

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

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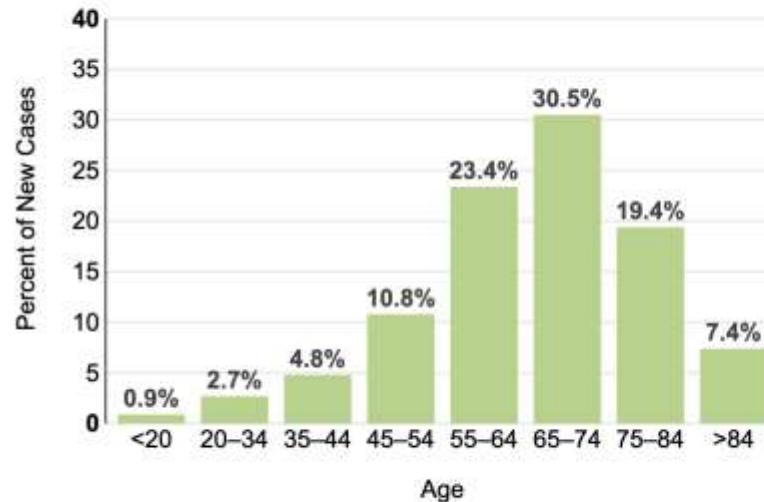
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# Conflict of interest

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)

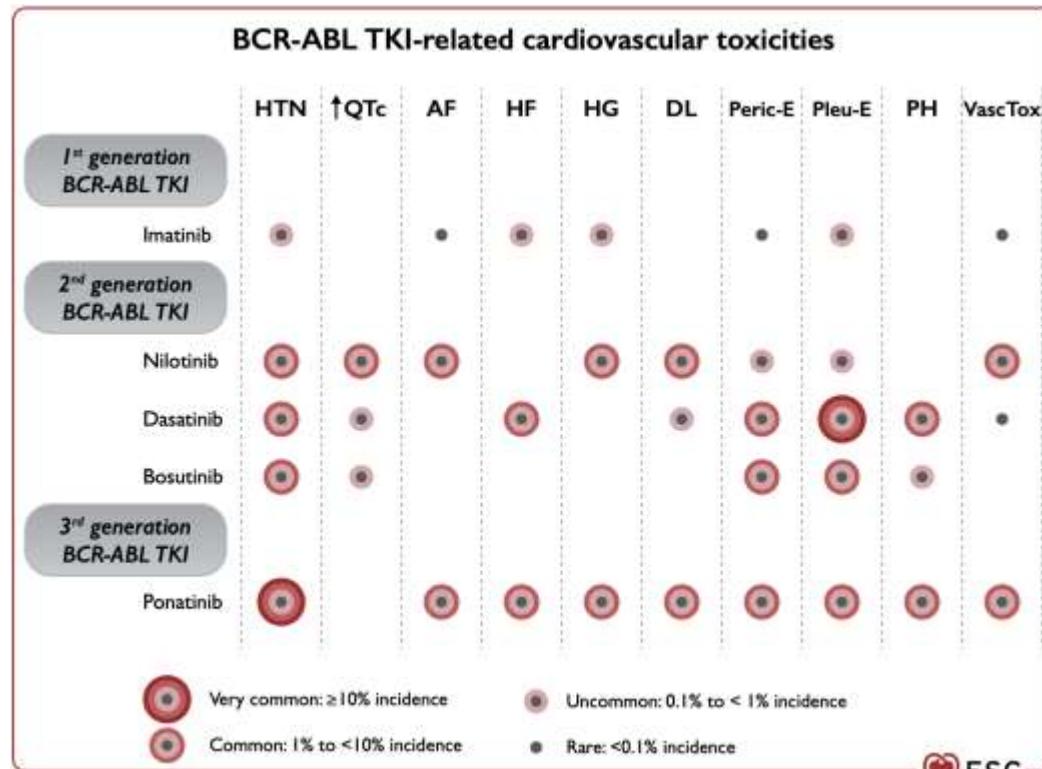
# Prevalence of cardiac comorbidities in the general population

- **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

	Arrhythmia	Cardio-myopathy	Arterial vascular disease	Venous thrombo-embolism	Pulmonary hypertension	Systemic hypertension	Pericardial disease	Valvular heart disease
<b>Conventional chemotherapy</b>								
Antracyclines (doxorubicin)		X						
Alkylating agents (cyclophosphamide, melphalan)	X	X	X					
Antimetabolites (cytarabine)							X	
Arsenic trioxide	X							
<b>Targeted agents</b>								
Immunomodulatory drugs (thalidomide, lenalidomide)	X			X				
Proteasome inhibitors (bortezomib, carfilzomib)		X	X			X		
BCR::ABL1 inhibitors (dasatinib, nilotinib, ponatinib)	X		X	X			X	
BTK inhibitors(ibrutinib)	X				X (dasatinib)			

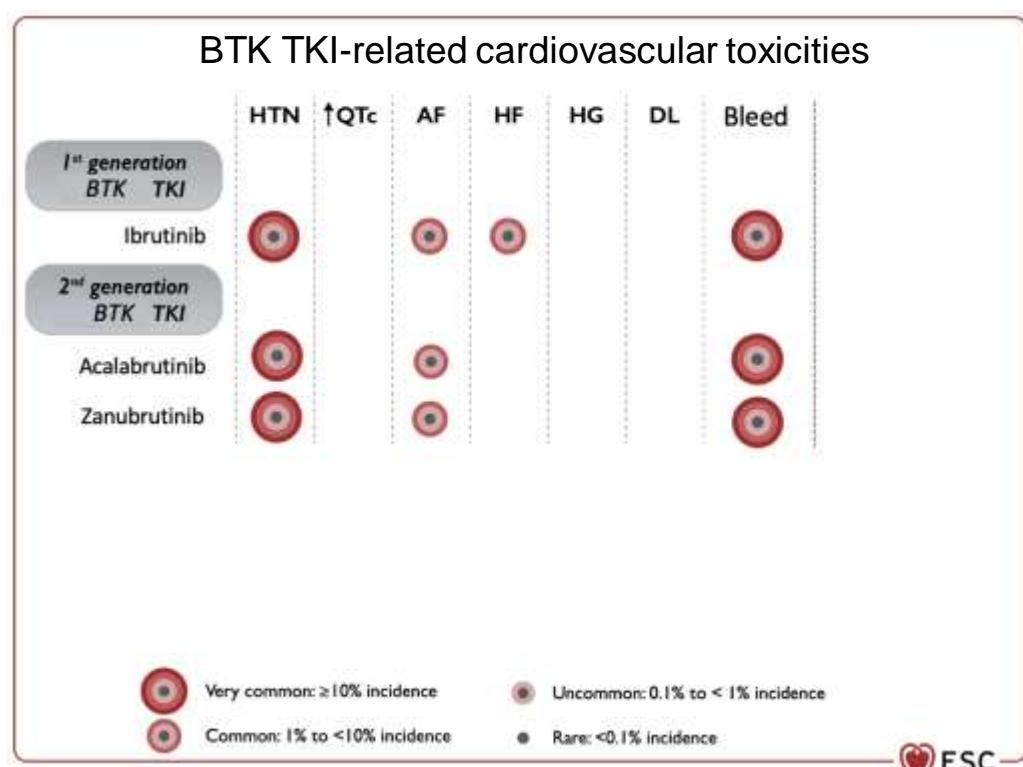
# CV toxicities of BCR::ABL inhibitors



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

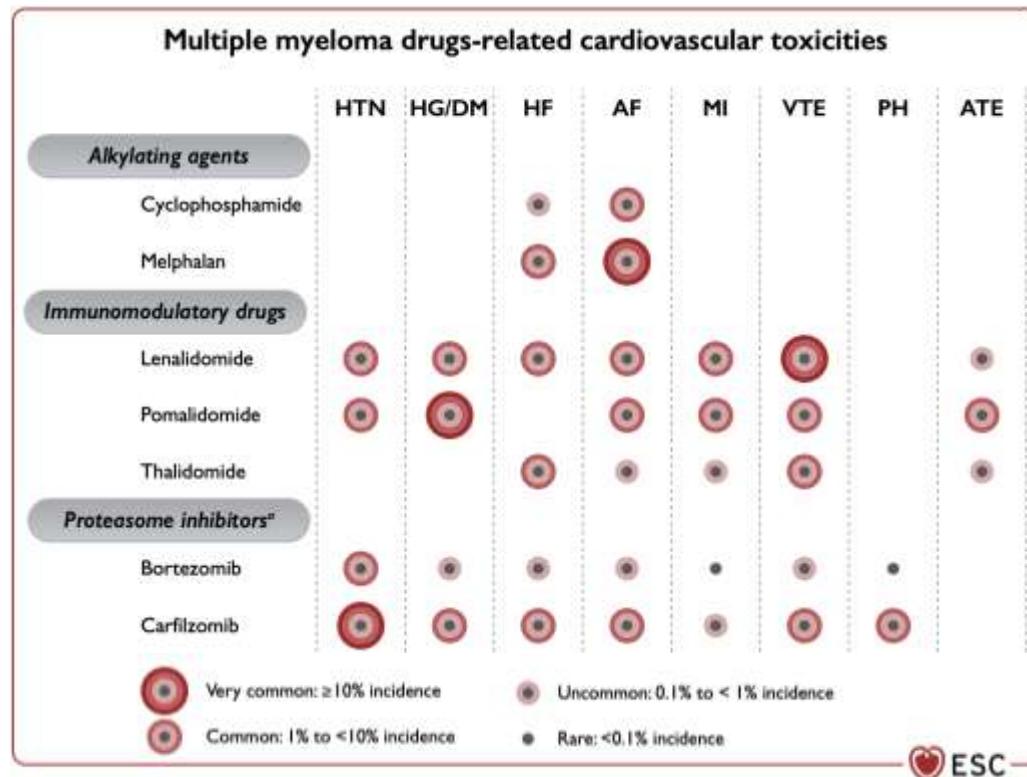
HTN: hypertension, AF: atrial fibrillation, HF: heart failure; HG: hyperglycaemia, DL: dyslipidaemia, Peric-E: pericardial effusion, Pleu-E: pleural effusion, PH: pulmonary hypertension

# CV toxicities of BTK inhibitors



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

# CV toxicities of BTK inhibitors



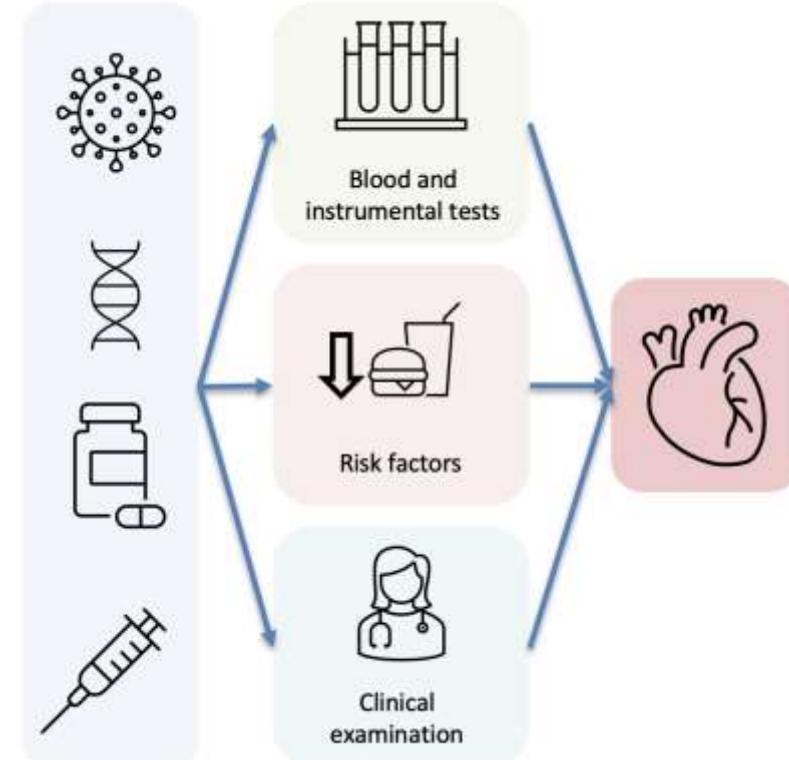
HTN: hypertension, AF: atrial fibrillation, HF: heart failure; HG: hyperglycaemia, DM: diabetes mellitus, MI: myocardial infarction, VTE: venous thromboembolism, PH: pulmonary hypertension, ATE: arterial thromboembolism

Immunomodulatory drugs are associated with a higher risk of thrombosis.

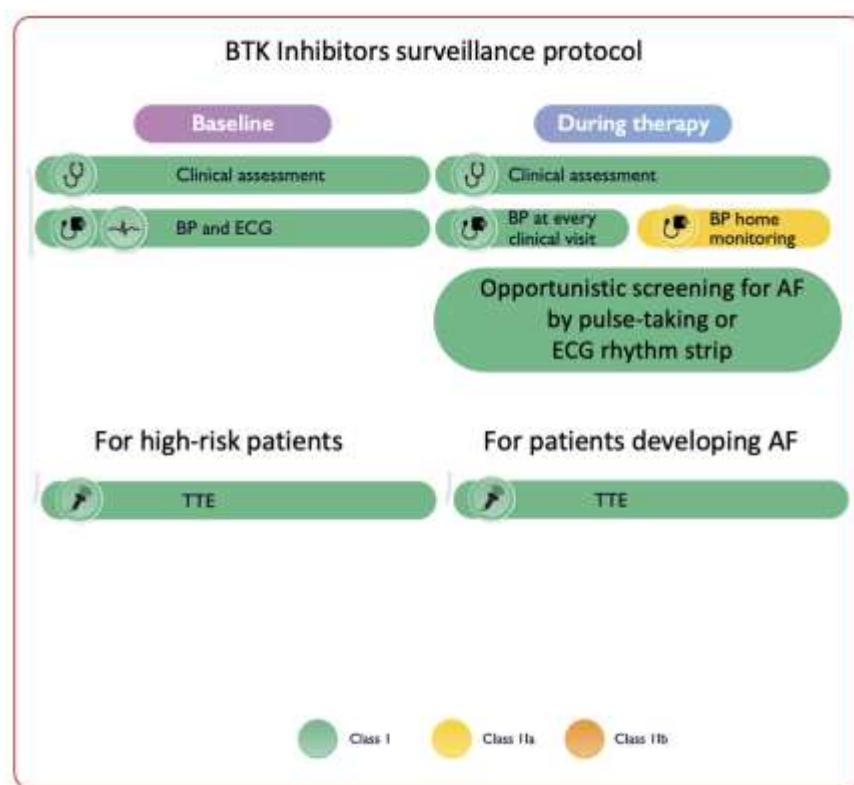
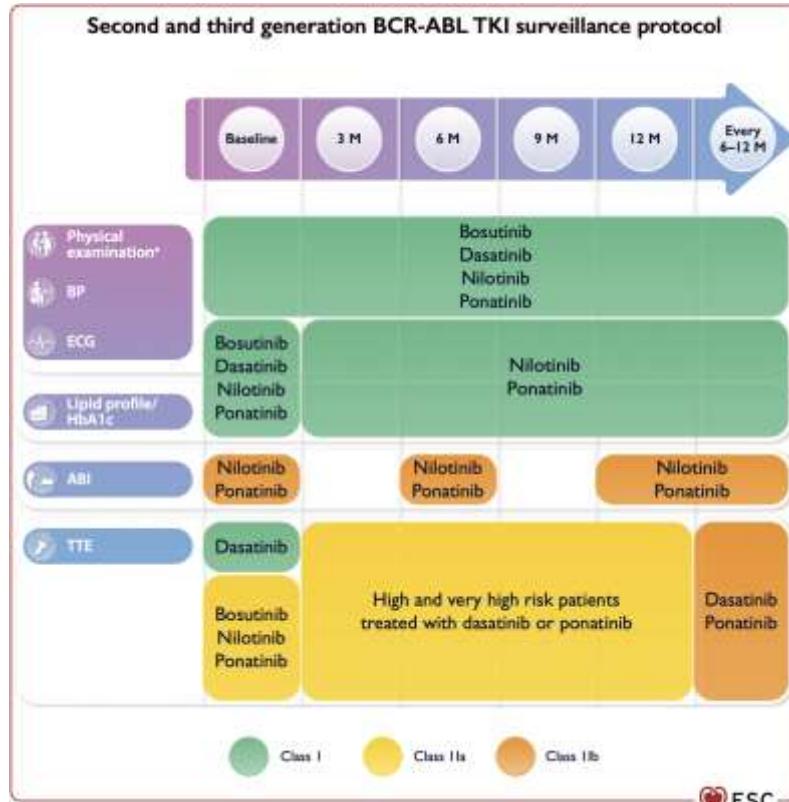
Among proteasome inhibitors, Carfilzomib is associated with a higher risk of hypertension

# How to integrate these drugs in our therapy

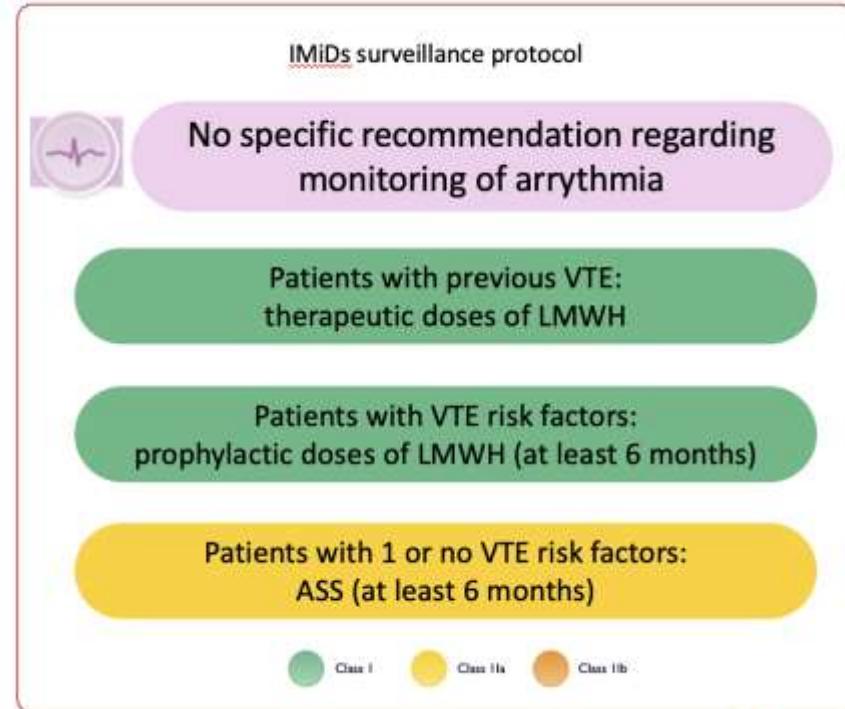
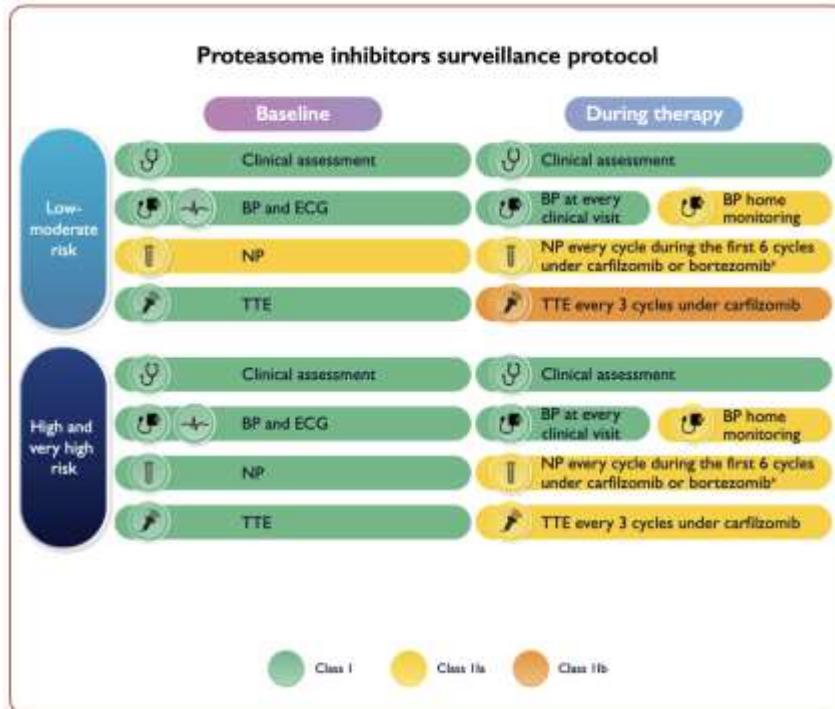
- Optimal monitoring is the key (2022 ESC Guidelines on cardio-oncology)
- Reducing risk factors before starting therapy
- Medical and behavioural therapy
- ...don't underestimate the effect of sport



# 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)	
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 underestimate 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!