VII CORSO del GRUPPO ITALIANO DI EMATOPATOLOGIA

La DIAGNOSTICA EMATOPATOLOGICA nell'ERA della MEDICINA di PRECISIONE

A case of fibrotic myeloid neoplasm

Giorgia Caniato

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Bologna, Aula Prodi | 11-12 maggio 2026

Clinical history

Female, 41y

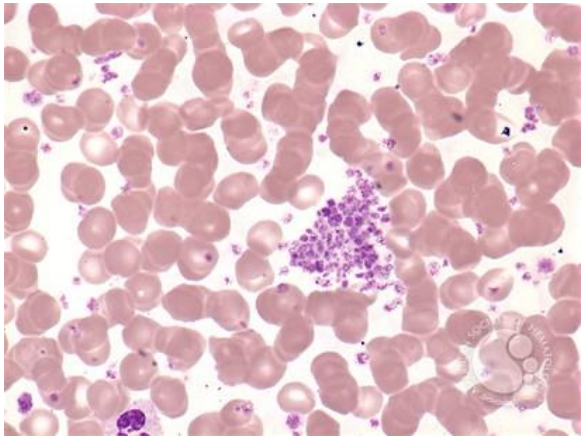
Clinical presentation

- 3y history of CML treated with Imatinib
- Referred to the hematology unit for severe thrombocytosis and anemia

Complete blood count

Laboratory tests

- WBC = 3.94 x 10^9/L
- Hb = **103** g/L (MCV = 80.9 fL)
- Plts = **1278** x 10^9/L



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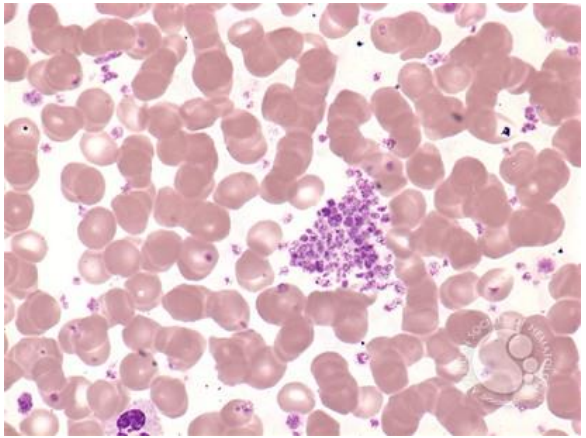
Differential count

- ANC = 1.77 x 10^9/L (44.9%)
- Lymph = 1.63 x 10^9/L (41.4%)
- Eos = 0.07 x 10^9/L (1.8%)
- Baso = 0.04 x 10^9/L (1.0%)
- Mono = 0.08 x 10^9/L (2.0 %)



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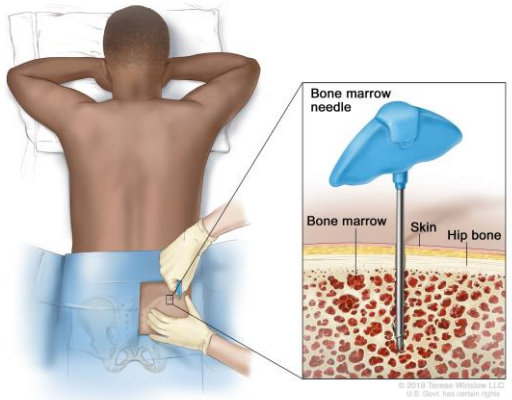
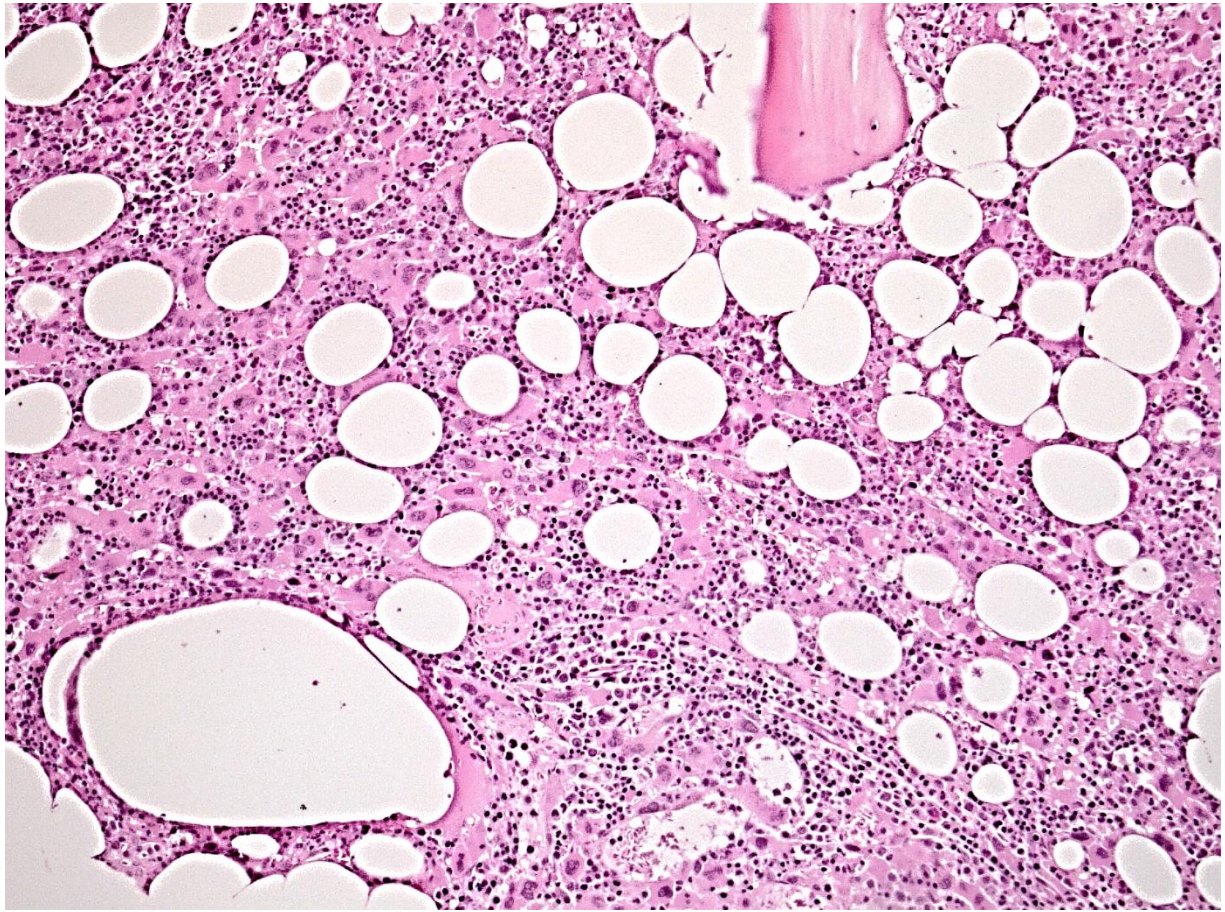
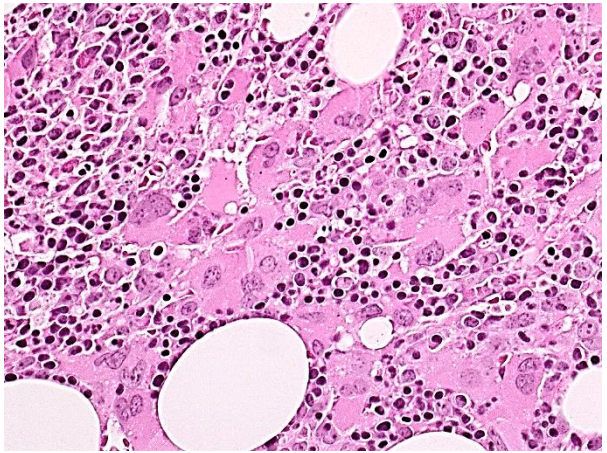
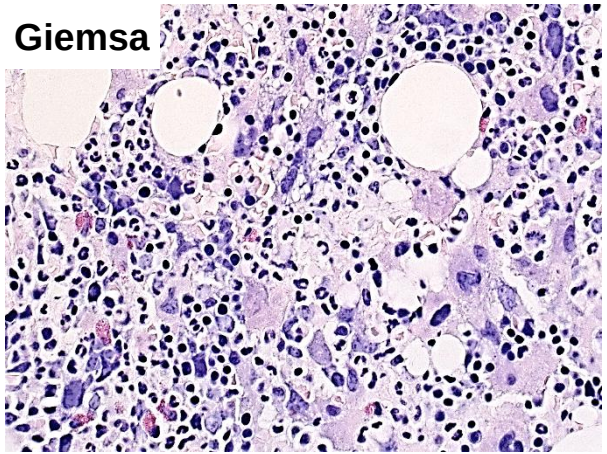


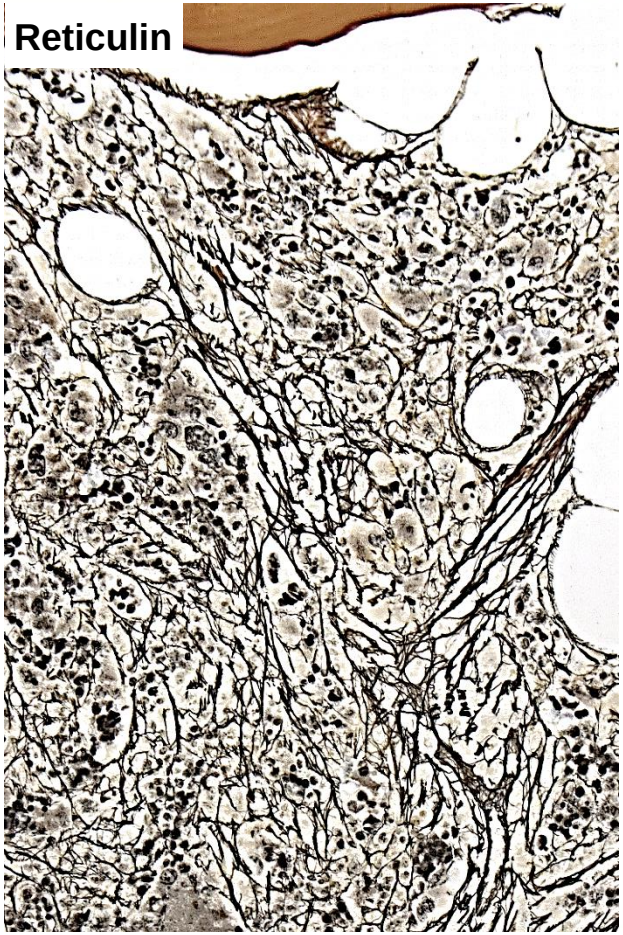
Bone marrow biopsy was performed



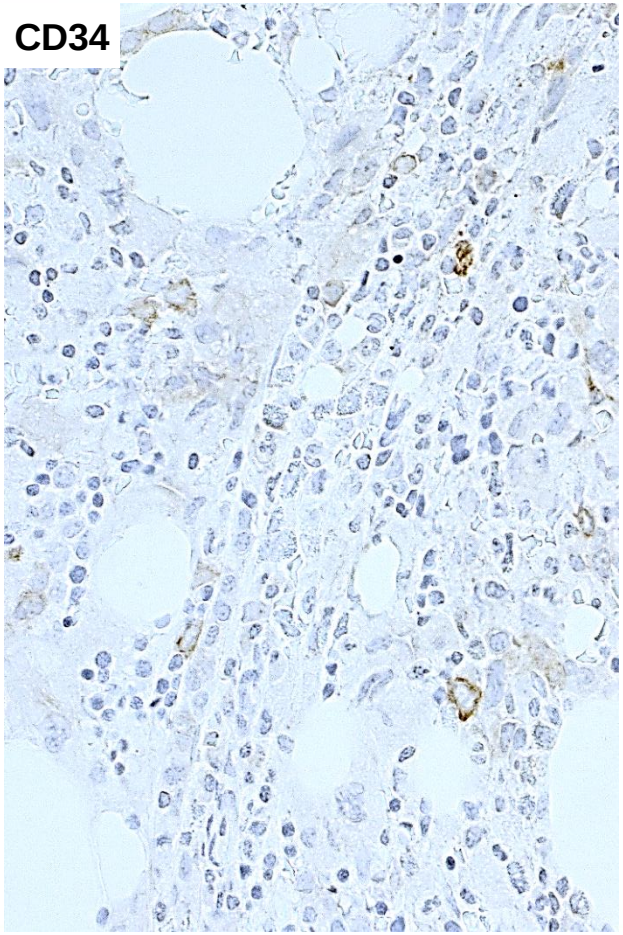



Giemsa

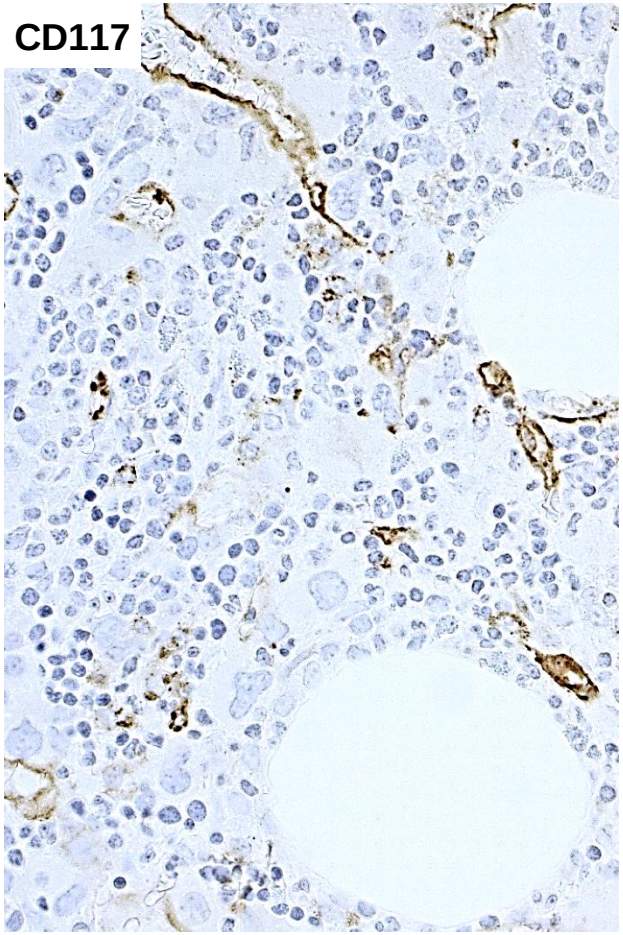
Reticulin



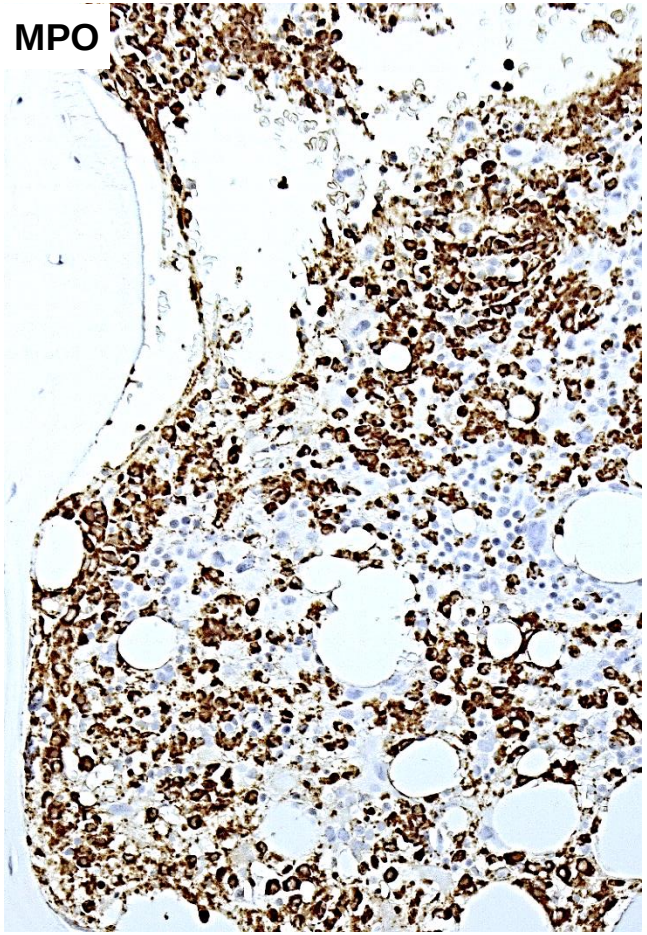
CD34



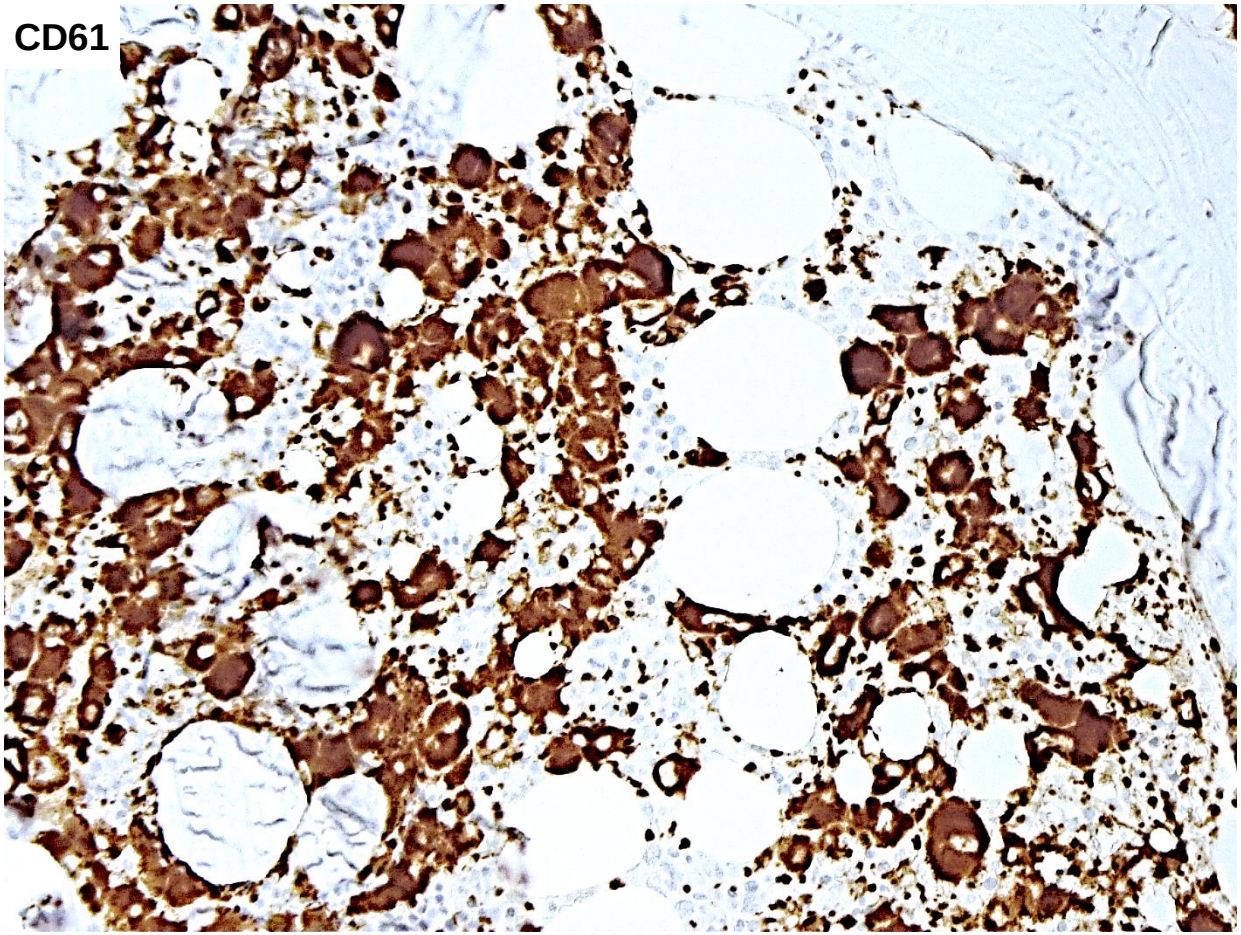
CD117



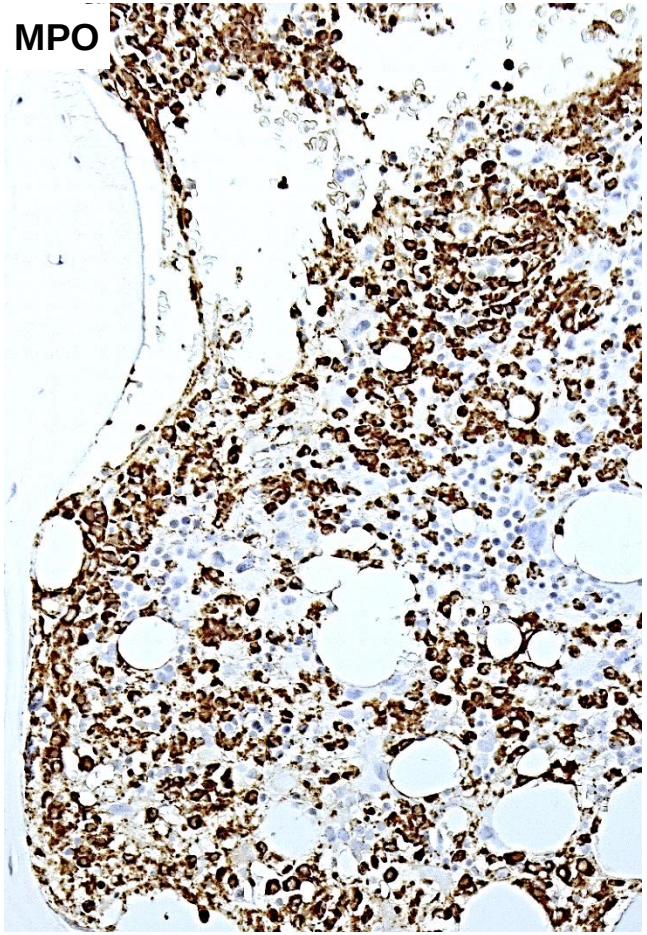
MPO



CD61



MPO



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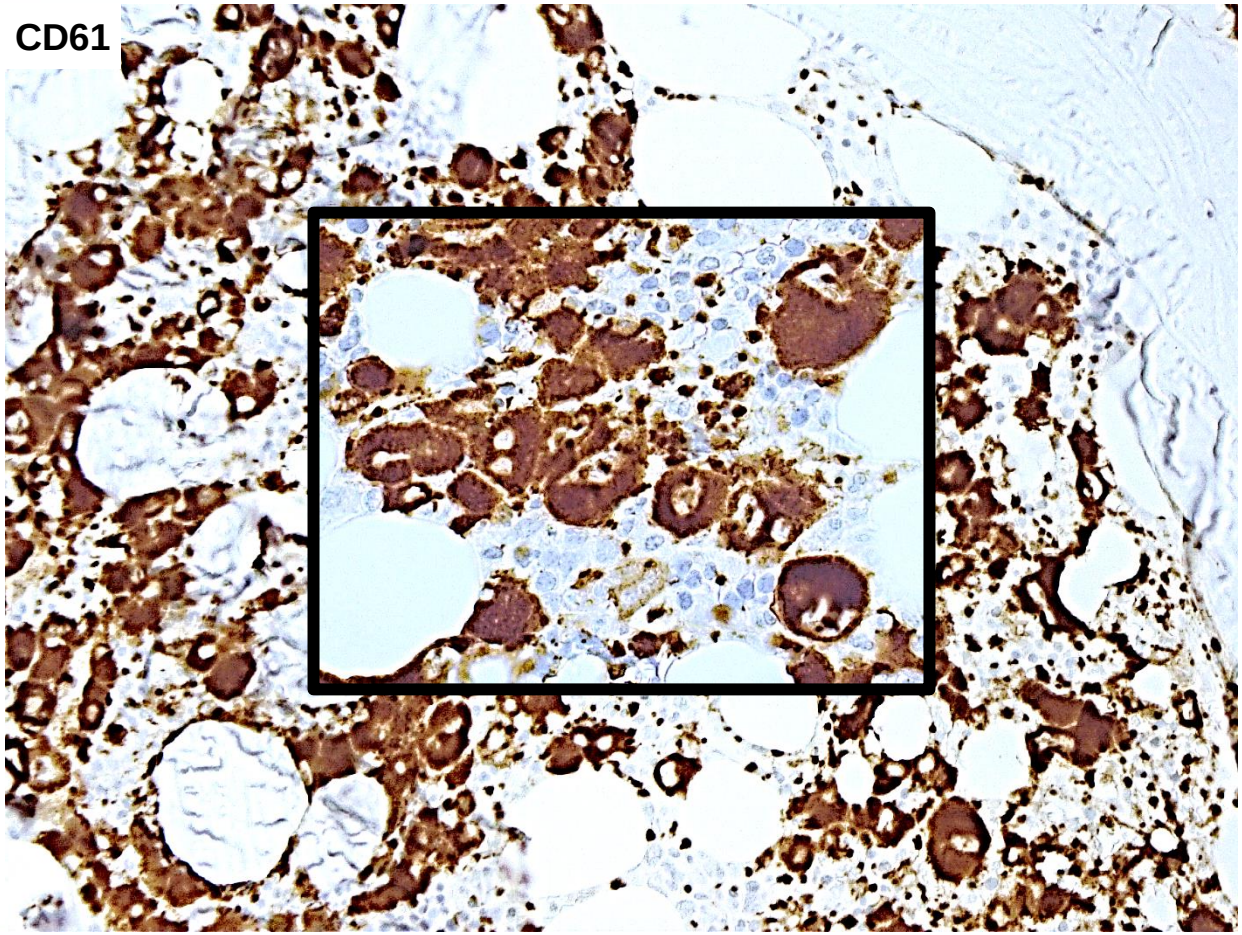

Genetic tests

Cytogenetic analysis

- Not performed due to dry tap

Molecular analysis

- No *JAK2, CALR or MPL* mutations
- *BCR::ABL1* fusion (p210; VAF = 49.0%)

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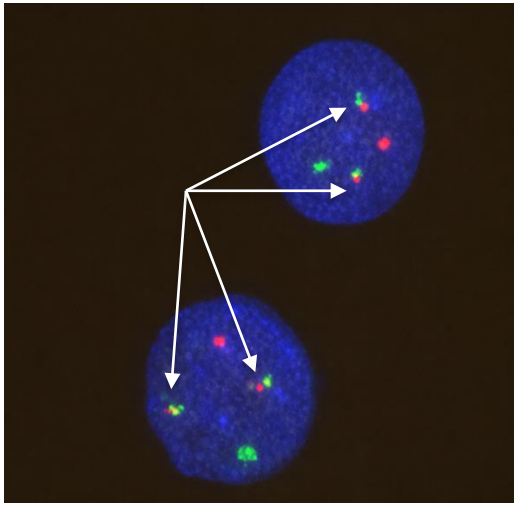
FISH analysis

- *BCR::ABL1* fusion (27% of analysed cells)



BCR/ABL1 double fusion probe

Final diagnosis

Chronic myeloid leukemia, accelerated phase

CML – accelerated phase (WHO 2016)

Table 2. Criteria for CML, accelerated phase

CML, accelerated phase criteria	
Any 1 or more of the following hematologic/cytogenetic criteria or response-to-TKI criteria:	
• Persistent or increasing WBC (>10 × 10^9/L), unresponsive to therapy	**"Provisional" response-to-TKI criteria**
• Persistent or increasing splenomegaly, unresponsive to therapy	• Hematologic resistance to the first TKI (or failure to achieve a complete hematologic response* to the first TKI) or
• Persistent thrombocytosis (>1000 × 10^9/L), unresponsive to therapy	• Any hematological, cytogenetic, or molecular indications of resistance to 2 sequential TKIs or
• Persistent thrombocytopenia (<100 × 10^9/L) unrelated to therapy	• Occurrence of 2 or more mutations in *BCR-ABL1* during TKI therapy
• 20% or more basophils in the PB	
• 10%-19% blasts† in the PB and/or BM	
• Additional clonal chromosomal abnormalities in Ph^+ cells at diagnosis that include "major route" abnormalities (second Ph, trisomy 8, isochromosome 17q, trisomy 19), complex karyotype, or abnormalities of 3q26.2	
• Any new clonal chromosomal abnormality in Ph^+ cells that occurs during therapy	

Large clusters or sheets of small, abnormal megakaryocytes, associated with marked reticulin or collagen fibrosis in biopsy specimens may be considered as presumptive evidence of AP, although these findings are usually associated with 1 or more of the criteria listed above.

*Complete hematologic response: WBC, <10 × 10^9/L; platelet count, <450 × 10^9/L, no immature granulocytes in the differential, and spleen nonpalpable.

†The finding of bona fide lymphoblasts in the blood or marrow, even if <10%, should prompt concern that lymphoblastic transformation may be imminent and warrants further clinical and genetic investigation; 20% or more blasts in blood or BM, or an infiltrative proliferation of blasts in an extramedullary site is CML, blast phase.

WHO Classification of Tumours series, 4th ed.

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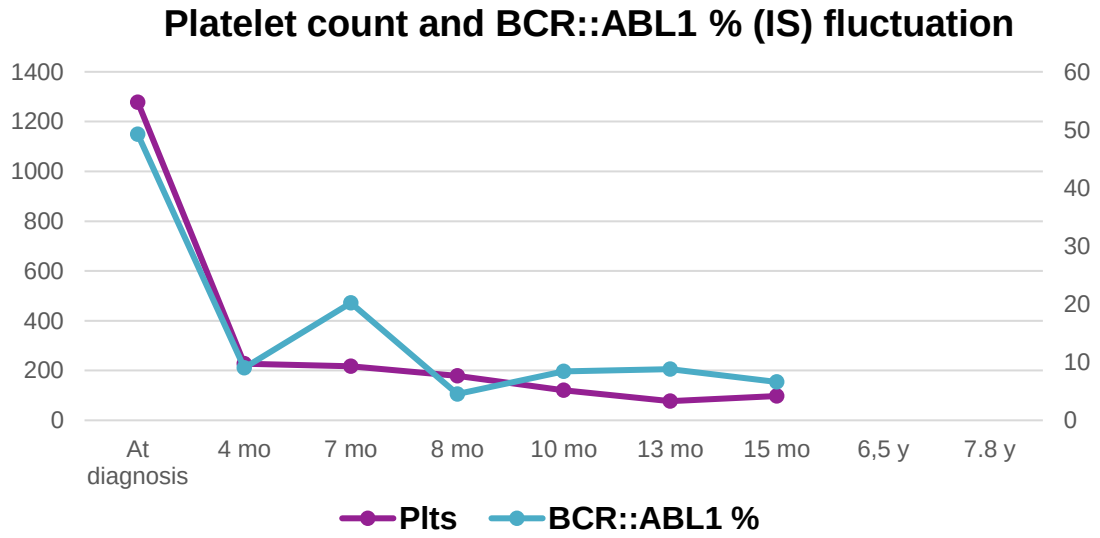
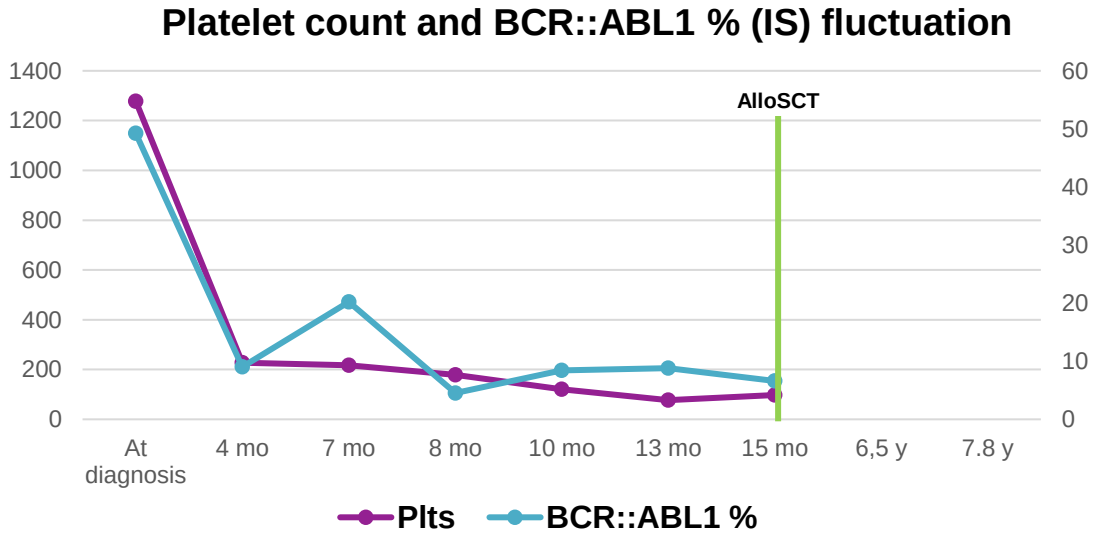
Management and outcome

- Double TKI (Dasatinib and Ponatinib) with partial molecular response



Management and outcome

- Double TKI (Dasatinib and Ponatinib) with partial molecular response
- Failure to achieve major molecular response → alloSCT



Management and outcome

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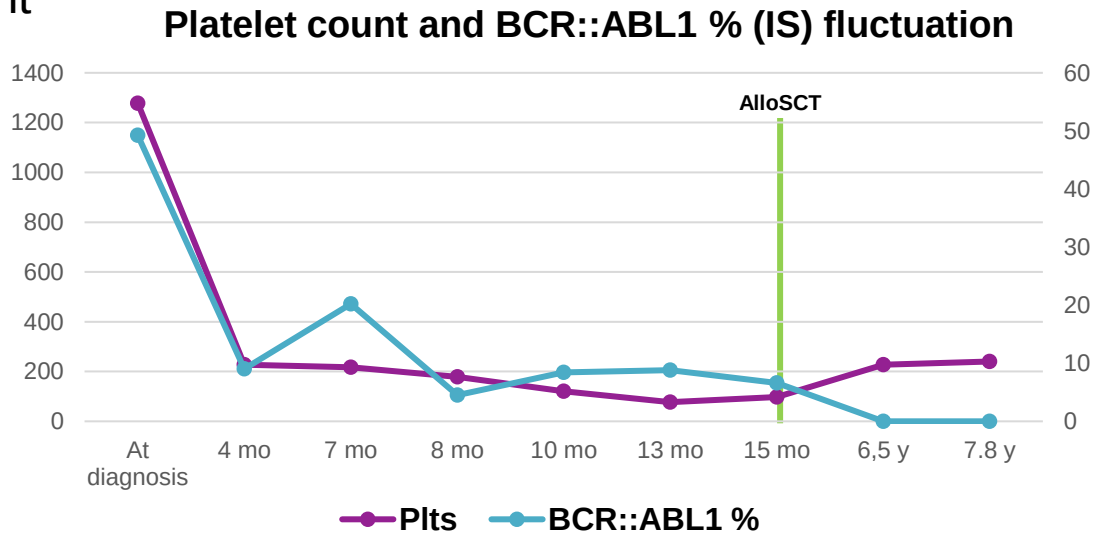
- Failure to achieve major molecular response → alloSCT
- Alive with MR5 7y after transplant



Accelerated phase of CML in WHO/ICC 2022

2022 ICC diagnostic criteria

Accelerated phase
Bone marrow or peripheral blood blasts 10%-19%
Peripheral blood basophils ≥ 20%
Presence of additional clonal cytogenetic abnormality in Ph+ cells (ACA)*

Ph, Philadelphia chromosome.

*Second Ph, trisomy 8, isochromosome 17q, trisomy 19, complex karyotype, or abnormalities of 3q26.2.

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No longer recognized in the **2022 WHO Classification**

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2022 WHO CML with high - risk features

At diagnosis or emerging on treatment

- 10% blasts in peripheral blood and/or bone marrow
- ≥ 20% basophils in peripheral blood
- Additional chromosomal abnormalities in Ph+ cells

At diagnosis

•	ELTS score	$[0.0025 \times (age/10)^3] + [0.0615 \times spleen\ size] + [0.1052 \times peripheral\ blood\ blasts] + [0.4104 \times (platelet\ count/1000)^{-0.5}]$	Low risk: < 1.5680 Intermediate risk: 1.5680-2.2185 High risk: > 2.2185

Emerging on treatment

- Resistance to TKI as defined by the European LeukemiaNet (ELN) in 2020, including loss of prior responses
- Emergence of additional chromosomal abnormalities
- BCR::ABL1 kinase domain mutations

Accelerated phase of CML in WHO/ICC 2022

2022 ICC diagnostic criteria

Accelerated phase
Bone marro blood bla
Peripheral b ≥ 20%
Presence of cytogene Ph+ cells

No BM morphological **findings** included **in either classification**

2022 WHO CML with high - risk features

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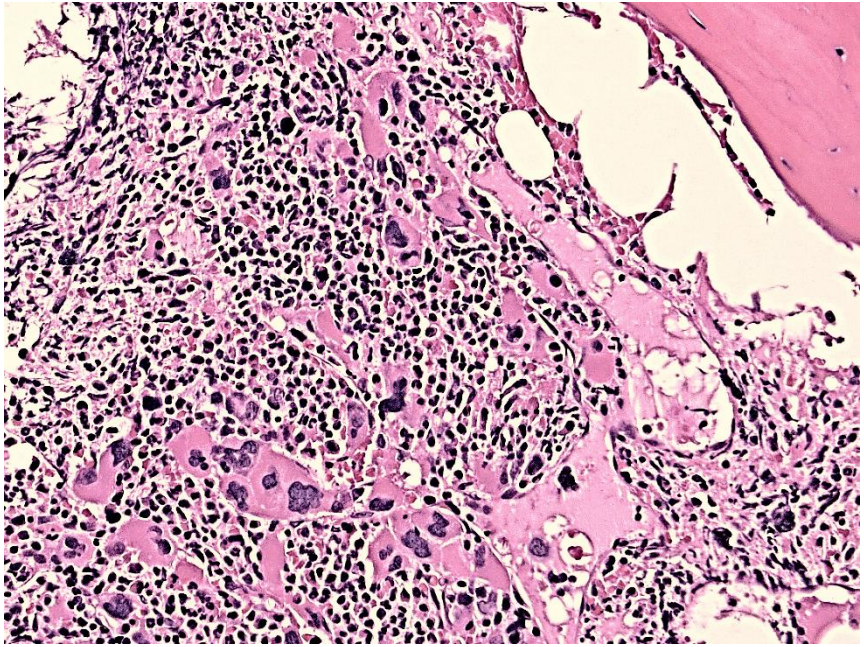
Final diagnosis - nowadays

2022 WHO — **Chronic myeloid leukemia with high–risk features**

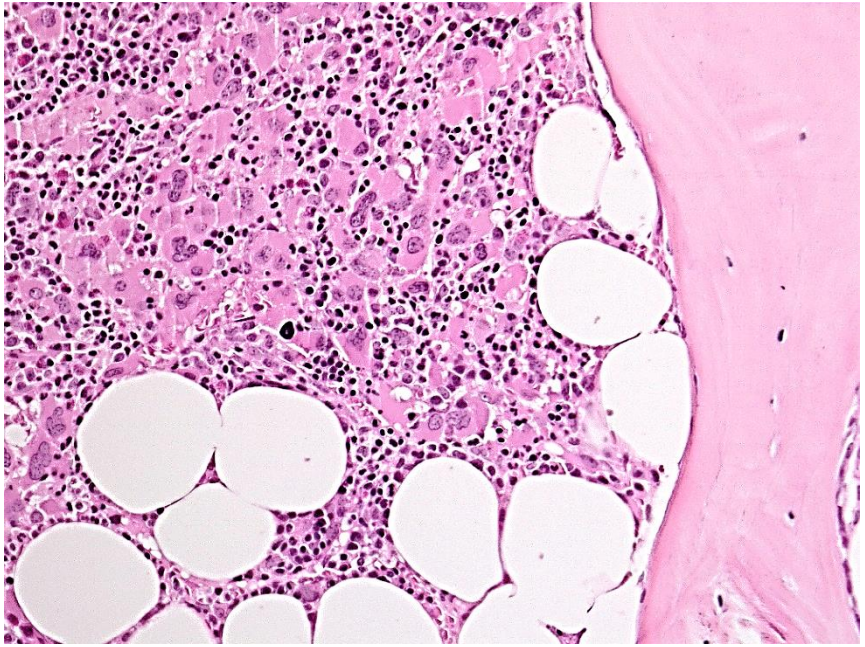
2022 ICC — **Chronic myeloid leukemia, chronic phase (CML– CP)**

CML with fibrosis *versus* Primary Myelofibrosis

Primary Myelofibrosis

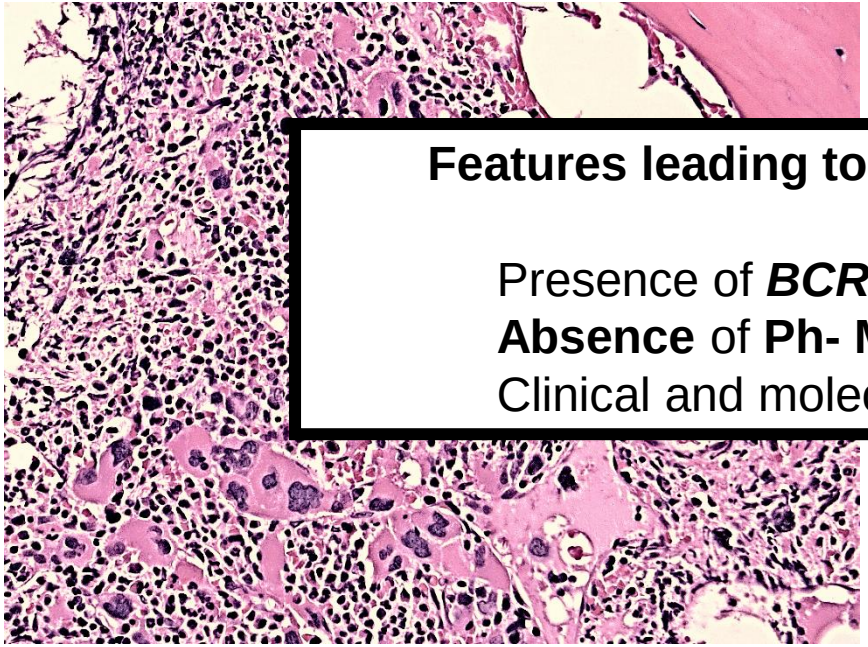


CML with PMF-like features



CML with fibrosis *versus* Primary Myelofibrosis

Primary Myelofibrosis



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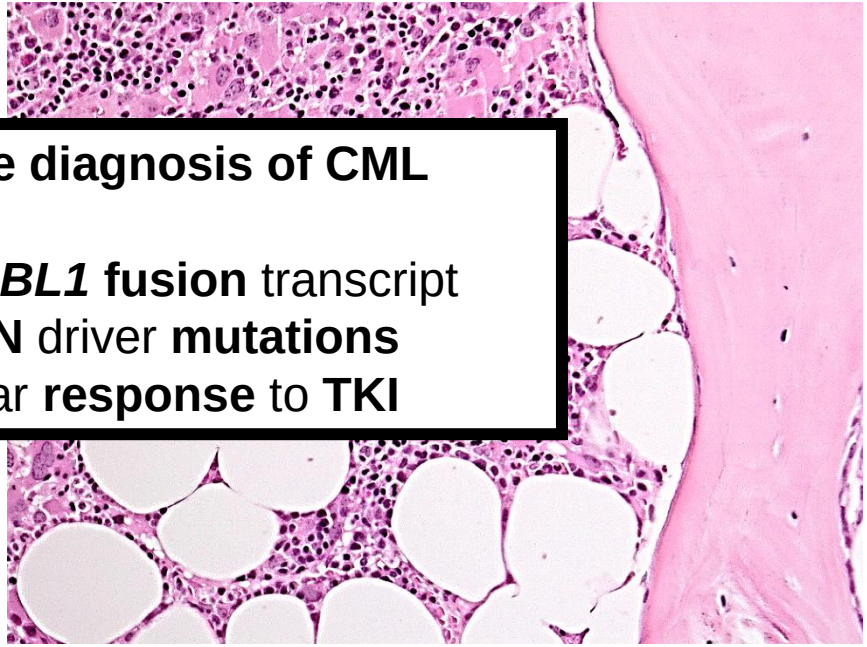

Features leading to the diagnosis of CML

Presence of ***BCR::ABL1*** **fusion** transcript
Absence of **Ph- MPN** driver **mutations**
Clinical and molecular **response** to **TKI**

Conclusions

- CML with fibrosis is a rare morphological finding

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- Integration of clinical, morphological and molecular data is key for the diagnosis

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- CML with fibrosis is a rare morphological finding
- Integration of clinical, morphological and molecular data is key for the diagnosis
- Response to TKIs contributes to confirm the diagnosis