

The Onco-hematologist's View: Integrating Novel Therapies and Cardiovascular Safety

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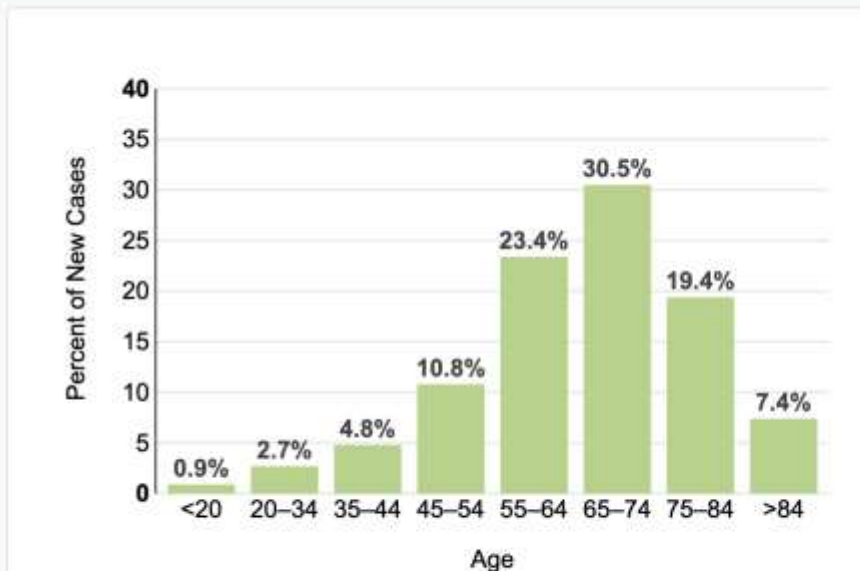
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Conflict of interest

Name of Company	Research support	Employee	Stockholder	Speaker's Bureau	Scientific Advisory Board	Other (Honoraria and/or travel support)
GSK					X	X
Menarini/ StemLine					X	X
BMS/Celgene					X	X
Sanofi					X	X
Janssen					X	X
AstraZeneca					X	X
Pfizer					X	X

Cancer is a disease of the “elderly”

Percent of New Cases by Age Group: Cancer of Any Site



Cancer of any site is most frequently diagnosed among people aged 65–74.

Median Age
At Diagnosis

67

SEER 21 2018–2022, All Races, Both Sexes

Age at diagnosis of haematological cancers

Most haematological cancers are diagnosed around 70 years of age

Non-Hodgkin lymphoma is most frequently diagnosed among people aged 65–74.

Median Age
At Diagnosis

68

Myeloma is most frequently diagnosed among people aged 65–74.

Median Age
At Diagnosis

69

Leukemia is most frequently diagnosed among people aged 65–74.

Median Age
At Diagnosis

68

Exception: Hodgkin Lymphoma

Hodgkin lymphoma is most frequently diagnosed among people aged 20–34.

Median Age
At Diagnosis

39









...but HL is rare! (5% of HC)

Prevalence of cardiac comorbidities in the general population

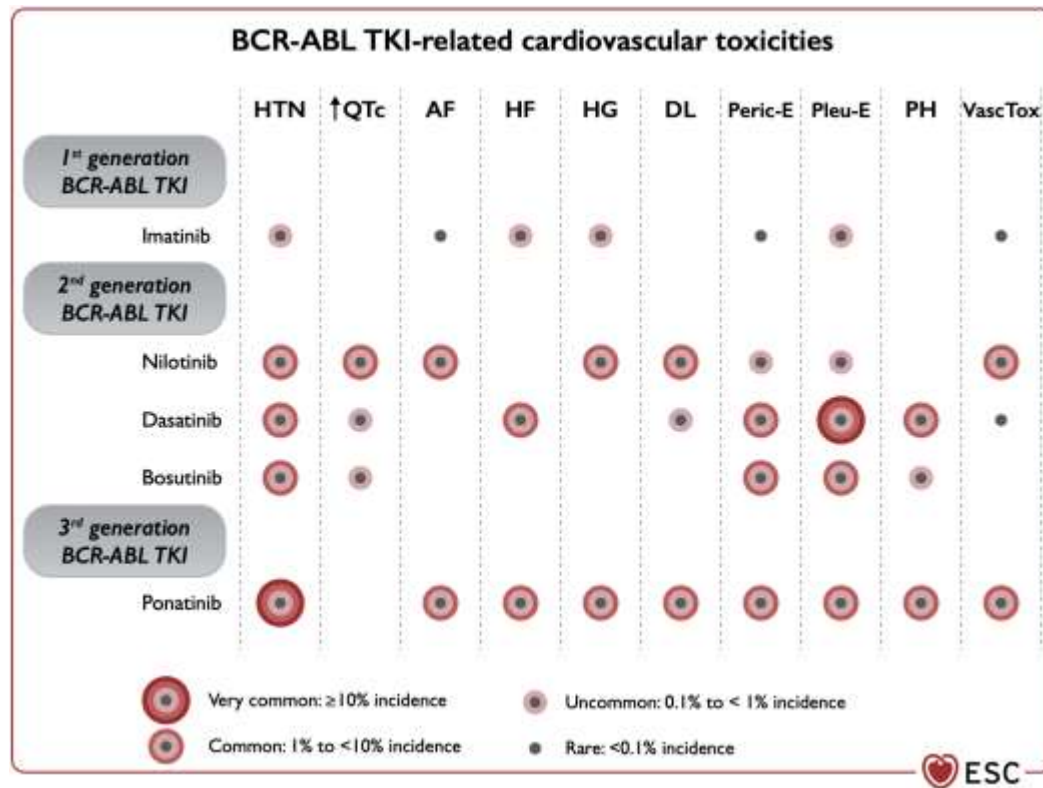
- **70%** of people **70 yrs or older** will develop CVD
- CVD frequently coexists with diabetes (37%–47%), anaemia (39%–51%), and arthritis (41%–46%)
- **70%** of people **65 yrs or older** have hypertension
- Prevalence of heart disease (coronary heart disease, angina pectoris or myocardial infarction) in US: **14.3%** in adults aged **65–74**, and **24.2%** in adults aged **75 or older**
- Prevalence of chronic ischemic heart disease in a German cohort (median age **74 yrs**): **27.5%**

Major CV toxicities in haematologic cancers

Cardiovascular Round Table

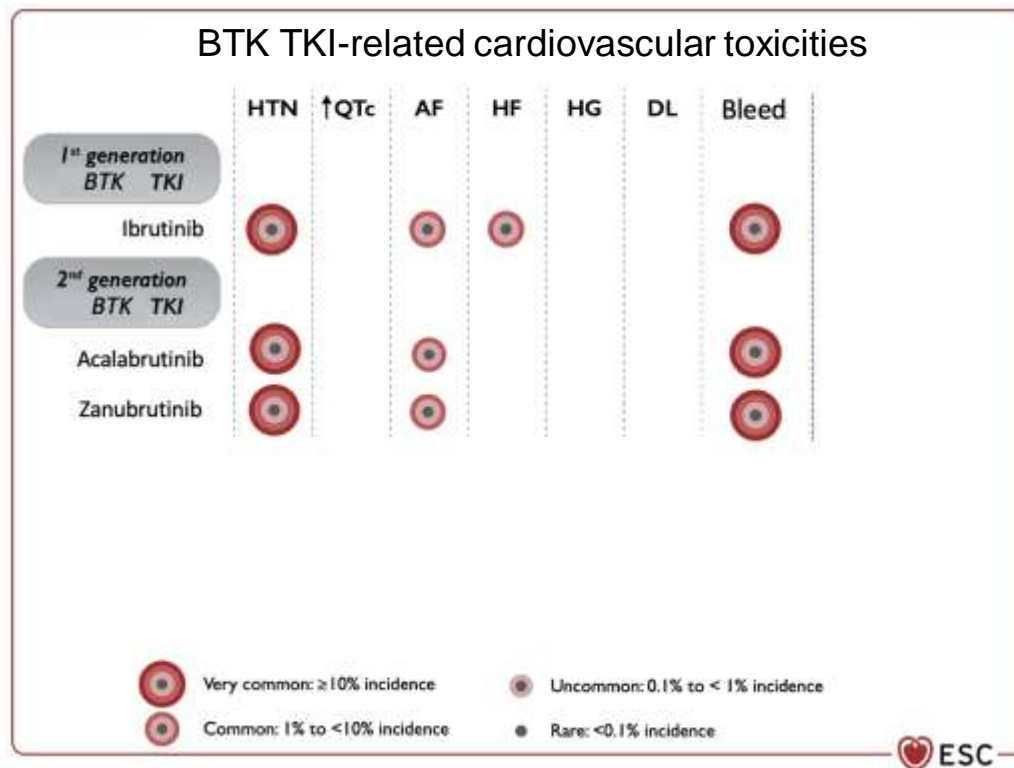
	 Arrhythmia	 Cardiomyopathy	 Arterial vascular disease	 Venous thromboembolism	 Pulmonary hypertension	 Systemic hypertension	 Pericardial disease	 Valvular heart disease
Conventional chemotherapy								
Antracyclins (doxorubicin)		X						
Alkylating agents (cyclophosphamide, melphalan)	X	X	X					
Antimetabolites (cytarabine)							X	
Arsenic trioxide	X							
Targeted agents								
Immunomodulatory drugs (thalidomide, lenalidomide)	X			X				
Proteasome inhibitors (bortezomib, carfilzomib)		X	X			X		
BCR::ABL1 inhibitors (dasatinib, nilotinib, ponatinib)	X		X	X	X (dasatinib)			
BTK inhibitors (ibrutinib)	X							

CV toxicities of BCR::ABL inhibitors



Cardiovascular complications of BCR::ABL1 TKI are due to their typical off target effects

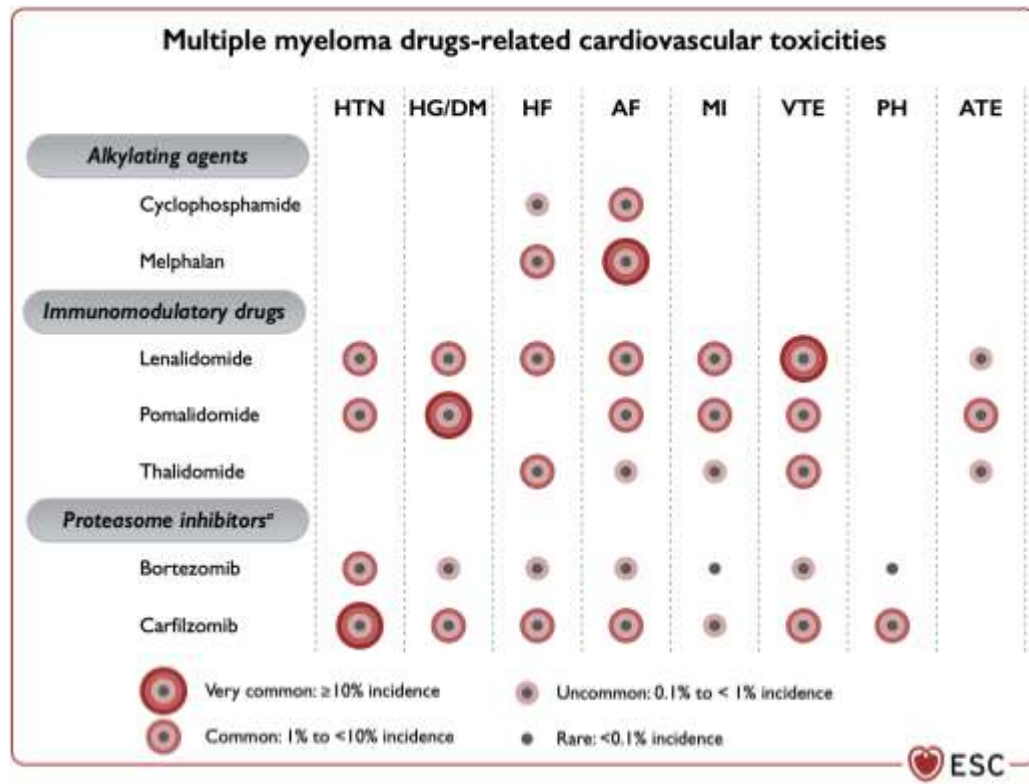
CV toxicities of BTK inhibitors



BTK are associated with bleeding diathesis, and an increased risk of hypertension, AF and HF

BTK: Burton tyrosine kinase; HTN: hypertension, AF: atrial fibrillation, HF: heart failure; HG hyperglycaemia, DL: dyslipidaemia, Bleed: bleeding

CV toxicities of BTK inhibitors



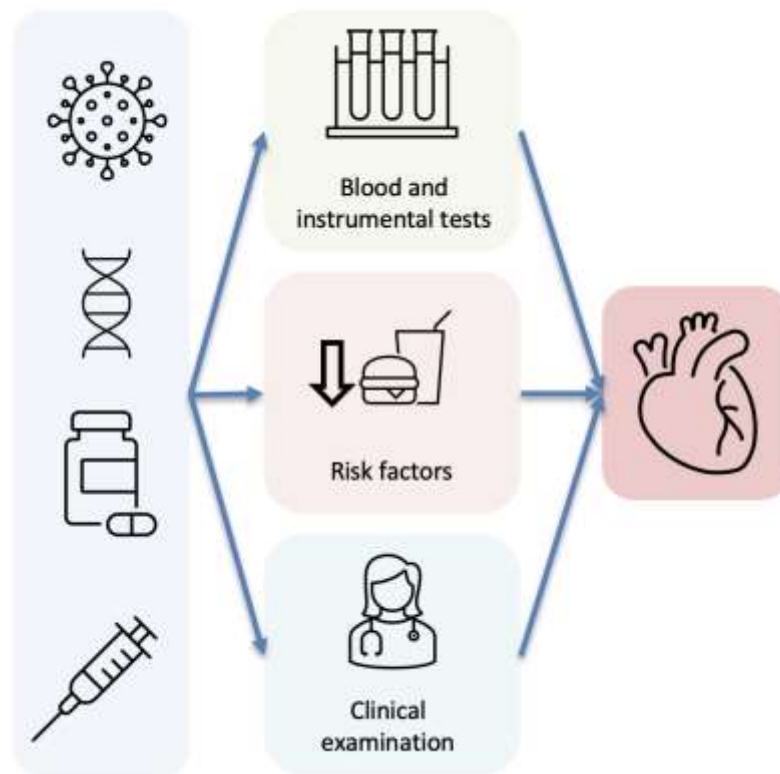
Immunomodulatory drugs are associated with a higher risk of thrombosis.

Among proteasome inhibitors, Carfilzomib is associated with a higher risk of hypertension

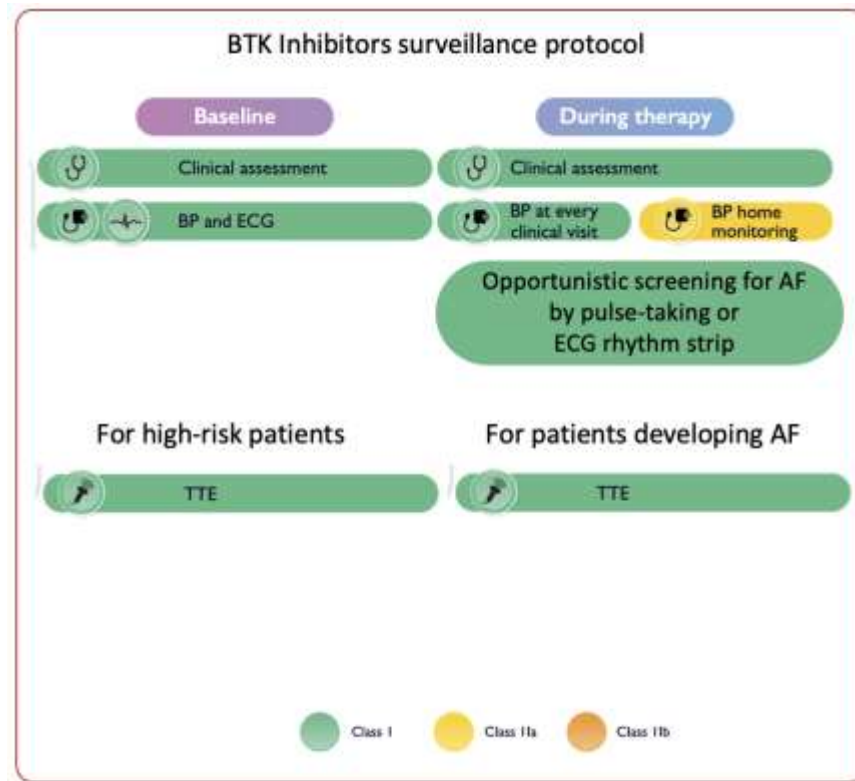
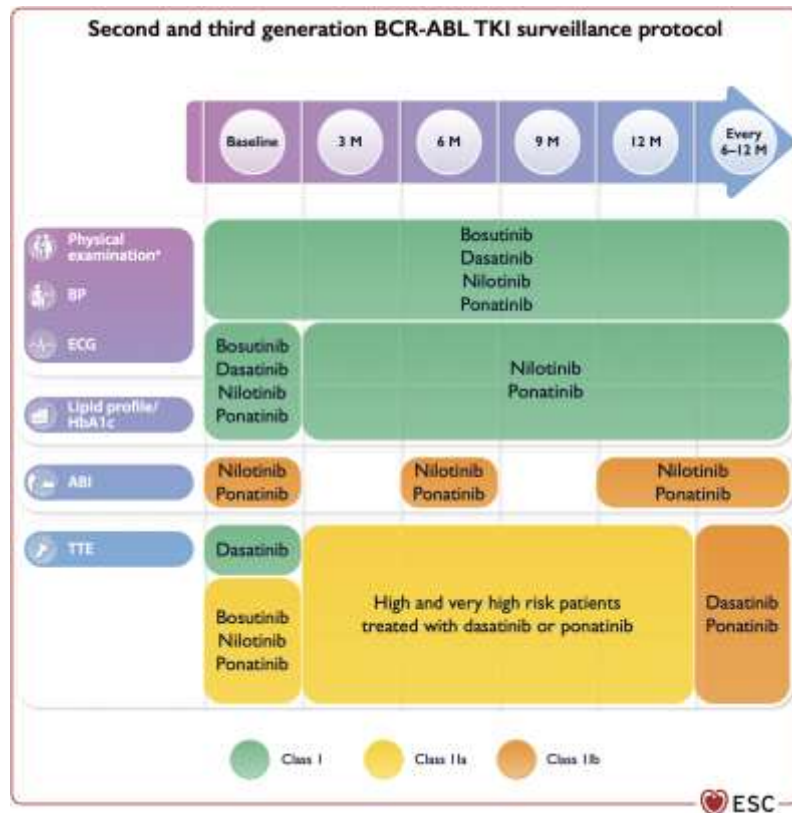
HTN: hypertension, AF: atrial fibrillation, HF: heart failure; HG hyperglycaemia, DM: diabetes mellitus, MI: myocardial infarction, VTE: venous thromboembolism, PH: pulmonary hypertension, ATE: arterial thromboembolism

How to integrate these drugs in our therapy

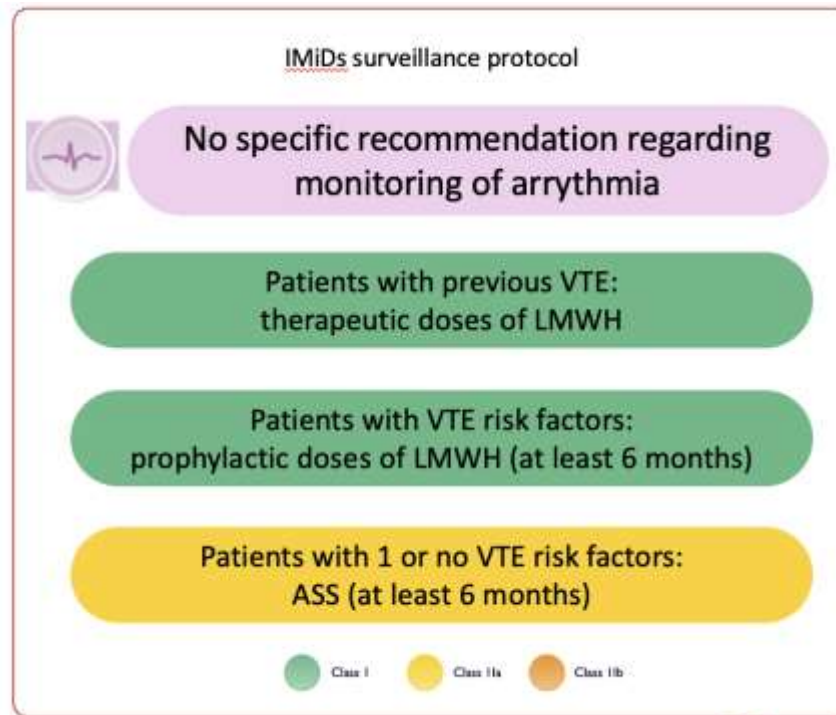
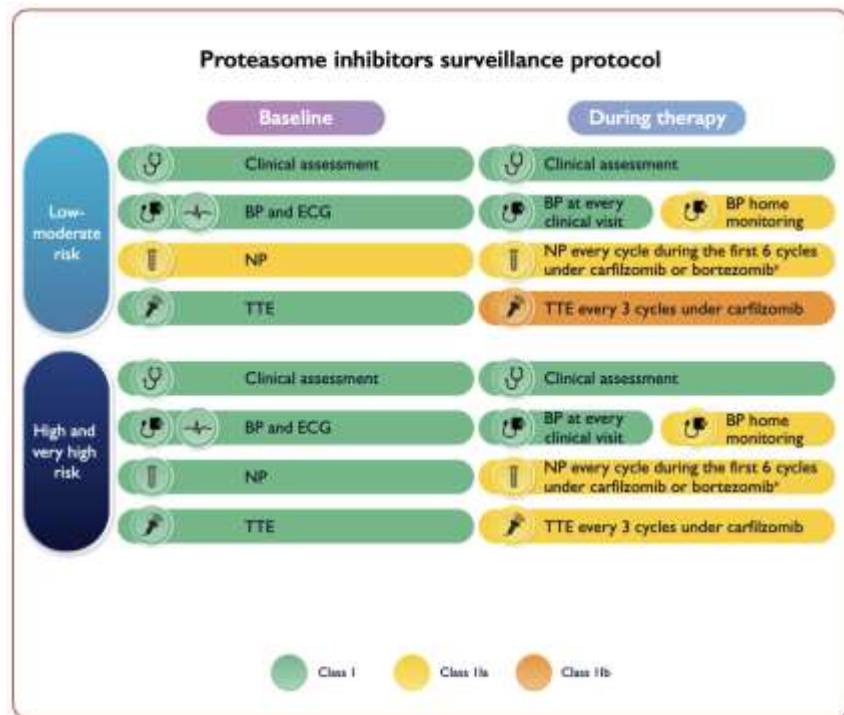
- Optimal monitoring is the key (2022 ESC Guidelines on cardio-oncology)
- Reducing risk factors before starting therapy
- Medical and behavioural therapy
- ...don't underestimate the effect of sport



Examples of monitoring



Examples of monitoring



Let's spice things up a little bit...

It is not all that easy...comorbidities and side effects of drugs are different also according to sex at birth

Example of multiple myeloma

	Male, N = 363 (55%), n/N (%)	Female, N = 292 (45%), n/N (%)	p value
Risk according to IMWG			
High	31/137 (23)	32/119 (27)	0.378
Standard	89/137 (65)	78/119 (65)	
Low	17/137 (12)	9/119 (8)	
	Male, n = 179 (57%), n/N (%)	Female, n = 134 (43%), n/N (%)	p value
Toxicity*			
Haematological	168/171 (98)	132/132 (100)	0.260
Infections	131/179 (73)	93/134 (69)	0.527
Gastrointestinal	91/179 (51)	88/133 (66)	0.107
Mucositis	39/173 (23)	54/132 (41)	0.001
Cardiovascular tox	18/179 (10)	13/134 (10)	0.792
ICU admission	2/172 (1)	3/131 (2)	0.655
Comorbidities*			
Renal insufficiency CKD > Grade 2 before SCT	25/110 (23)	21/100 (21)	0.868
Cardiac (general)	122/179 (68)	73/134 (55)	0.018
Hypertension	111/179 (62)	65/134 (49)	0.021
Coronary heart disease	23/179 (13)	2/134 (2)	<0.001
COPD	13/179 (7)	3/134 (2)	0.067
DM type II	18/179 (10)	8/134 (6)	0.220

Conclusions

- We have wonderful drugs that significantly increase survival of our patients
- Most of these compounds have a cardiovascular toxicity, often underestimated by onco-haematologist
- Patients bring their own burden of comorbidities which also affect cardiovascular risk profile
- Younger patients → evaluation of long-term survival and side effects

We are getting there, but we still need to improve cardiovascular safety assessment by improving risk stratification including better representation of diverse patient profiles (age, sex, behaviour, etc)

LET'S DO THIS TOGETHER



Grazie!