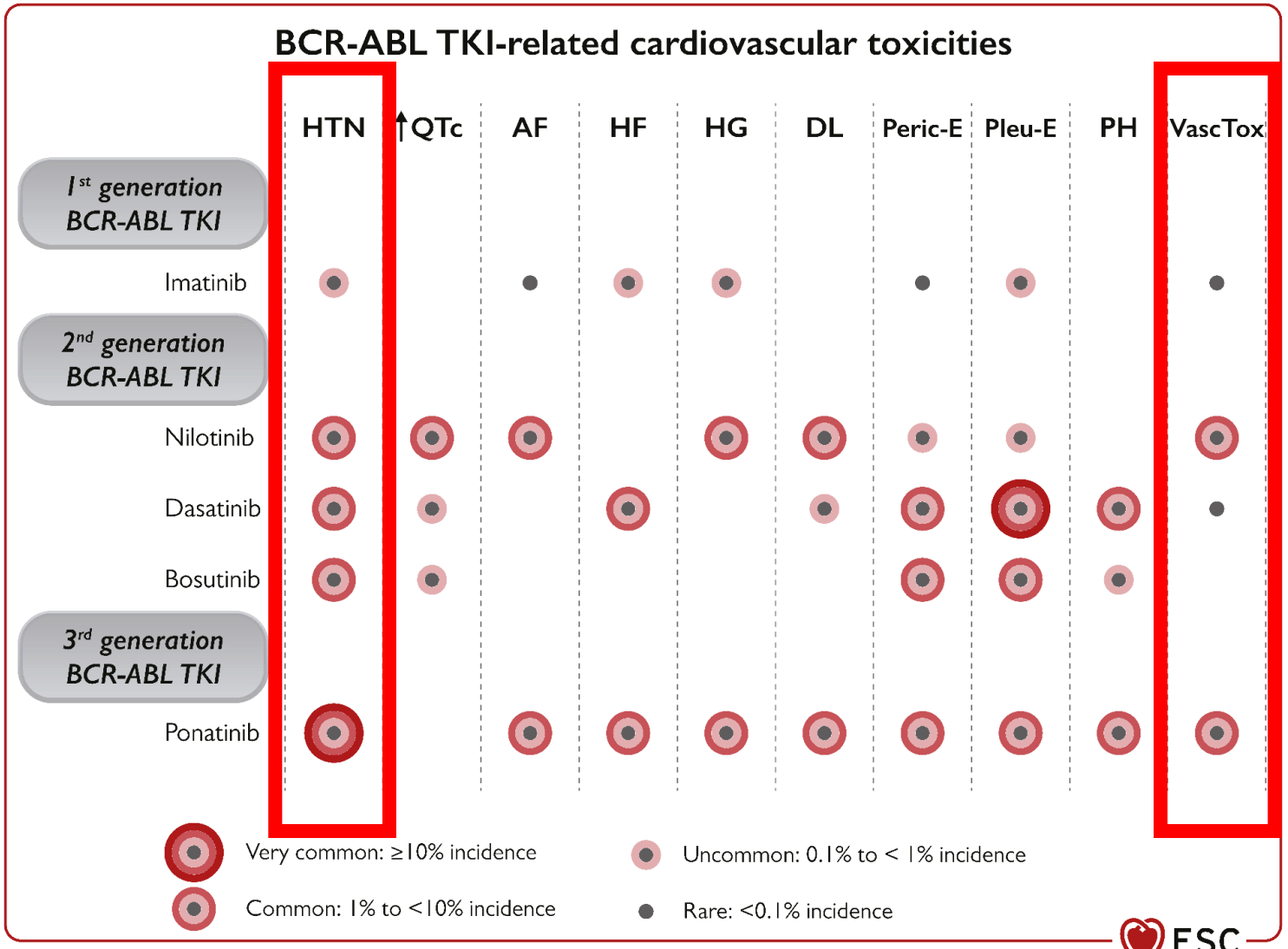
carcinoma metastatico del colon-retto

Carcinoma ovarico

Tossicità cardiovascolare correlata all'inibitore del fattore di crescita dell'endotelio vascolare

BCR-ABL tyrosine kinase inhibitor-related cardiovascular toxicities

Bcr/Abl è una **tirosino-chinasi intracellulare non recettoriale**
(dato che non risiede sulla membrana cellulare e non può essere quindi bloccata da anticorpi, sono necessarie piccole molecole in grado di superare la membrana cellulare e di legarsi al sito attivo dell'enzima).



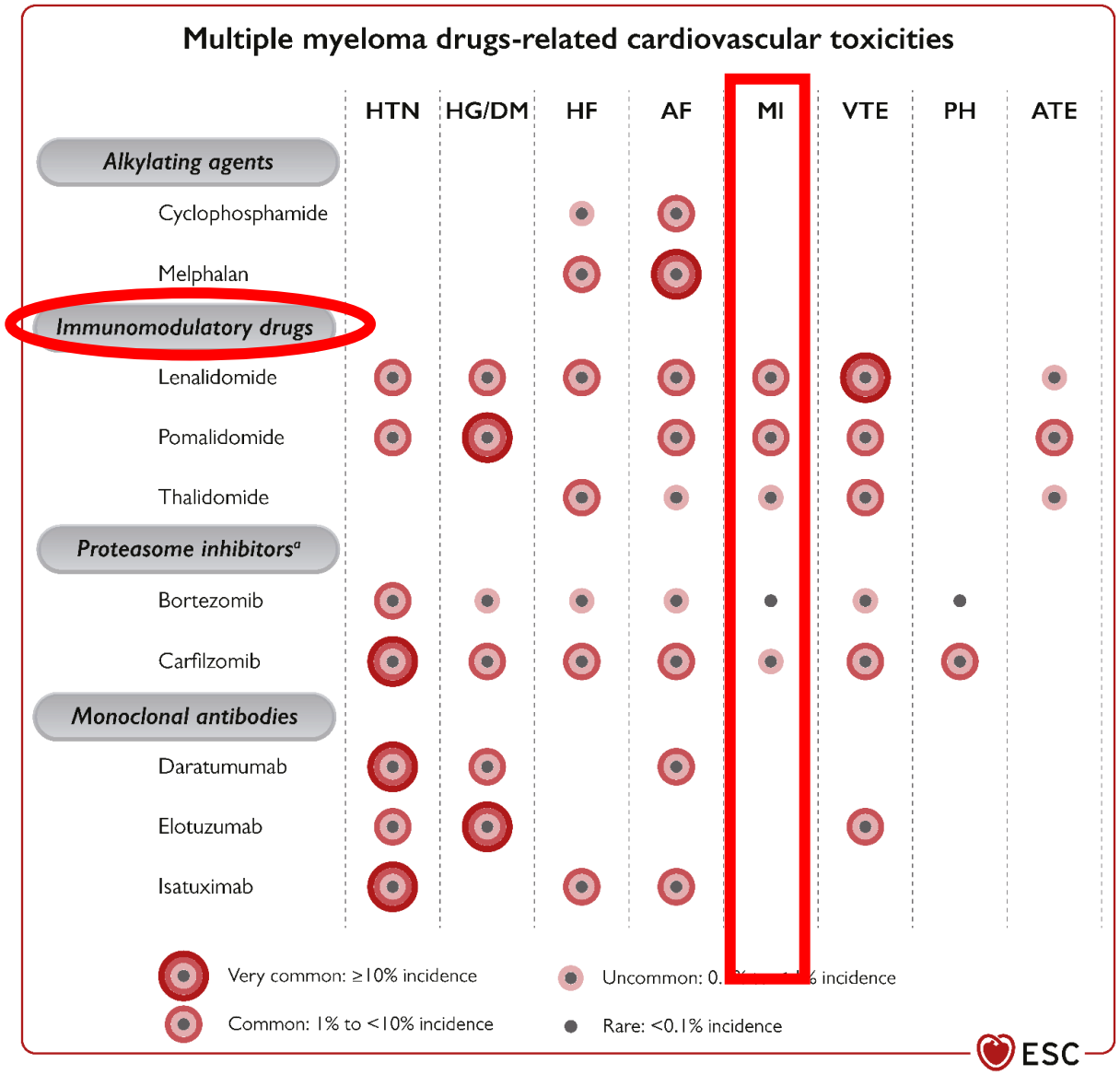
Leucemia mieloide cronica

Tossicità cardiovascolare correlata all'inibitore della tirosin Kinasi BCR-ABL

2022 ESC Guidelines on cardio-oncology
(*European Heart Journal*; 2022 – doi: 10.1093/eurheartj/ehac244)

Multiple myeloma drug-related cardiovascular toxicities

L'immunoterapia oncologica sfrutta farmaci particolari che agiscono sul sistema immunitario dell'organismo per stimolarlo ad attaccare le cellule tumorali

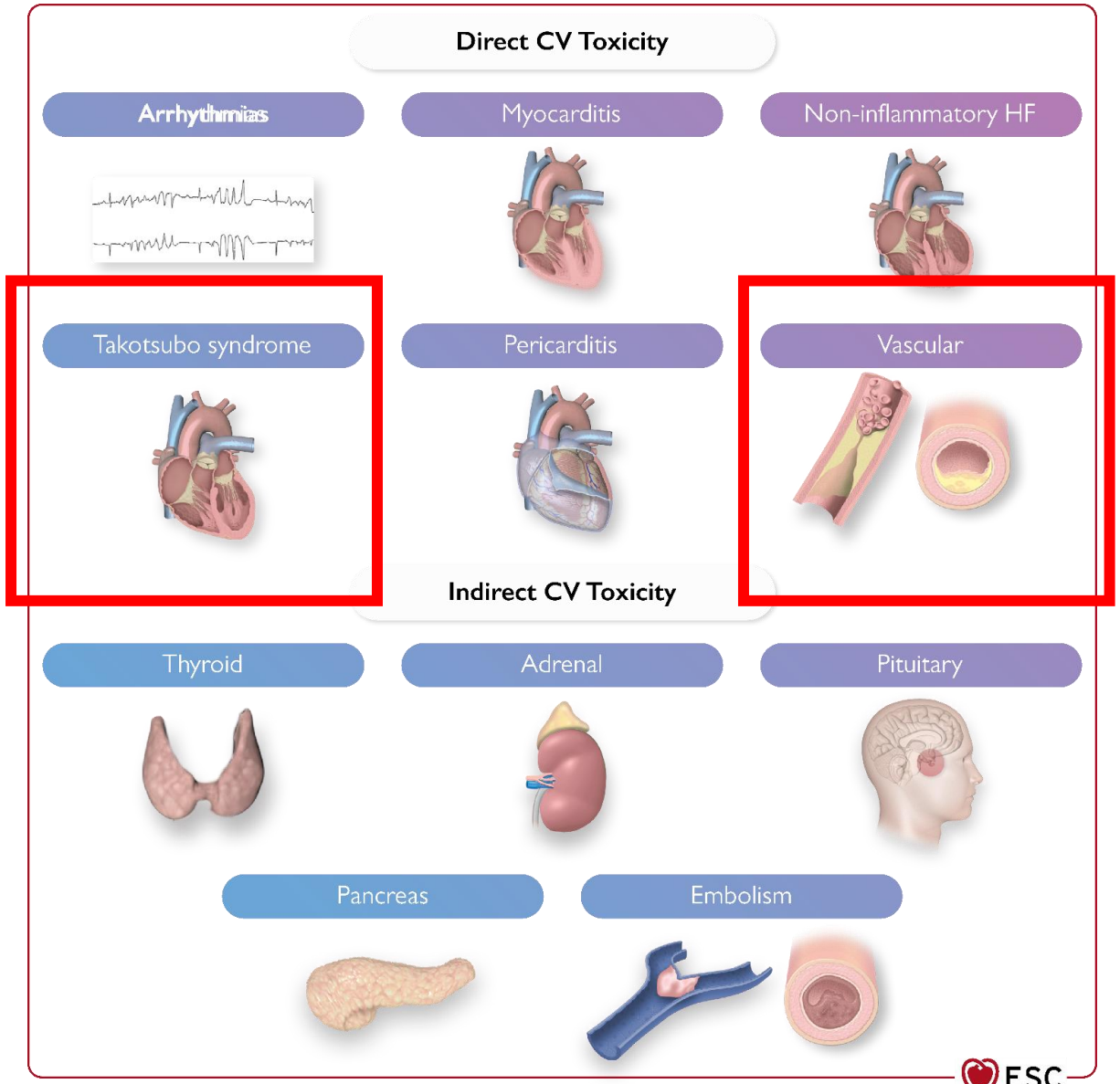


Mieloma multiplo

Tossicità cardiovascolare correlata alla immuno-terapia contro il mieloma multiplo

Direct and indirect immune checkpoint inhibitor-related cardiovascular toxicity

Gli inibitori del checkpoint immunitario (ICI) sono anticorpi monoclonali immunomodulatori, che aumentano l'immunità antitumorale dell'ospite, bloccando gli inibitori dell'attivazione e della funzione delle cellule T, quali i recettori T, definiti immuno-checkpoint, e facilitando le azioni mediate da cellule T contro i tumori



Tumore renale

www.escardio.org/guidelines

Tossicità cardiovascolare correlata alla terapia con inibitori del checkpoint immunitario

ESC European Society of Cardiology
European Heart Journal (2022) 43, 4229–4361
https://doi.org/10.1093/eurheartj/ehac244
ESC GUIDELINES

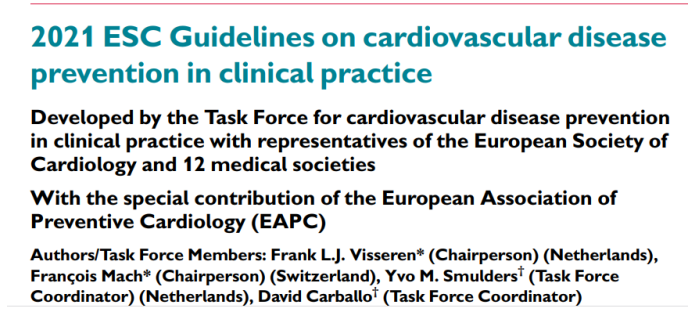
2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS)

Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC)

Coronary artery disease and RT treatment

- Any vascular location within the RT treatment volume is at i**ncreased risk for both accelerated atherosclerosis** and RT-related vasculopathy
- **RT-induced CAD depends on the location of the RT treatment volume** and most commonly affects either the proximal left anterior descending or the right coronary arteries.
- **RT-related vasculopathy is progressive and typically manifests in severe, diffuse, long, smooth and concentric angiographic lesions**

Prevention of cardiotoxicity and cardiovascular risk factors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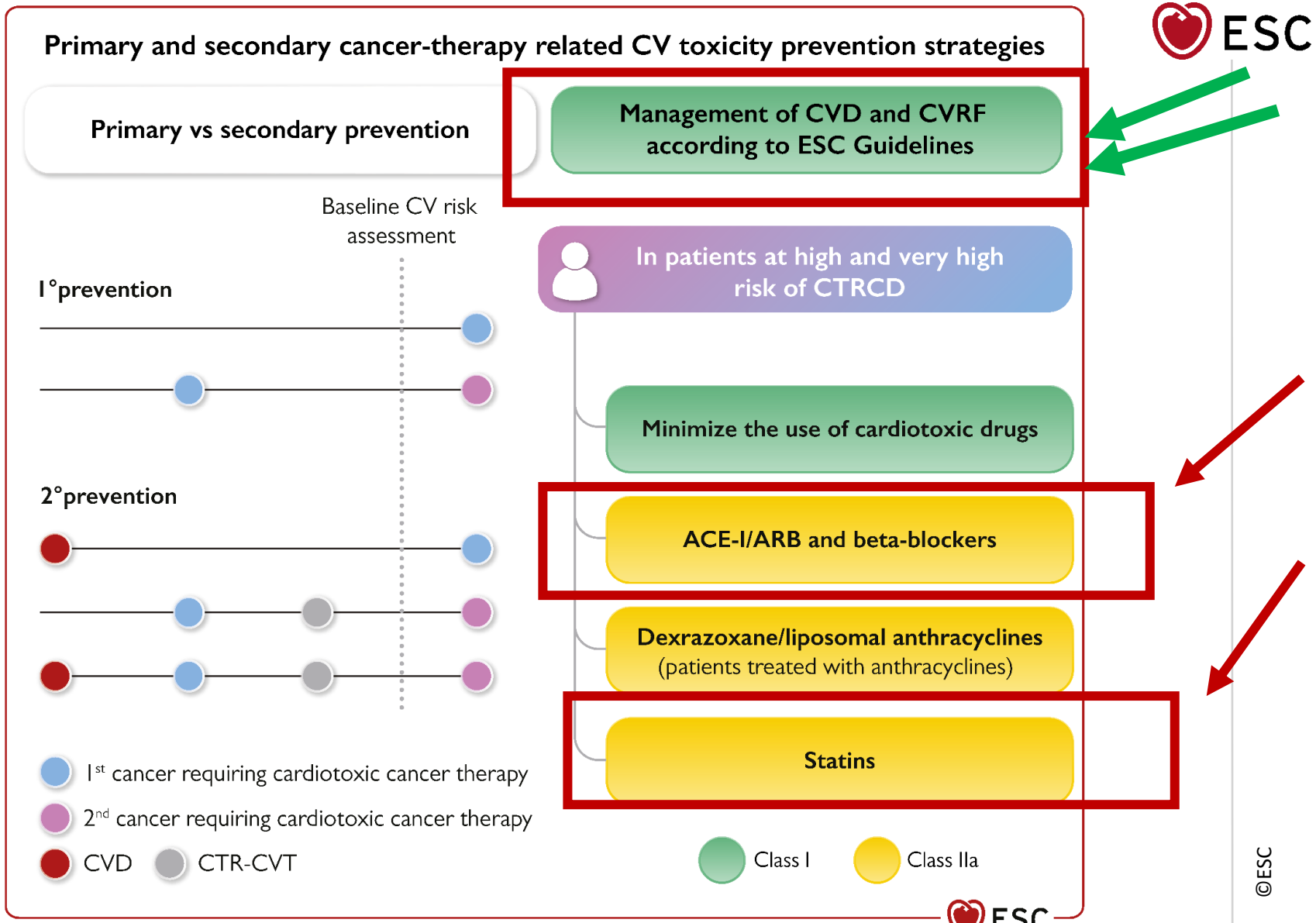
Management of CVD and CVRF according to ESC Guidelines

- **Exercise** should be strongly advised
- In particular, **aerobic exercise** is considered a promising non-pharmacological strategy to prevent and/ or treat chemotherapy toxicity
- A study showed a **significantly higher risk of CVD particularly in survivors of adult-onset cancer with underlying Coronary risk factors**
- Therefore, **aggressive management of ASCVD risk factors** in this population is recommended.

Primary and secondary cancer therapy-related cardiovascular toxicity prevention



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Coronary risk and antitumoral drugs

Key facts

- Diagnosis and screening
- Prevention of Cardiotoxicity and Cardiovascular risk factors
- Coronary risk stratification
- Coronary complications treatment
- Cardio-Oncological Care pathways

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Grazie
per l’attenzione

Conclusions

- Coronary toxicity risk is a dynamic variable
- A baseline CV risk assessment is recommended for all patients with cancer scheduled to receive a potentially cardiotoxic anticancer therapy
- Primary prevention of CV toxicity from cancer therapy aims to avoid or minimize the development of CTR-CVT in patients without CVD.
- Secondary prevention refers to interventions in patients with preexisting CVD, including prior or new CTR-CVT.

Conclusions 2

- Defining and delivering an appropriate prevention and surveillance plan for potential CV complications is recommended.
- Optimal management of CVRF and pre-existing CVD is mandatory to facilitate cancer therapy and to improve patients' prognosis.
- Detailed monitoring pathways during cancer therapy—*including 3D echocardiography, GLS, and cardiac biomarkers*—are provided to detect CV toxicity based upon specific cancer therapies and baseline coronary toxicity risk