



# ECD & concomitant diseases

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# Outline

## 1) Mixed histiocytosis

- ECD-LCH
- ECD-RDD

## 2) Clonal Hematopoiesis

## 3) Second cancer

- Hematologic
- Solid

# Outline

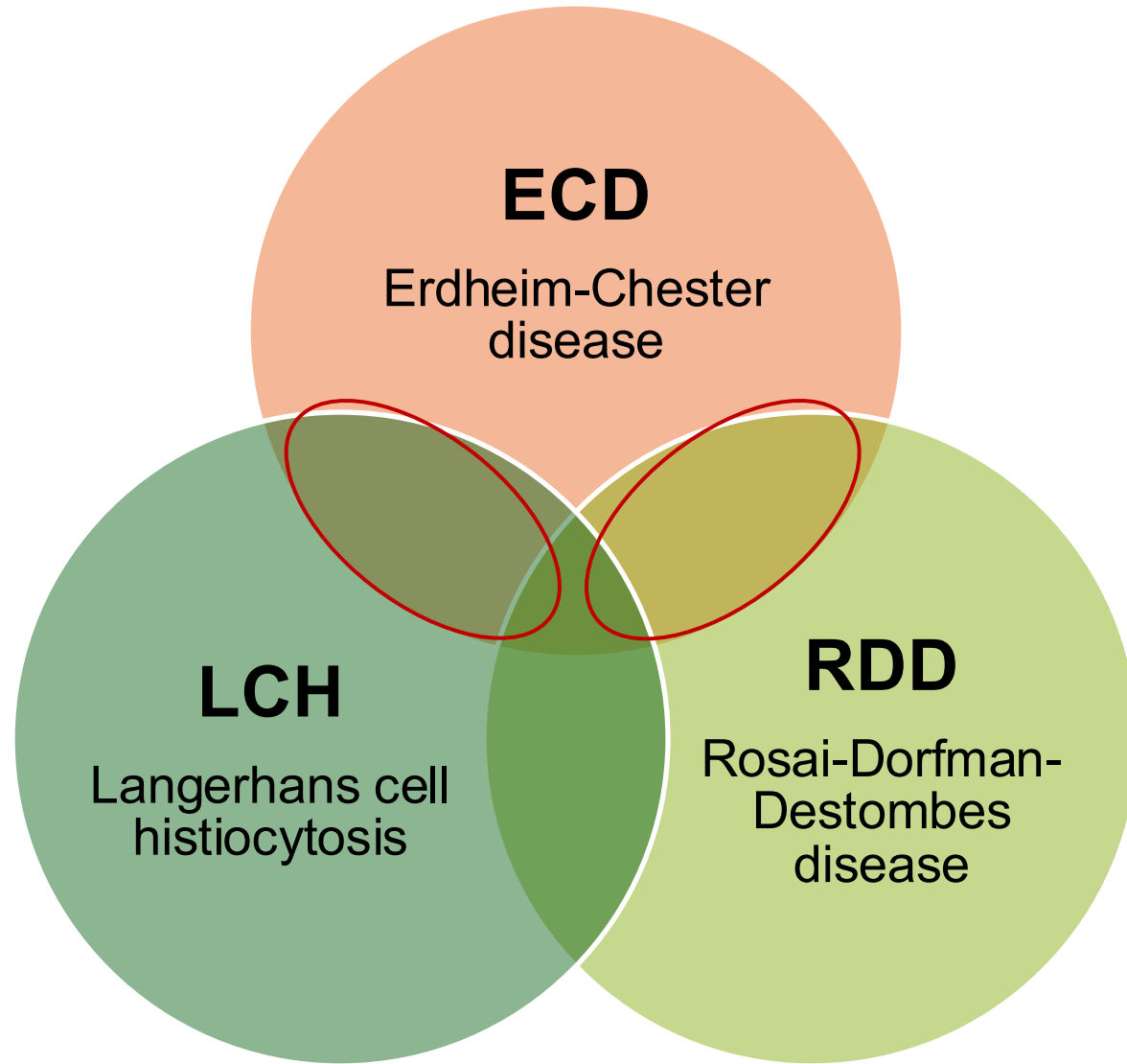
## 1) Mixed histiocytosis

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**ECD**

Erdheim-Chester  
disease

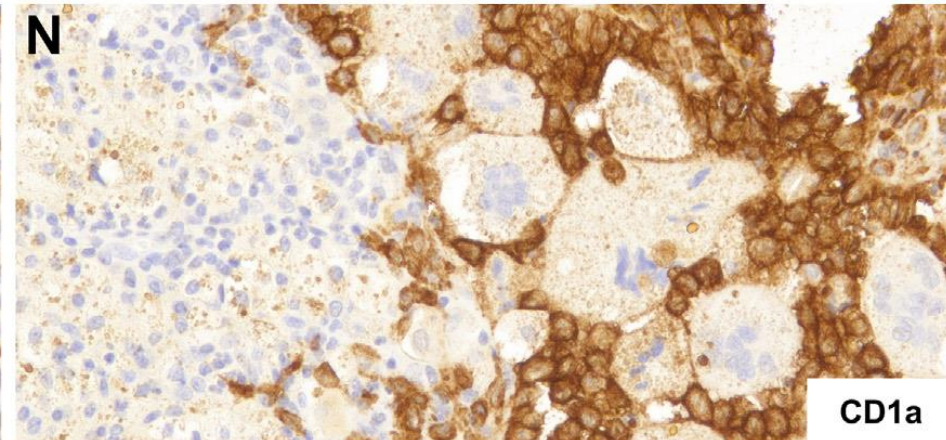
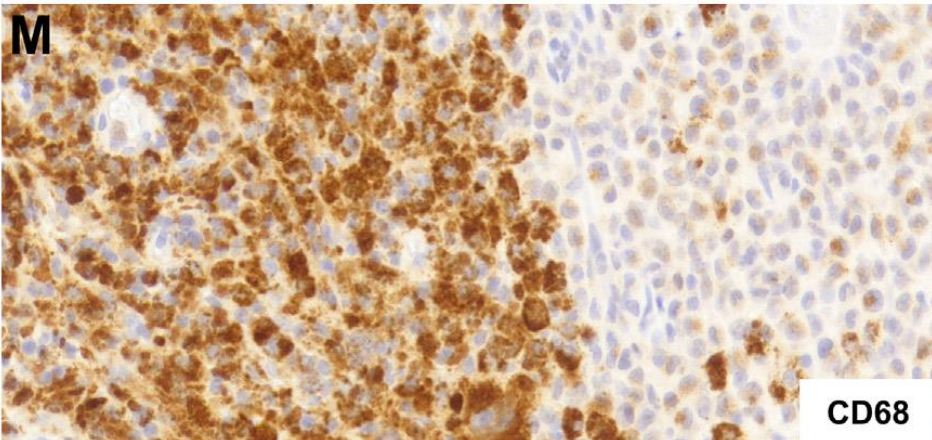
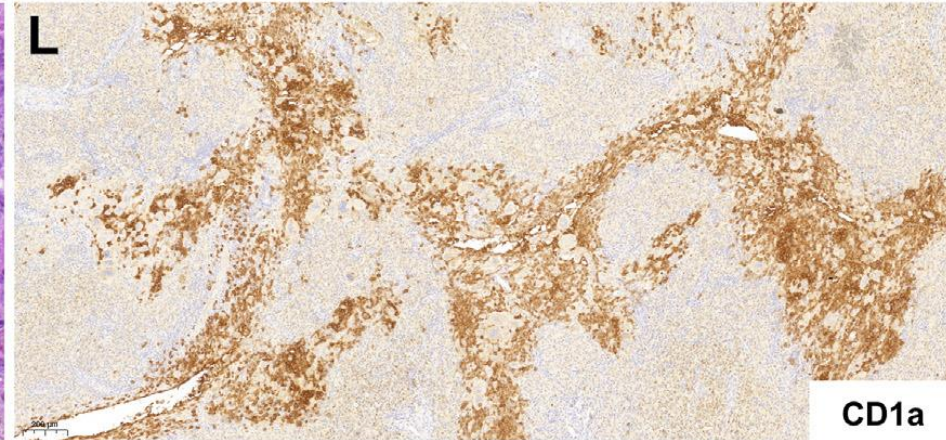
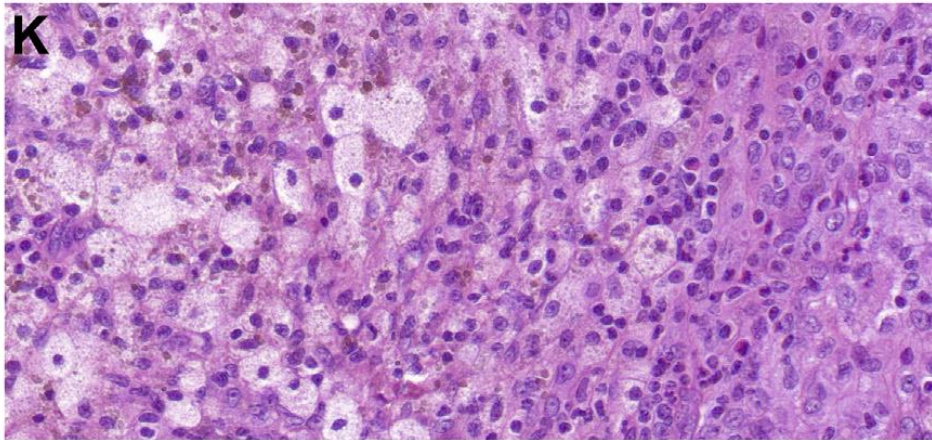
**LCH**

Langerhans cell  
histiocytosis

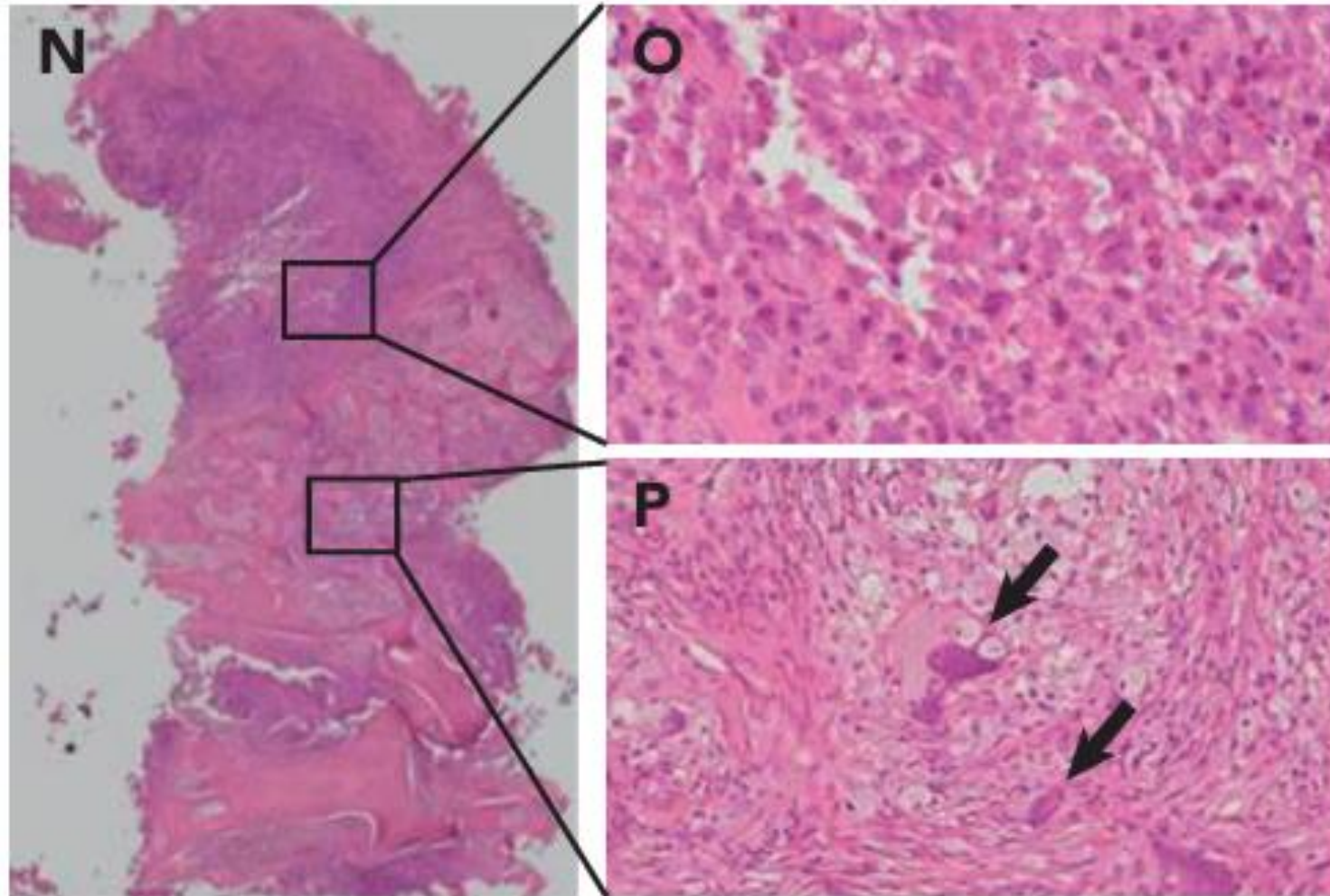
**RDD**

Rosai-Dorfman-  
Destombes  
disease

## Mixed histology (ECD-LCH)



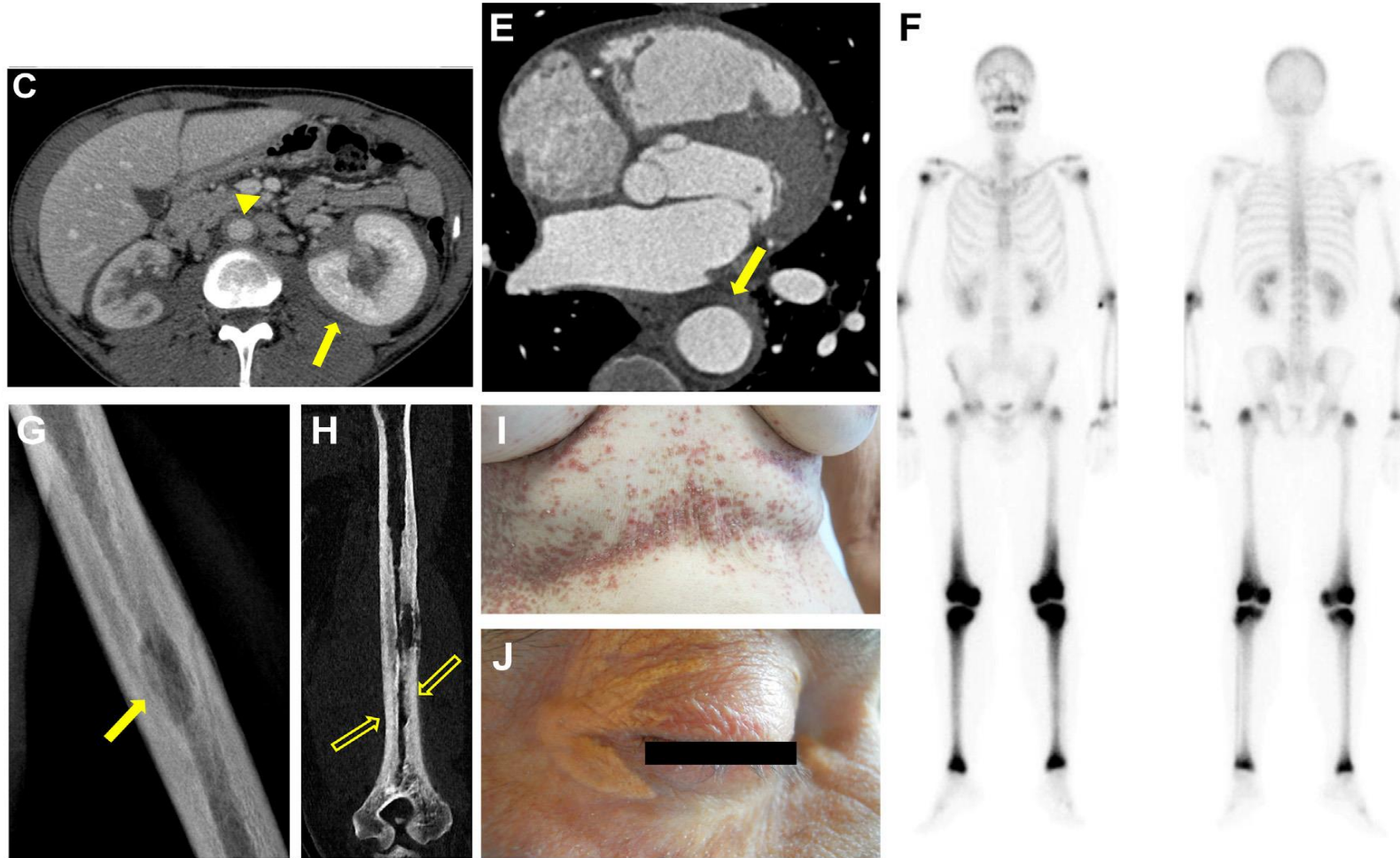
## Mixed histology (ECD-LCH)



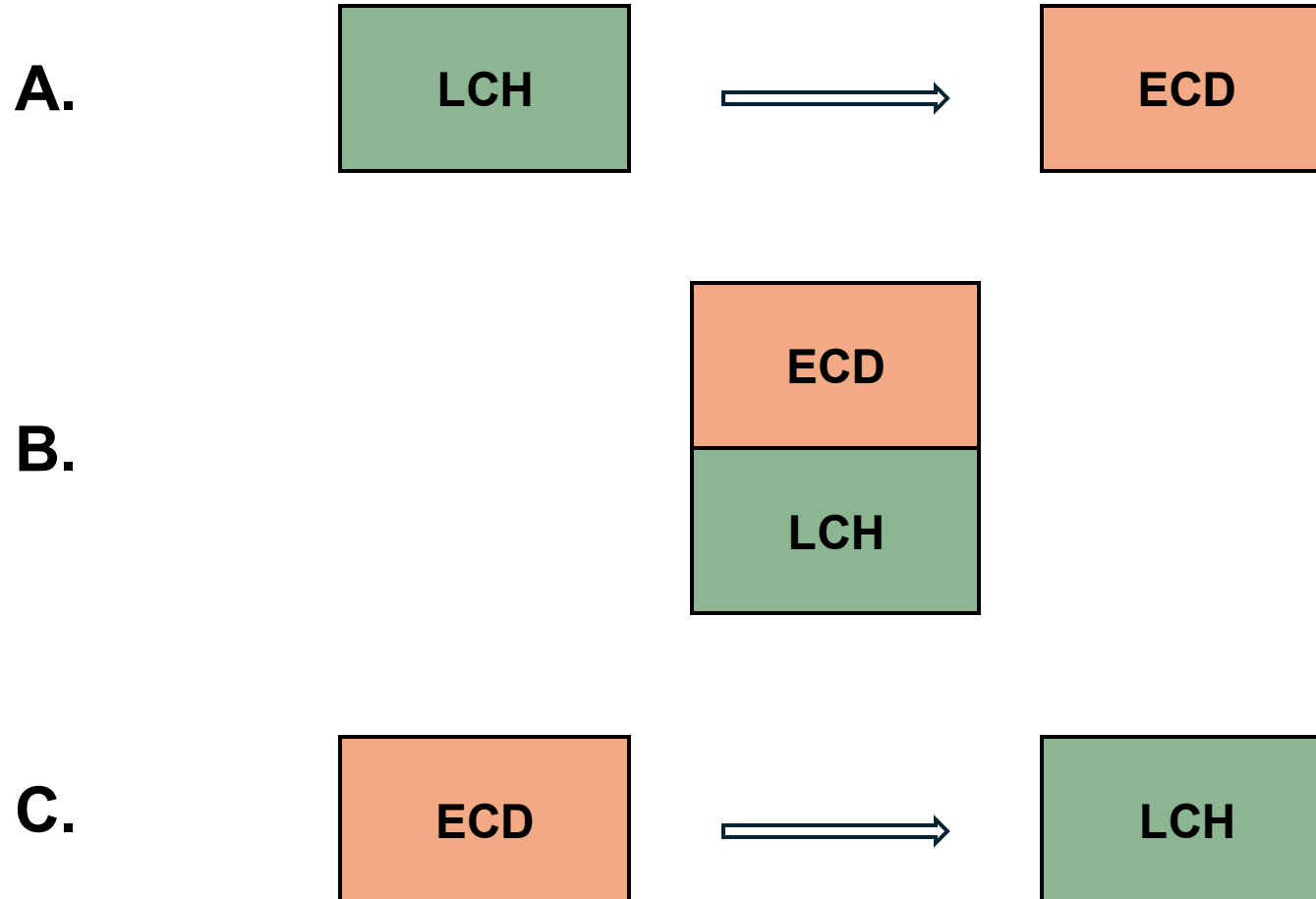
## Mixed clinic (ECD-LCH)

- Lytic bone lesions (fractures)
- Skin lesions
- Lymph node swelling
- Cysts / bullae in the upper lungs

# Mixed clinic (ECD-LCH)



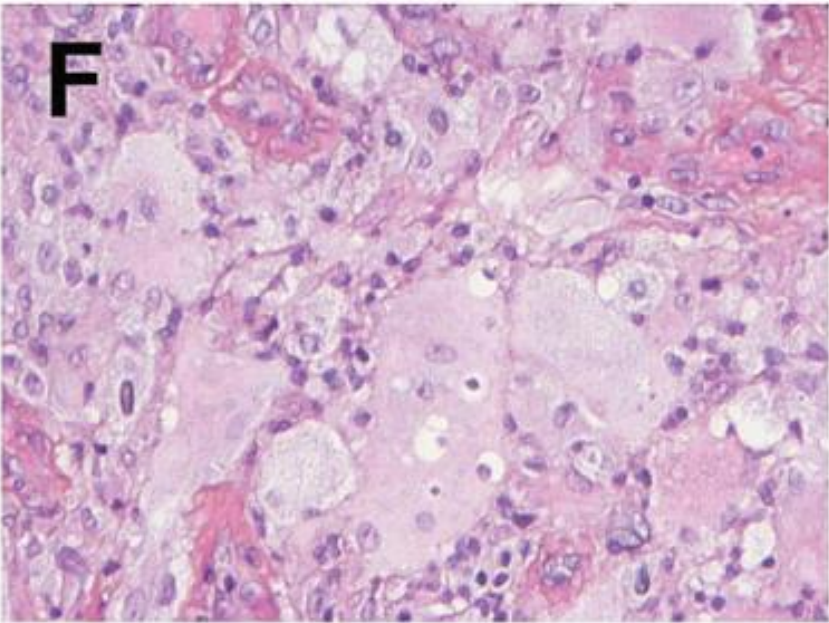
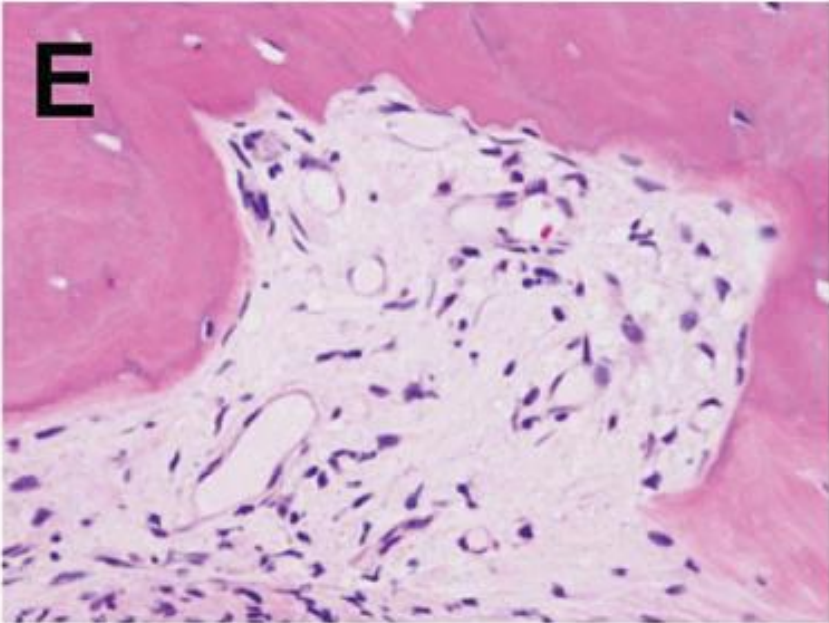
# Mixed clinic (ECD-LCH)



# Mixed histology (ECD-RDD)

ECD

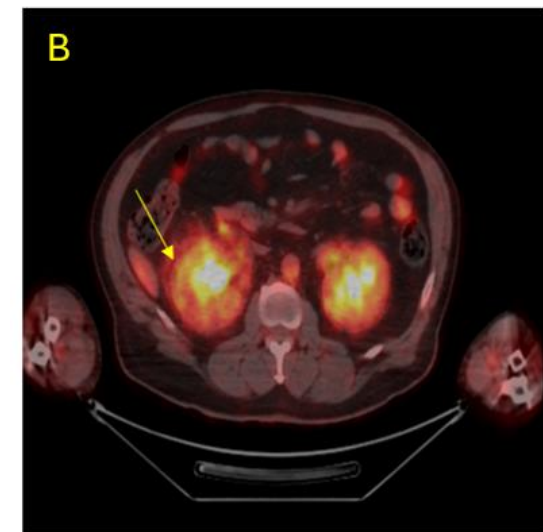
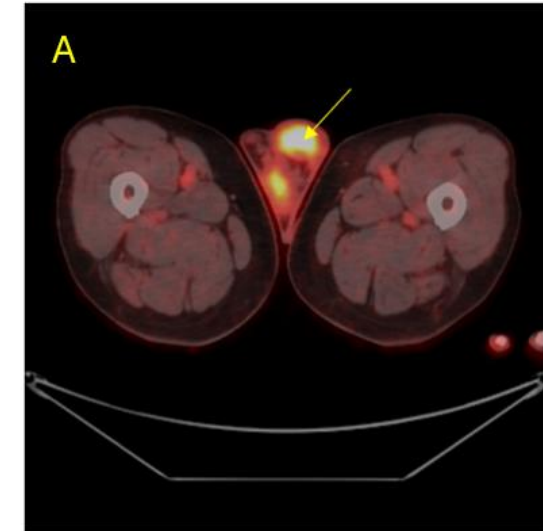
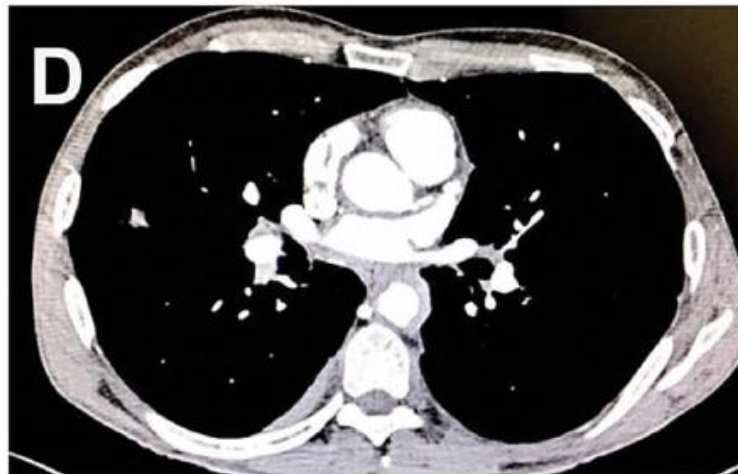
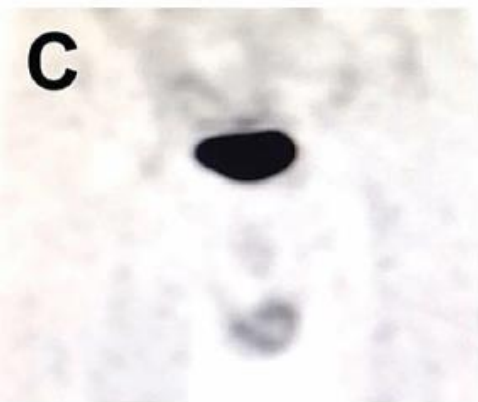
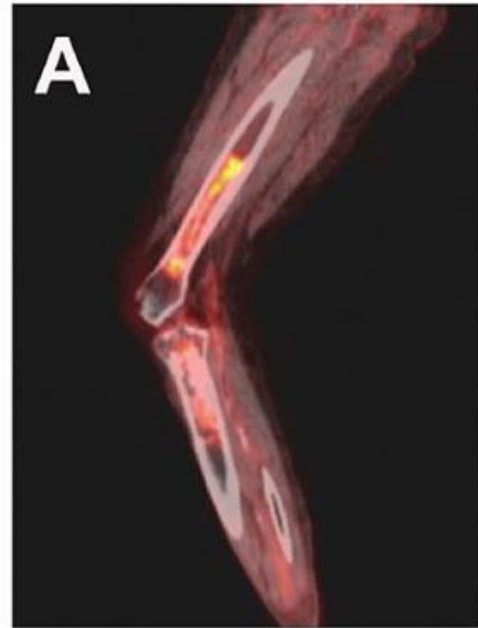
RDD

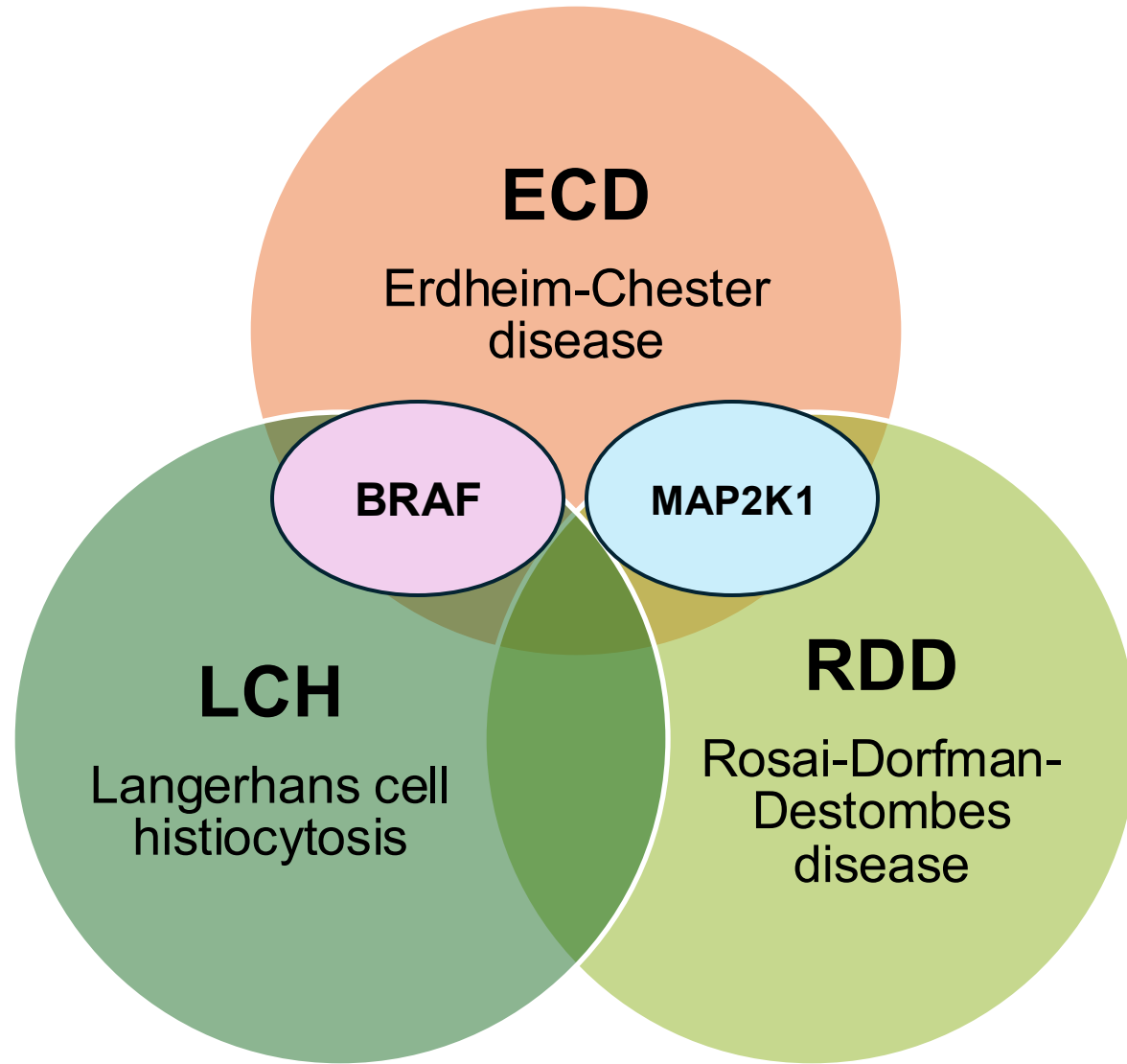


## Mixed clinic (ECD-RDD)

- Testicular swelling
- Lymph node swelling
- Soft tissue swelling
- Fibrosis around the kidneys

## Mixed clinic (ECD-RDD)





**ECD**

Erdheim-Chester  
disease

**BRAF**

**MAP2K1**

**LCH**

Langerhans cell  
histiocytosis

**RDD**

Rosai-Dorfman-  
Destombes  
disease

## Treatment in mixed histiocytosis

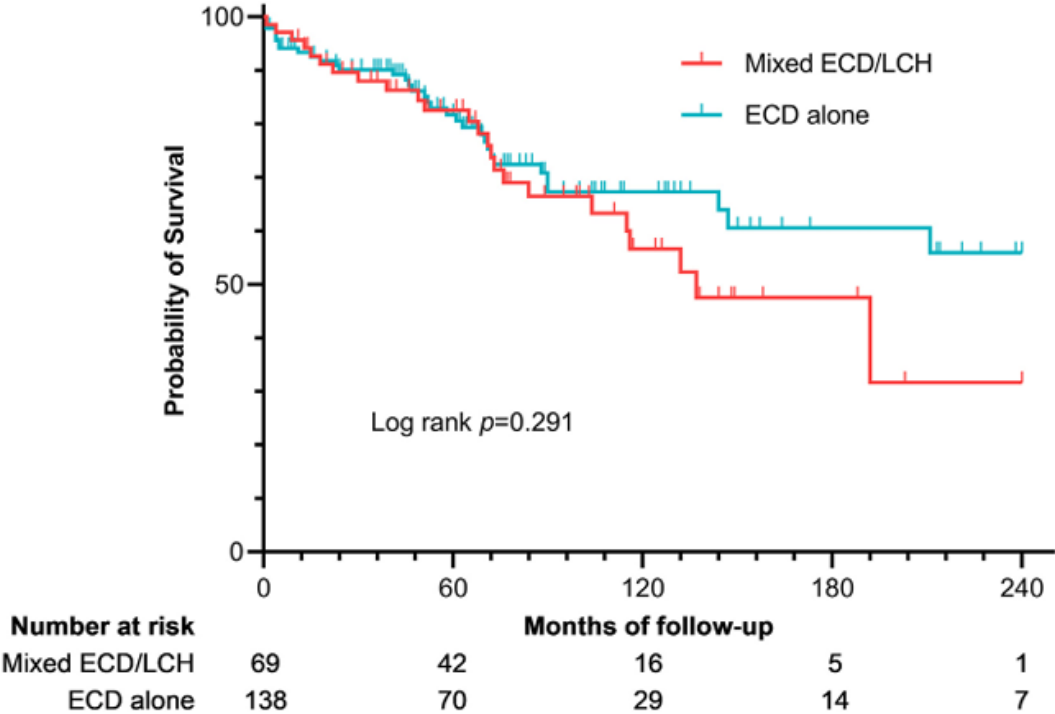
### Inhibitors!

- BRAFi (vemurafenib, dabrafenib)
- MEKi (cobimetinib, trametinib)

Response rates >>> than conventional treatments (chemo, IFNa)

# Prognosis of mixed histiocytosis

## B Age- and gender-matched cohorts



Better

→ Lytic bone lesions

Worse

→ Older age

→ Hematologic cancer

→ No response to treatment

# Outline

## 1) Mixed histiocytosis

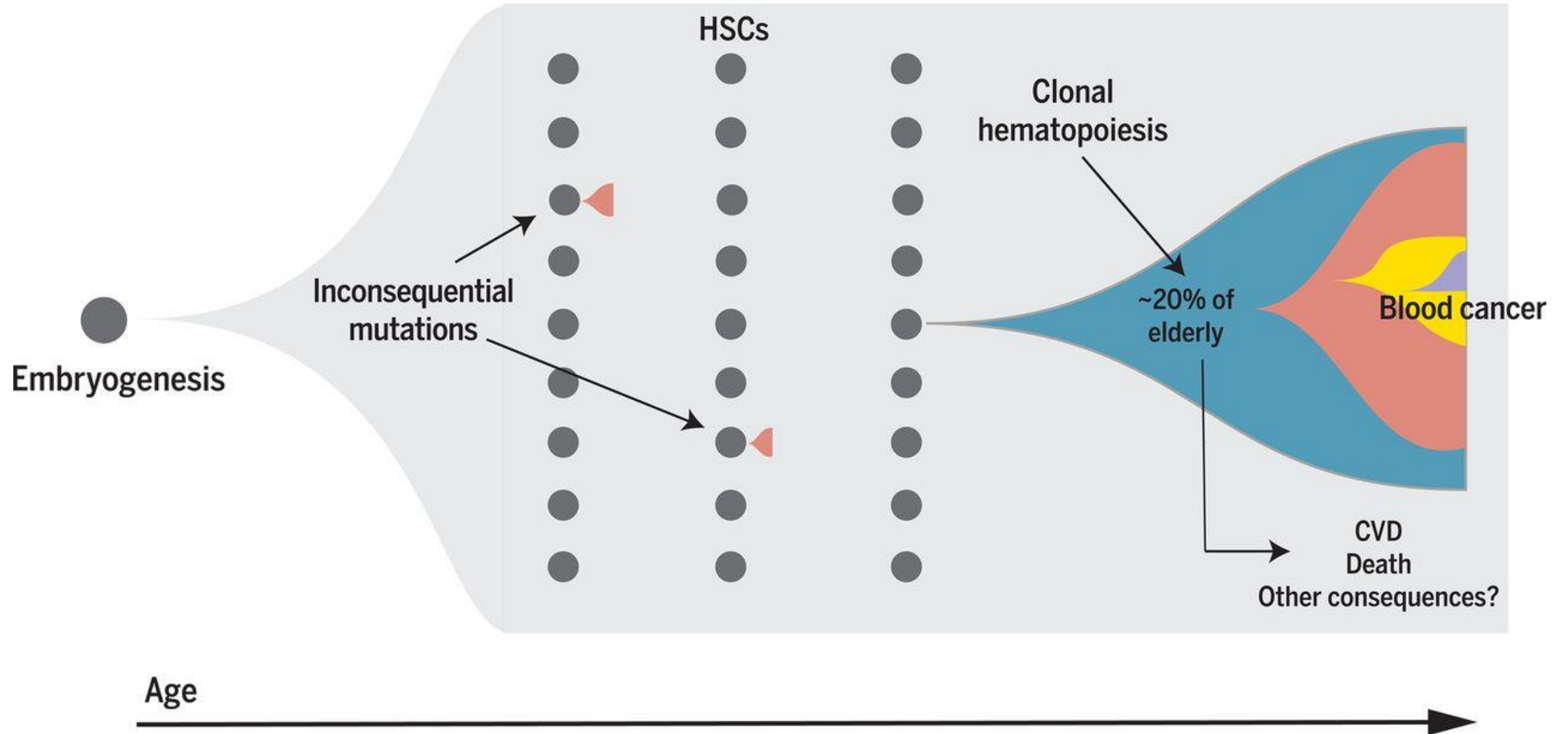
- ECD-LCH
- ECD-RDD

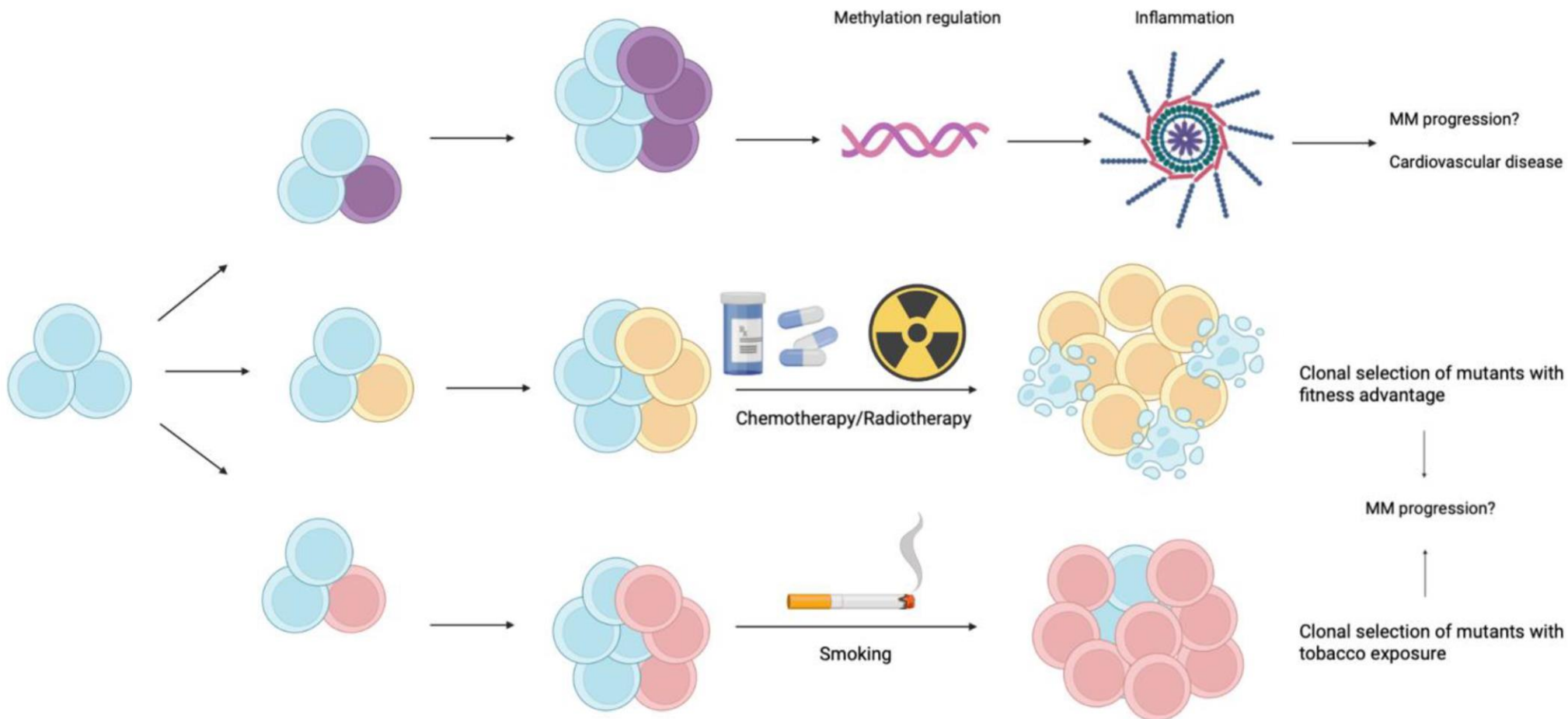
## 2) Clonal Hematopoiesis

## 3) Second cancer

- Hematologic
- Solid

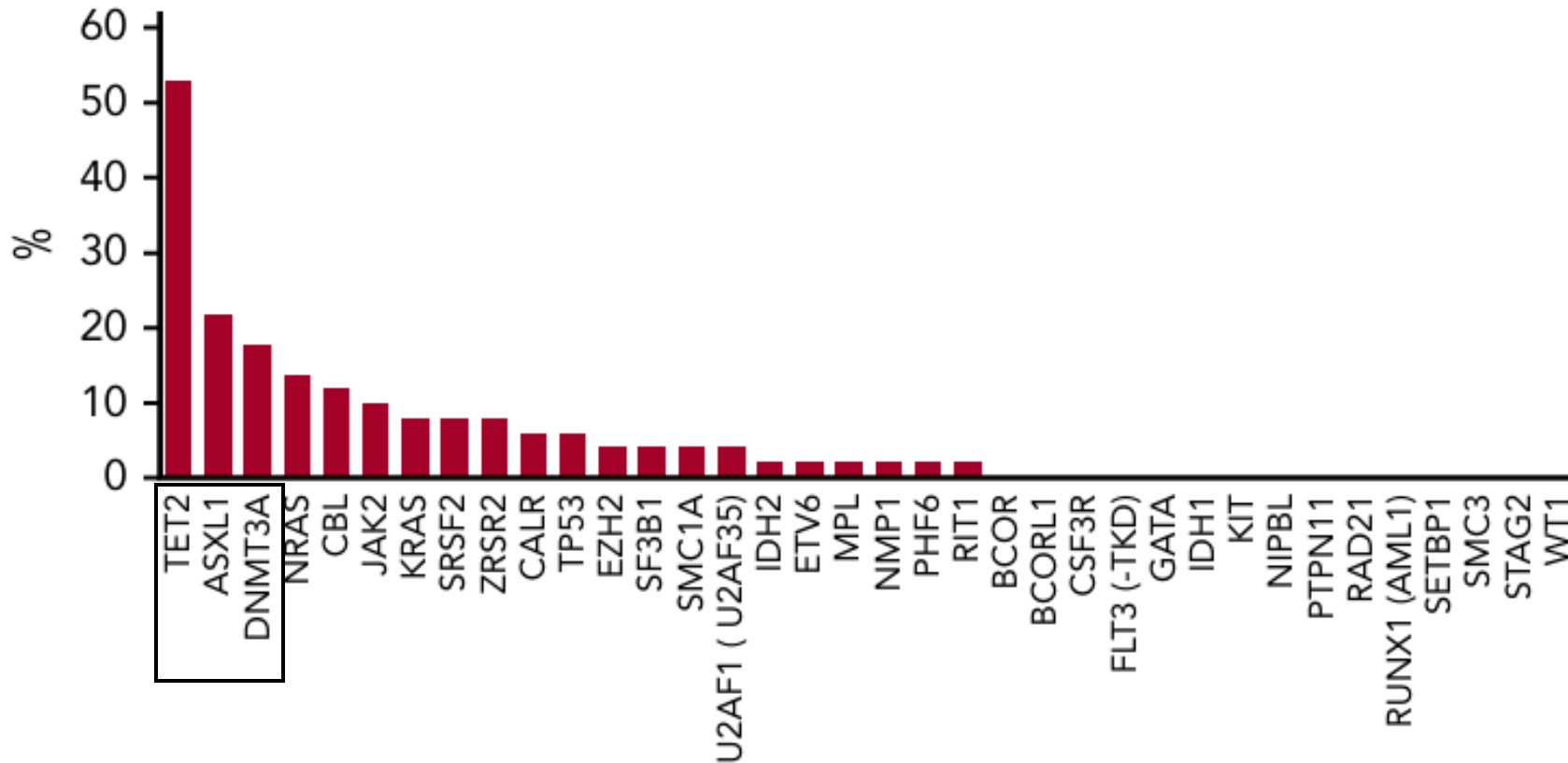
# What is clonal hematopoiesis?





# Clonal hematopoiesis in ECD

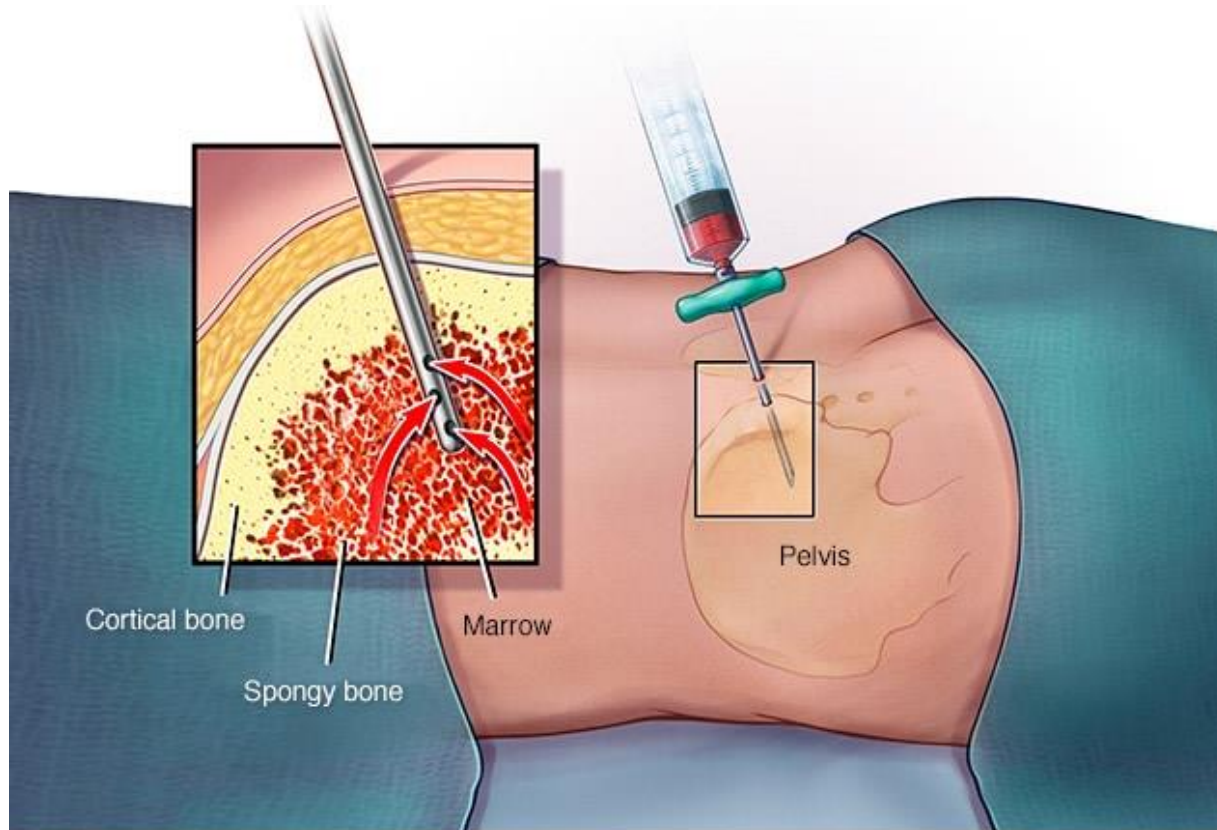
Up to 40% of patients



**KEY POINTS**

- ECD patients have a very high frequency of clonal hematopoiesis and concomitant overt myeloid malignancies.
- ECD patients with clonal hematopoiesis are older and have more frequent retroperitoneal involvement and BRAFV600E mutations.

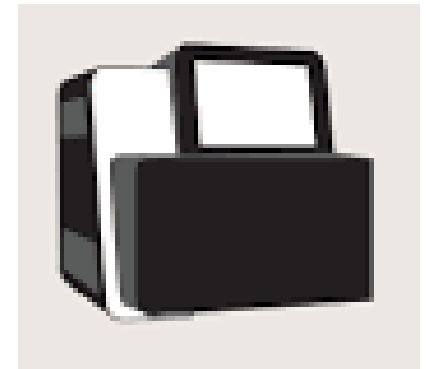
# How to look for clonal hematopoiesis?



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Next-generation  
sequencing

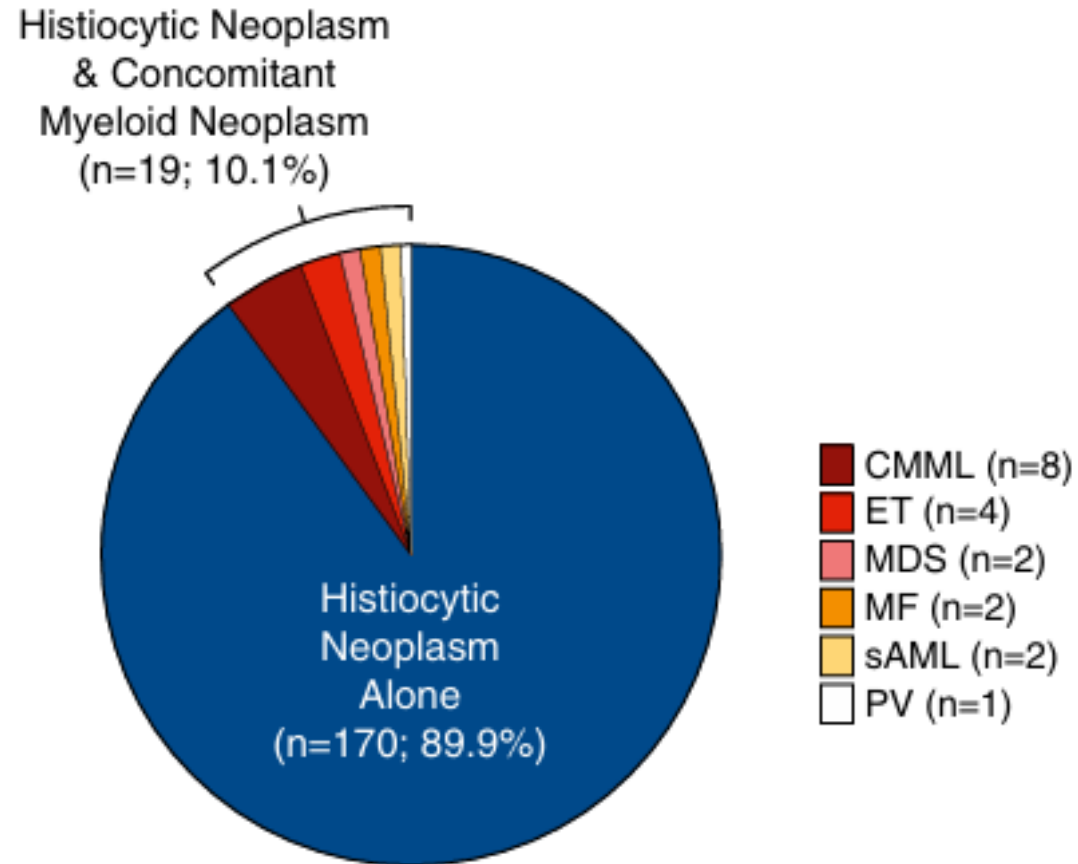


But why is this important in ECD?

# Outline

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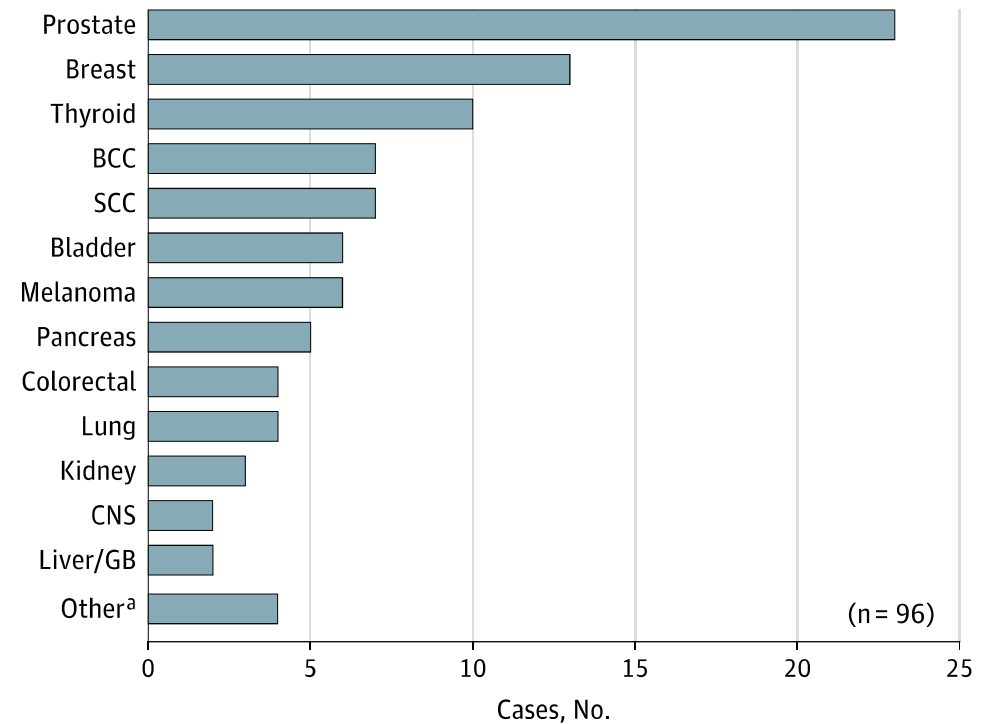
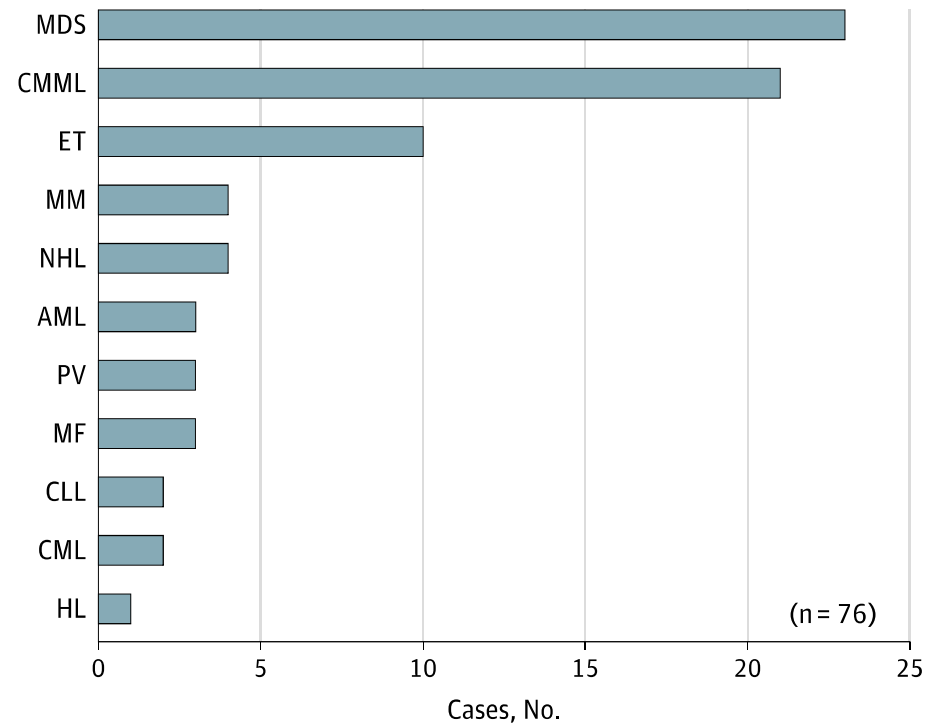
# Hematologic cancer in ECD



# Second cancer in ECD

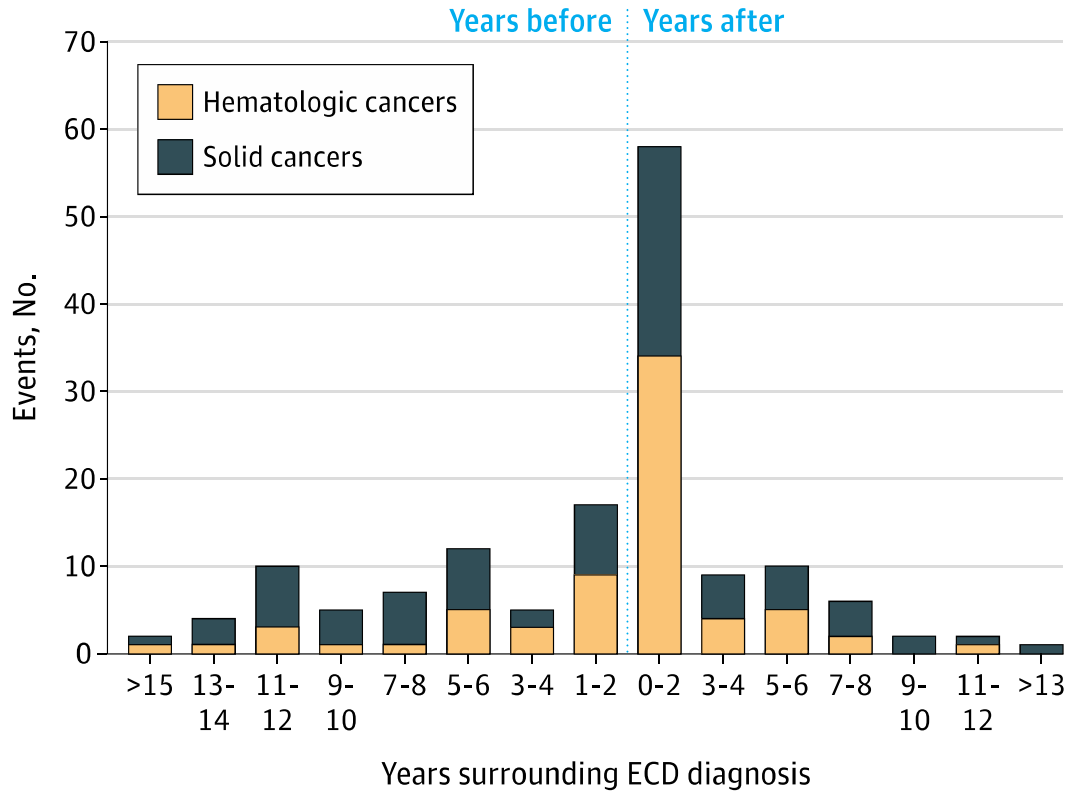
Up to 28% of patients

**A** Associated hematologic and solid cancers

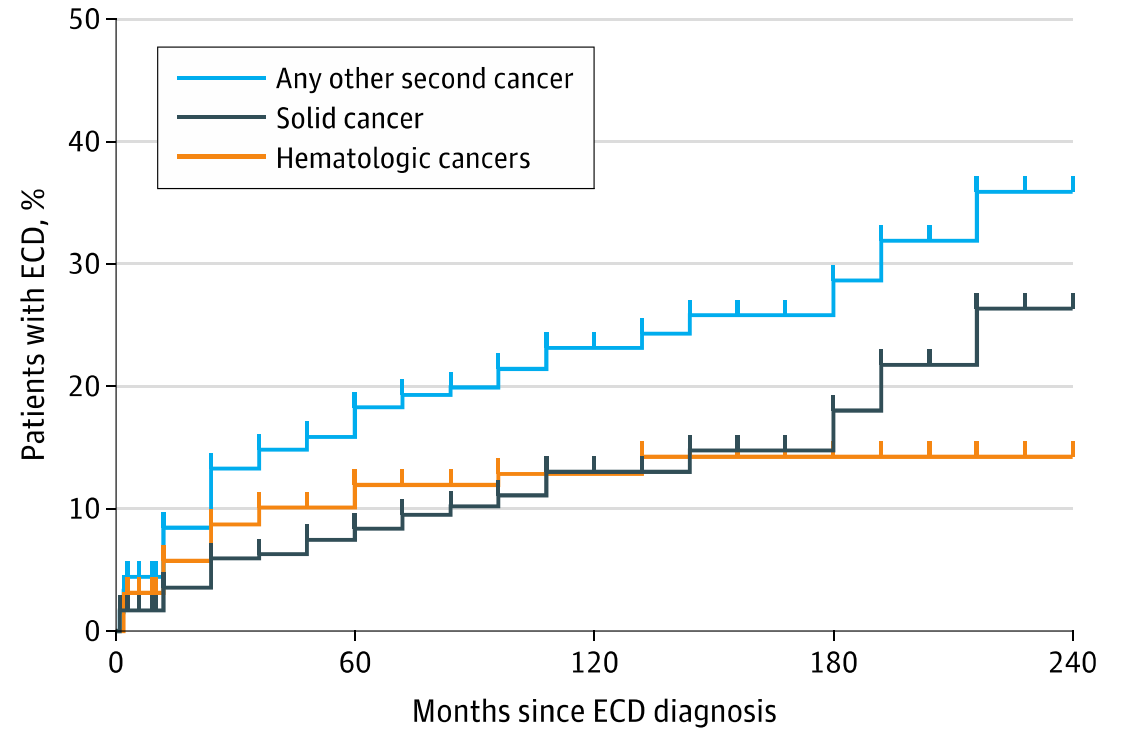


# Second cancer in ECD – when?

**B** Distribution of diagnoses of second cancers



**C** Estimated risk of second cancer



## Second cancer in ECD

Second cancer is frequent in ECD (4-fold risk)

Increased risk if

- Older age
- Multisystem ECD
- (Clonal hematopoiesis)

No increase in mortality (screening!!!)

## Screening

- Blood tests ( $\pm$  BM aspiration)
- Mammography
- PSA
- Occult blood in the stools + coloscopy
- Thyroid ultrasound
- Dermatologist (++ if on inhibitors)

## Conclusions

- Other histiocytosis can overlap with ECD  
(and mixed histio requires inhibitors)
- Clonal hematopoiesis is frequent and needs to be looked for
- Screening for second cancer is very important