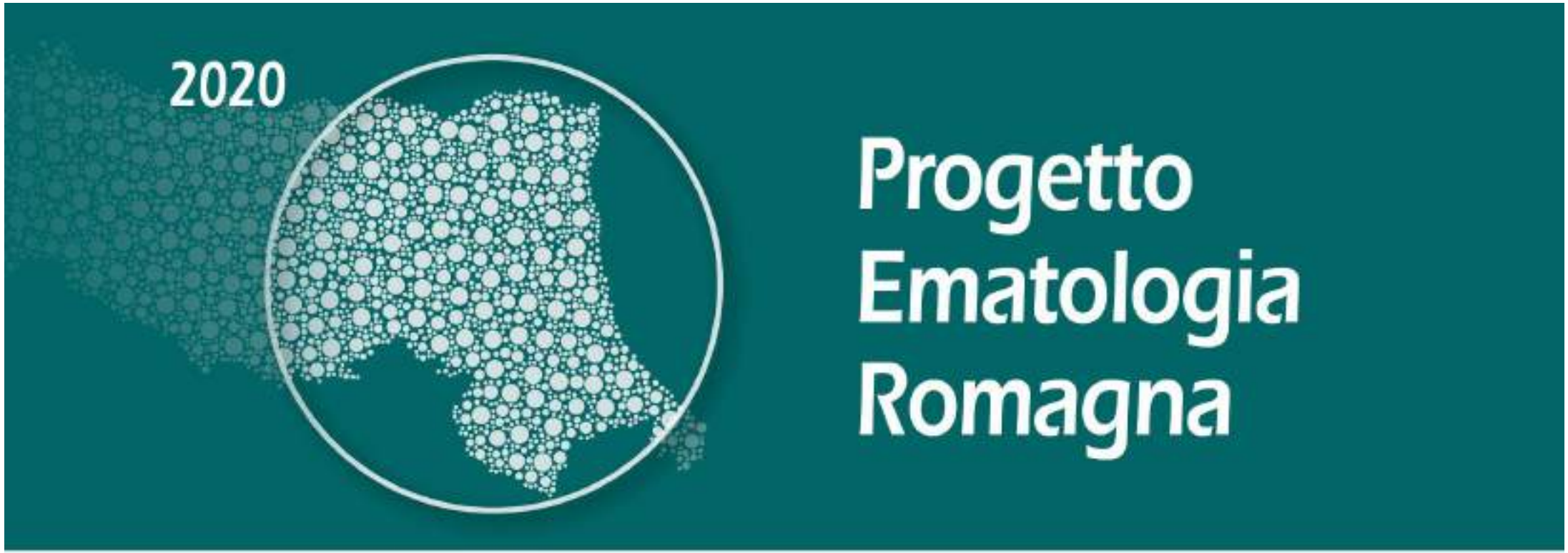

Il sarcoma Mieloide
La diagnostica istopatologica

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Definition of MS according to WHO 2017

- A **tumour mass** consisting of myeloblasts or haematopoietic precursors occurring at an anatomic site other than the bone marrow.

- Infiltration of any site by myeloid blasts in pt. with leukaemia is not classified as MS unless it presents with tumour masses in which the **tissue architecture is effaced**

- Extra-medullary myeloid tumour; Granulocytic sarcoma; Chloroma

Clinical features

- MS may occur de novo,
- may precede or concur with AML or CML or with other types of MPN or MDS or MDS/MPN,
- may be the first evidence of AML,
- may be the initial manifestation of relapse in a previously treated AML in remission.

Leukemia (2007) 21, 340–350
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ORIGINAL ARTICLE

Myeloid sarcoma: clinico-pathologic, phenotypic and cytogenetic analysis of 92 adult patients

SA Pileri[1], S Ascani[2], MC Cox[3], C Campidelli[1], F Bacci[1], M Piccioli[1], PP Piccaluga[1], C Agostinelli[1], S Asioli[4], D Novero[5], M Bisceglia[6], M Ponzoni[7], A Gentile[8], P Rinaldi[9], V Franco[10], D Vincelli[11], A Pileri Jr[12], R Gasbarra[13], B Falini[14], PL Zinzani[1] and M Baccarani[1]

Associated neoplasms

AML	41 (26)
MDS	11 (5)
CML	7 (1)
PMF	3
CMMoL	1
PV	2
ET	1
PTCL (1 NOS, 1 MF/SS)	2 (1)
FL grade 3	1 (1)
Prostatic carcinoma	2
Breast carcinoma	1 (1)
Colon poorly differentiated ca.	1
Colon tubular-villous adenoma	1 (1)
Embryonic carcinoma of the testis	1
Endometrial carcinoma	1
Larynx carcinoma	1
(Concomitant)	

In this setting/history
MS might be secondary
to prior chemotherapy

Clinical features

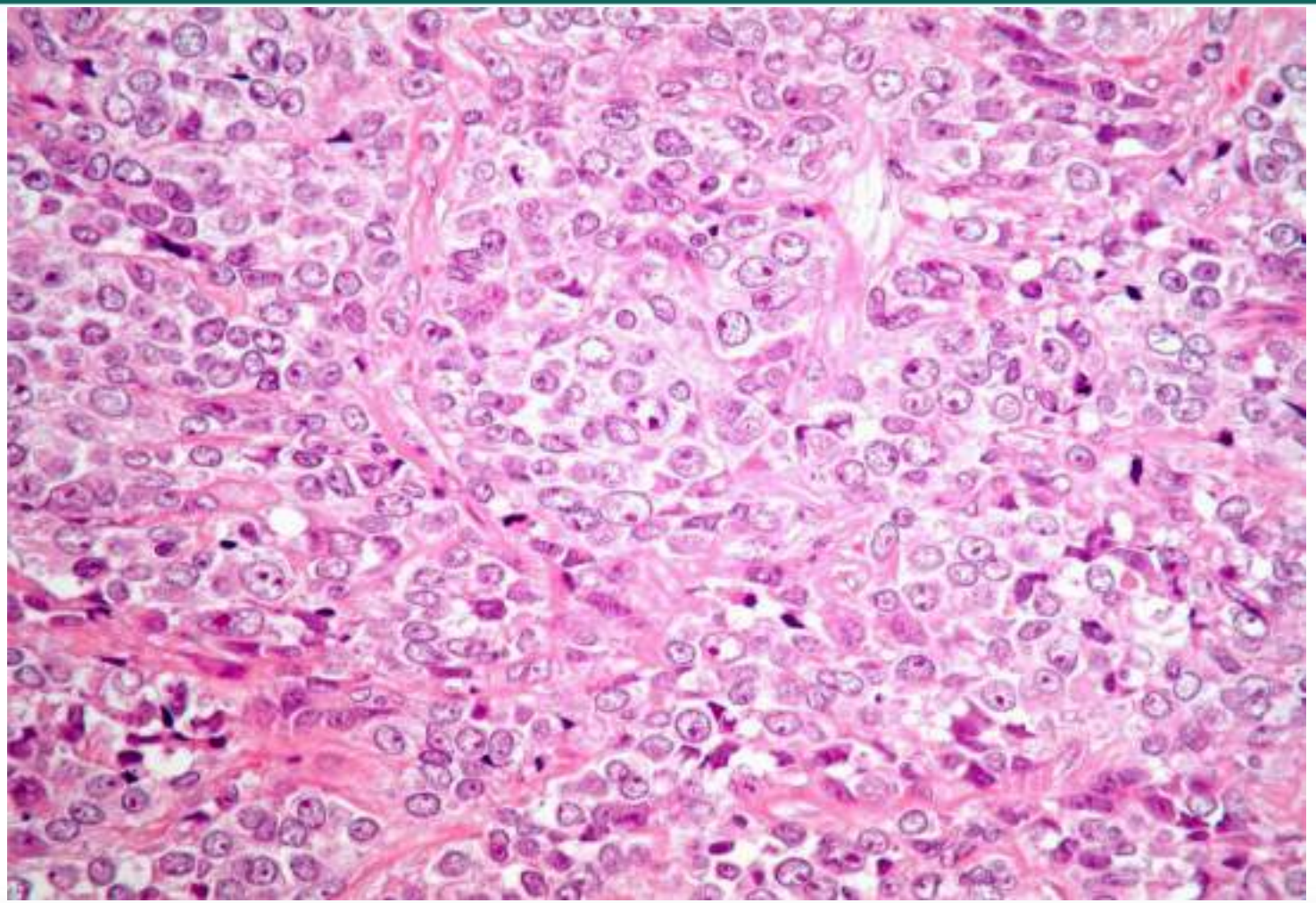
» **Epidemiology:**
M/F = 1.2/1
Median age = 56.5 years (1 month - 89 yrs).

» **Sites of involvement:** Almost every site of the body.
(skin, lymph node, gastro-intestinal tract, bone, soft tissue, and testis more frequently affected)

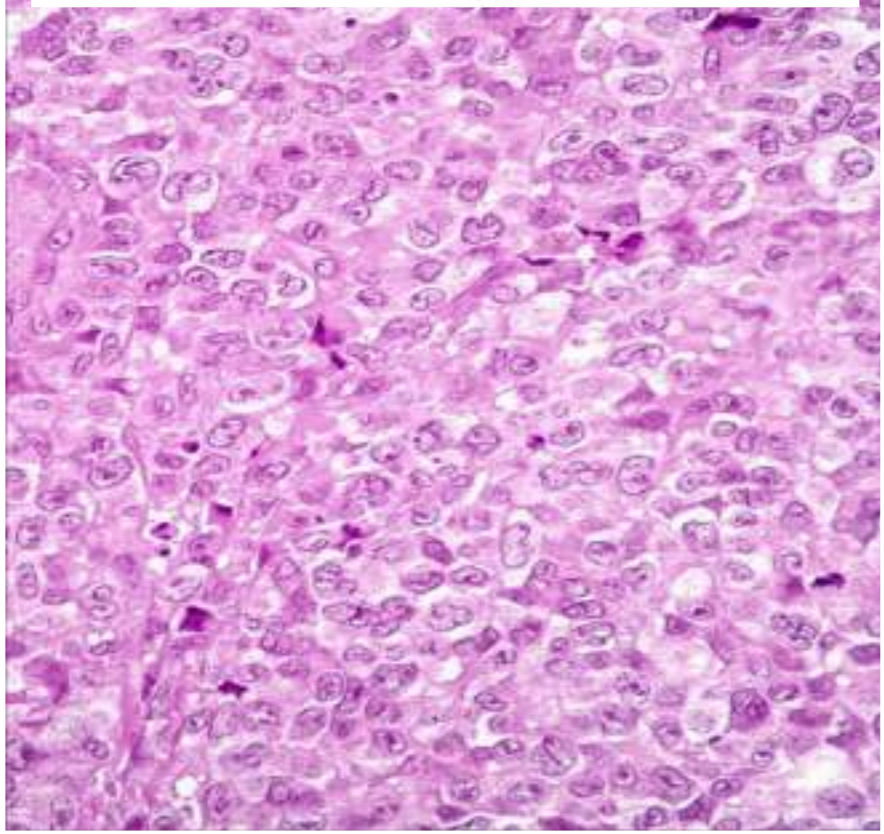
» In < 10%, **multiple anatomic sites**.

Microscopy

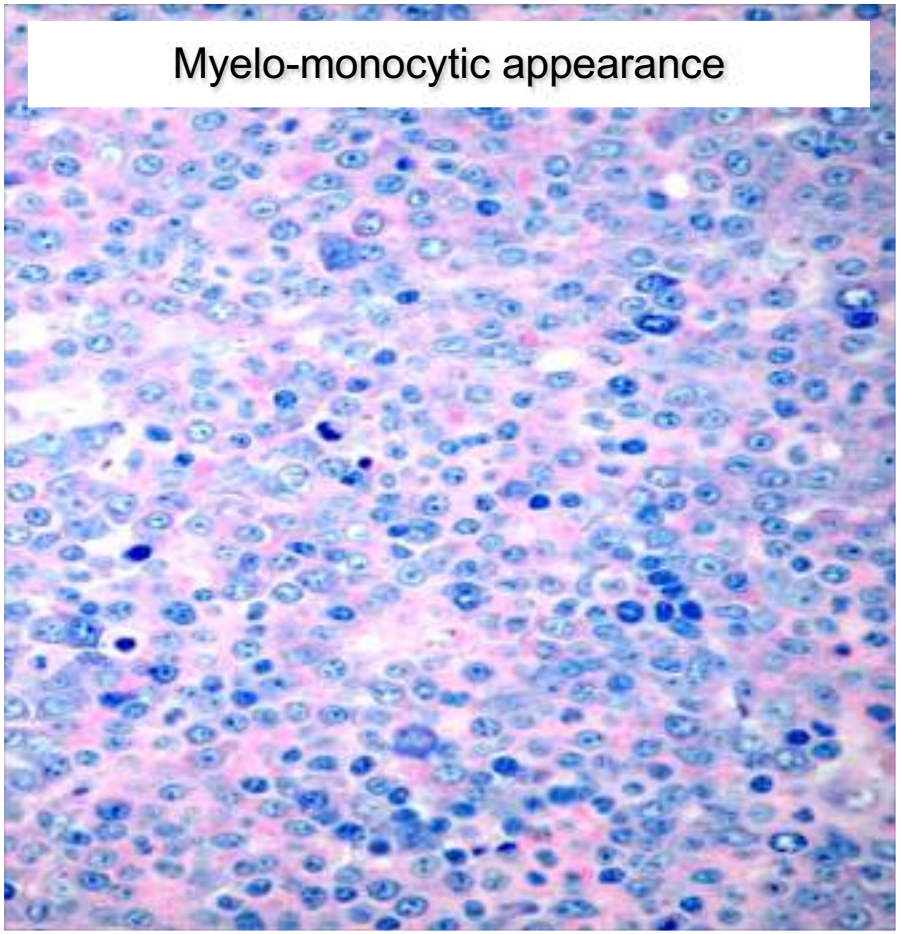
- MS more commonly consists of myeloblasts with or without maturation features.
- It often displays myelomonocytic or pure monoblastic morphology.
- Tumours with trilineage haematopoiesis or predominantly erythroid precursors or megakaryocytes are rare and may occur in conjunction with transformation of MPN.



Monoblastic appearance

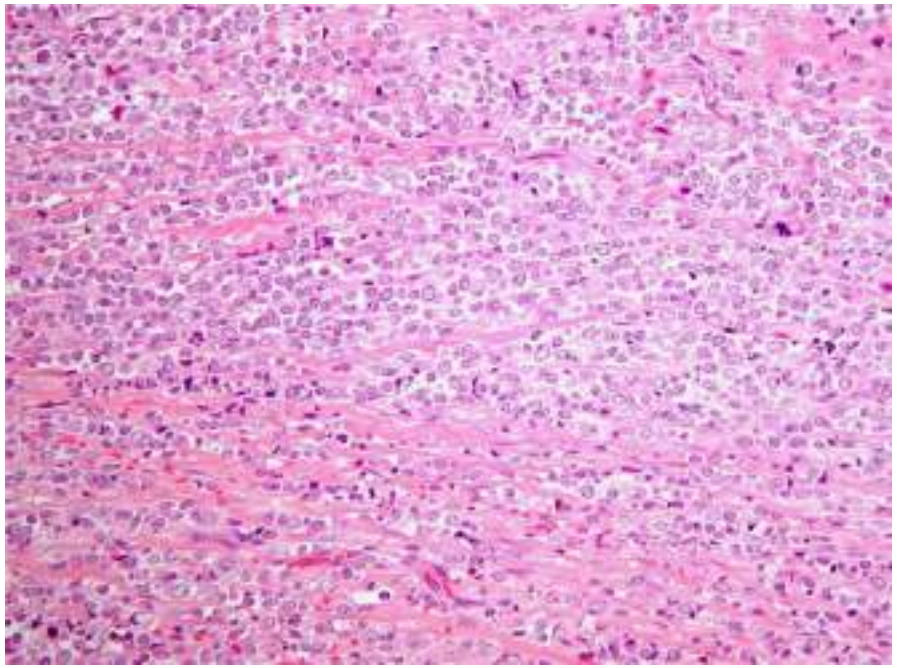


Myelo-monocytic appearance



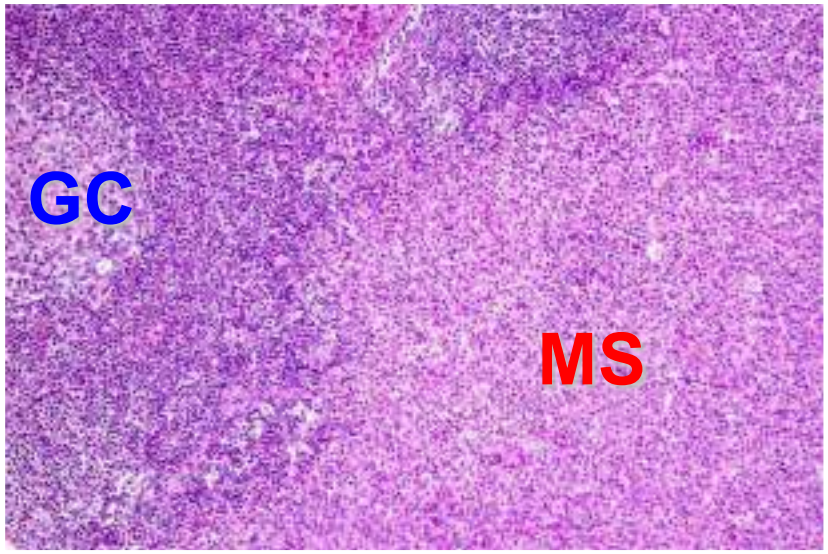
Morphologic findings

» At extra-nodal sites: indian-file growth pattern + varying degrees of fibrosis.



Morphologic findings

» In the lymph node: either intra-sinusoidal diffusion or para-cortical involvement with some residual follicles.



Phenotypic profile

- Commonest phenotypic profile: MPO^{+}, CD68/KP-1^{+}, CD68/PG-M1^{-}, GlyA^{-}, FVIIIRAg^{-}, CD3^{-}, and CD79a^{-}.
- In 20 cases, myelo-monocytic features: MPO$^{+/-}$, CD68/KP-1^{+}, CD68/PG-M1$^{-/+}$.
- In 20 cases, pure monoblastic population: MPO^{-}, CD68/KP-1^{+}, CD68/ PG-M1^{+}.
- CD117: in 71.7% of cases (17/20 MØ cases negative).
- CD34^{+} and TdT^{+} in 28.3% and 21.4% of cases.
- CD99^{+} in 53.4% of cases.
- Ki-67: high.

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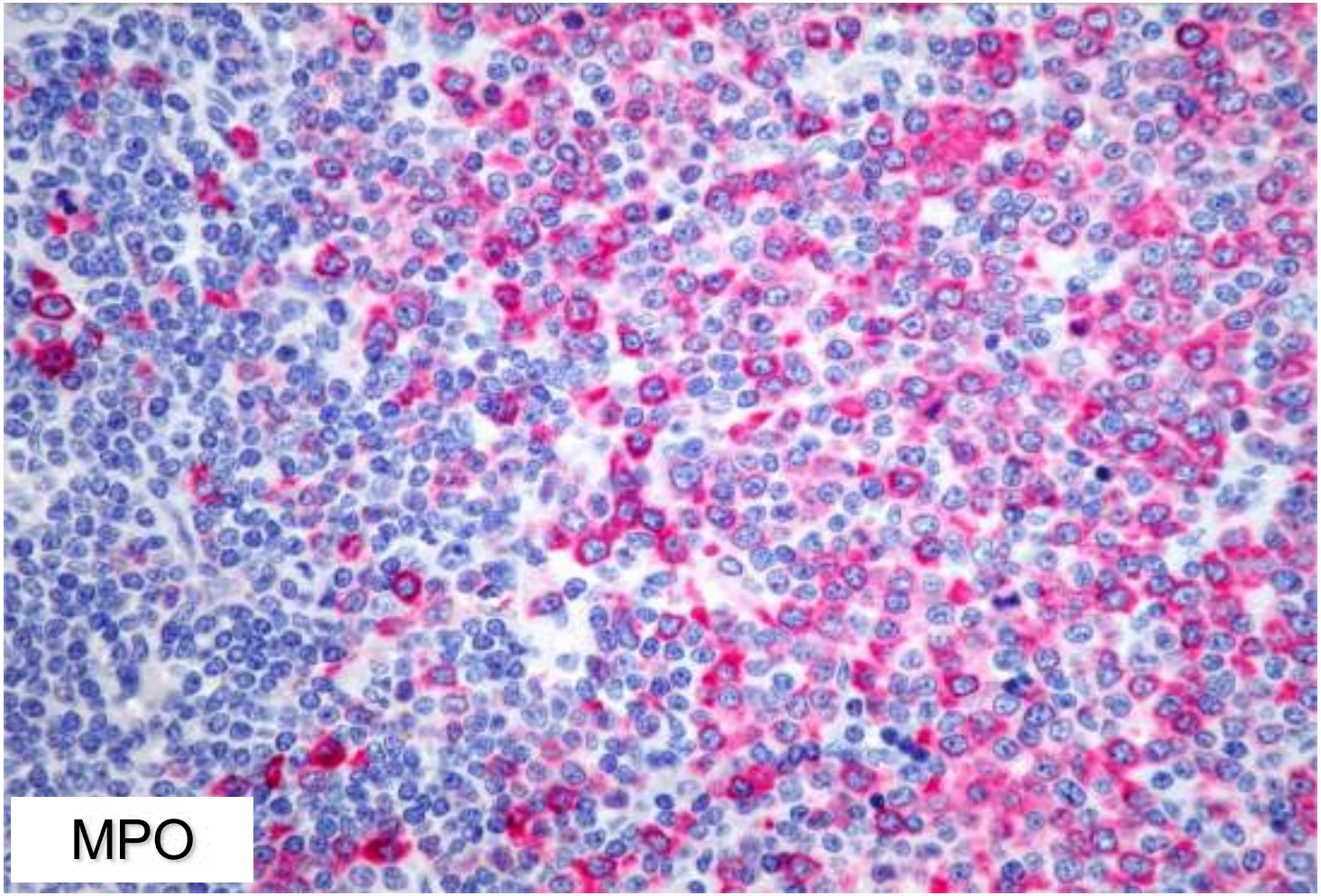
MPO

Phenotypic profile

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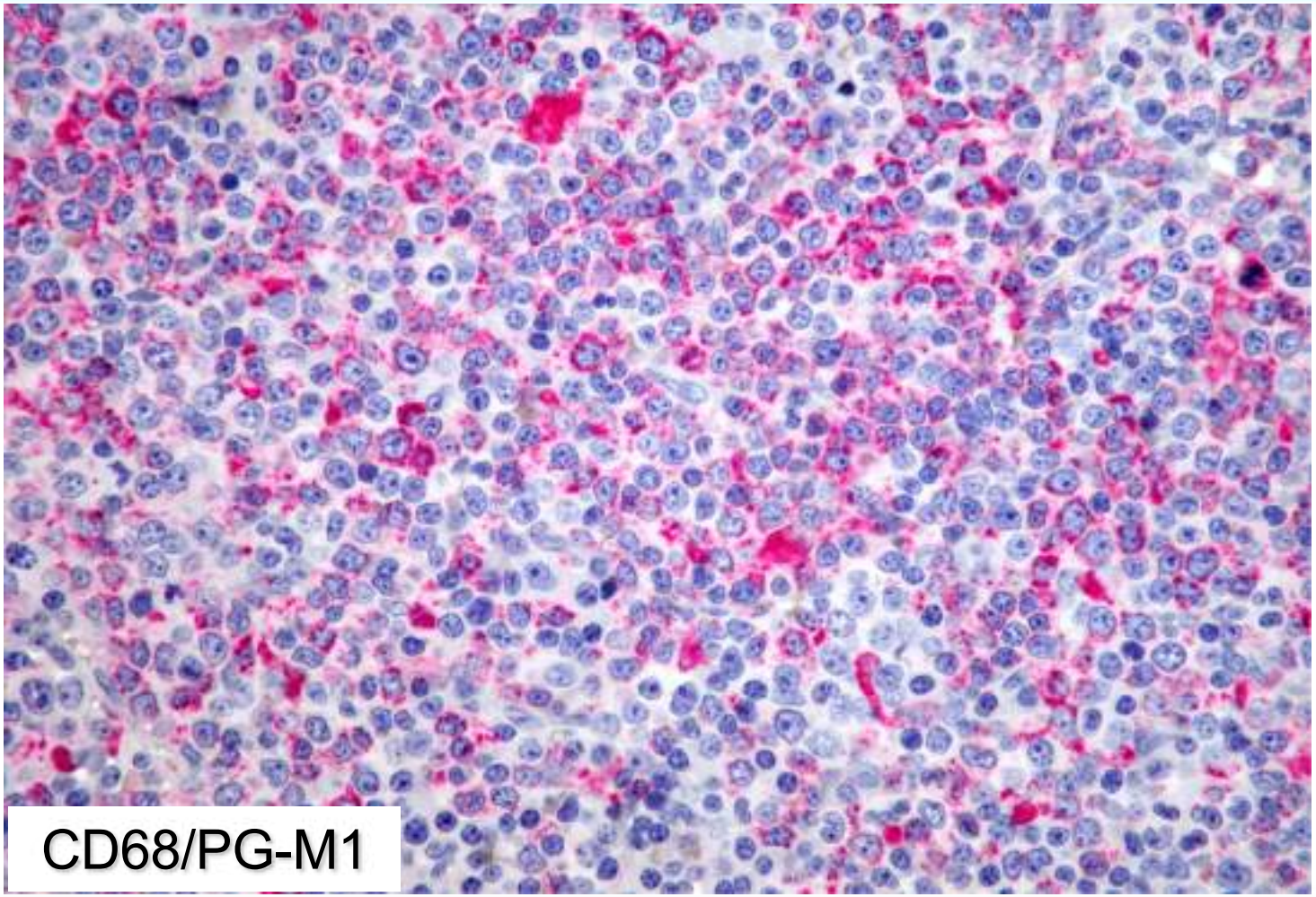

CD68/PG-M1

Phenotypic profile

- Commonest phenotypic profile: MPO^{+}, $CD68/KP\text{-}1^{+}$, $CD68/PG\text{-}M1^{-}$, $GlyA^{-}$, $FVIIIRAg^{-}$, $CD3^{-}$, and $CD79a^{-}$.
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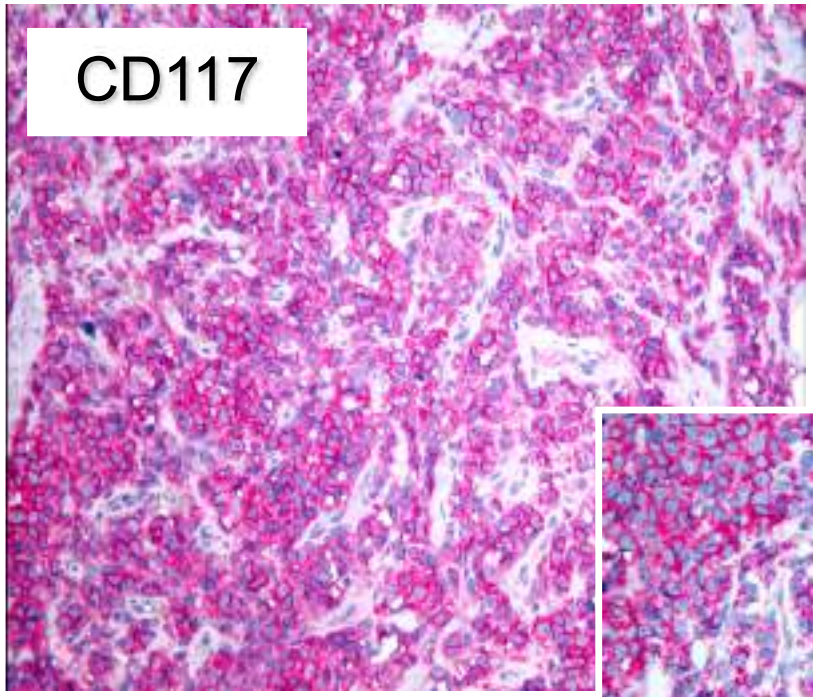
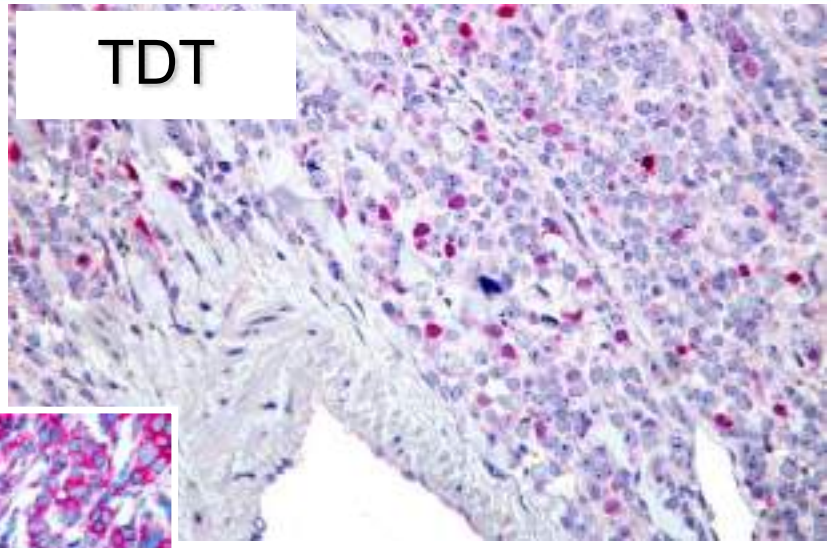
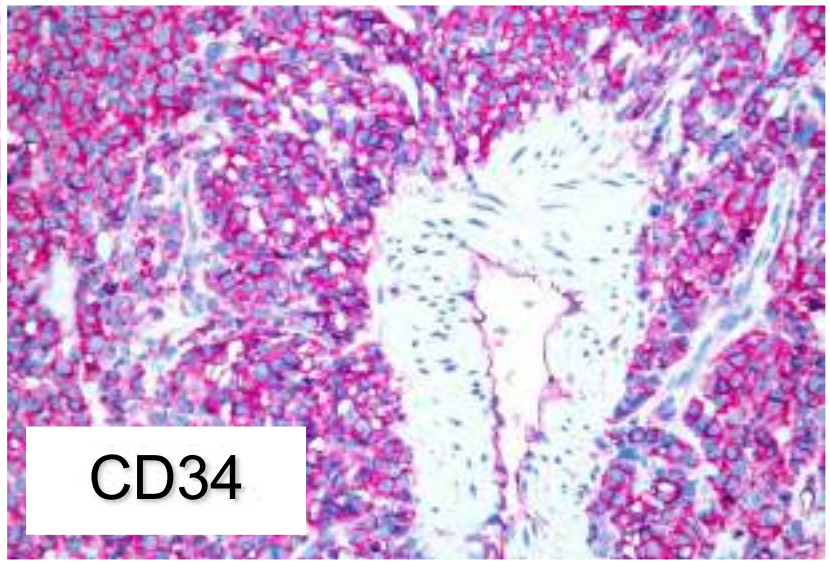
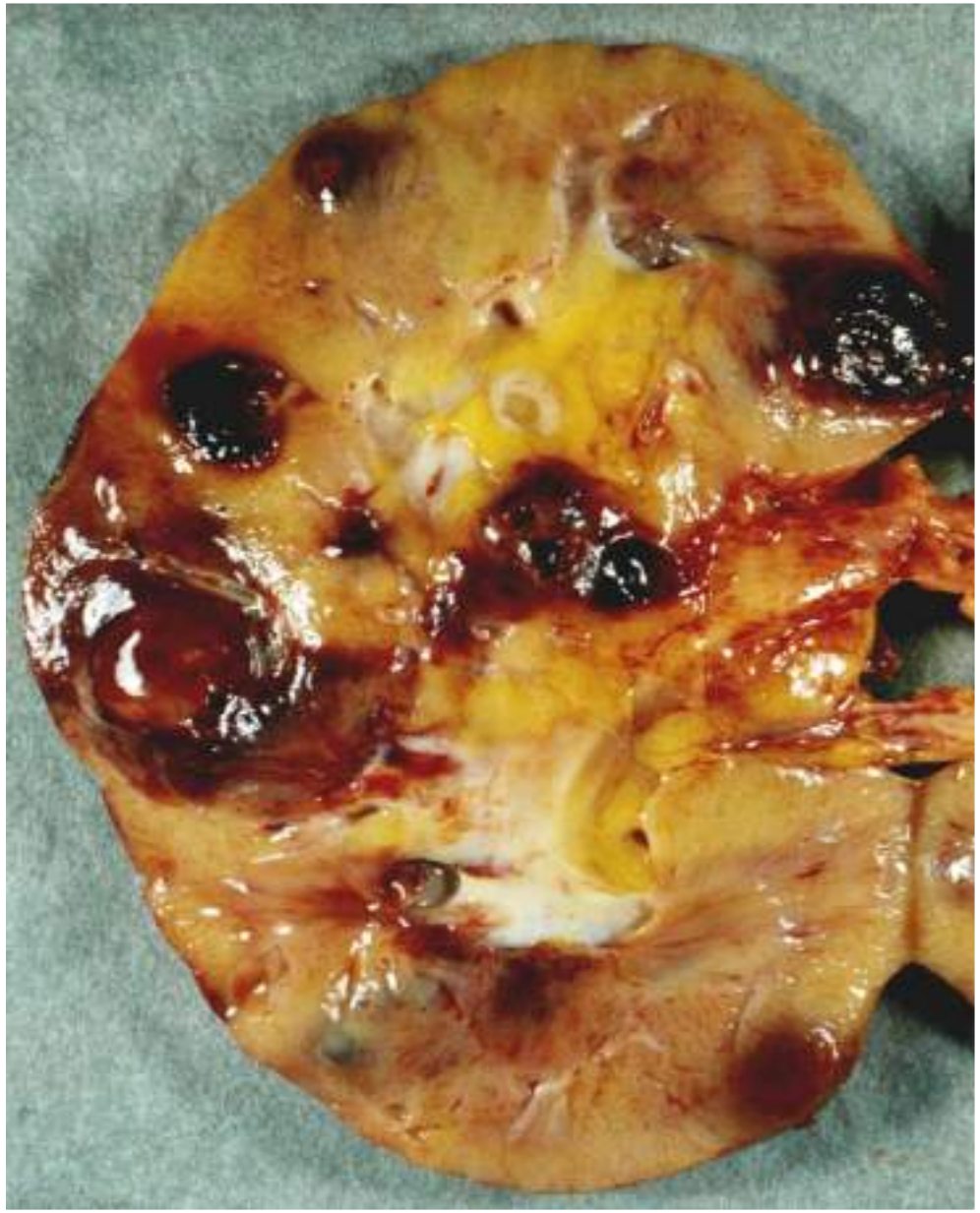
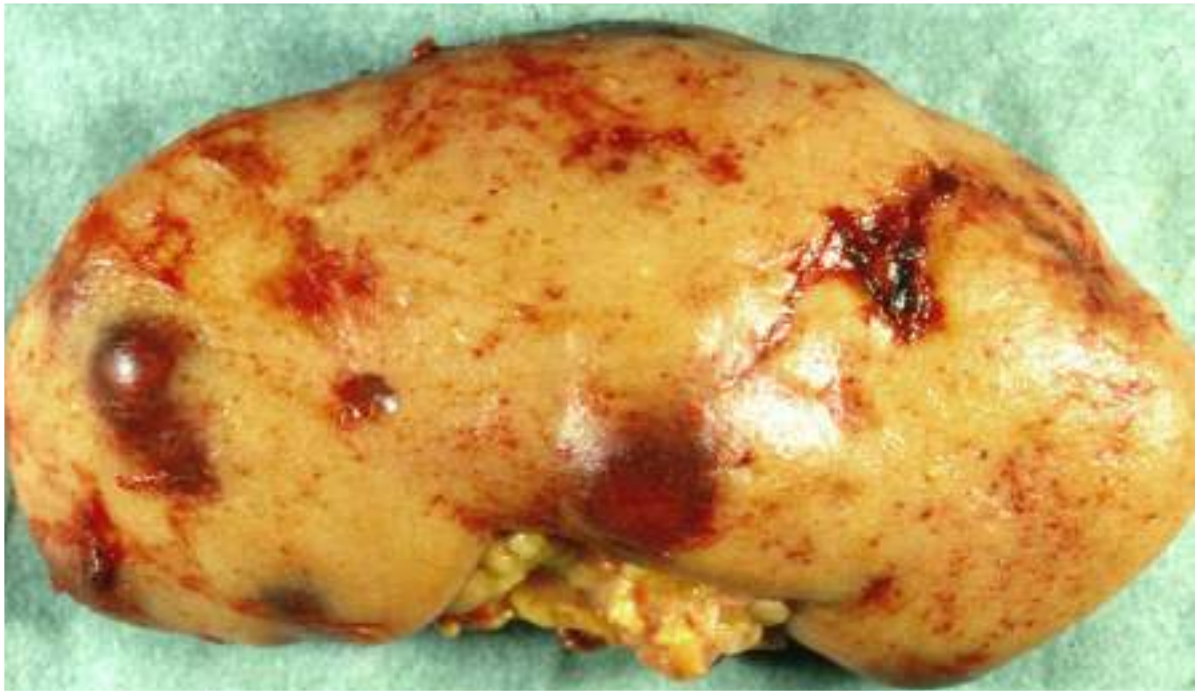
Pileri et al Leukemia 2007 21, 340-350

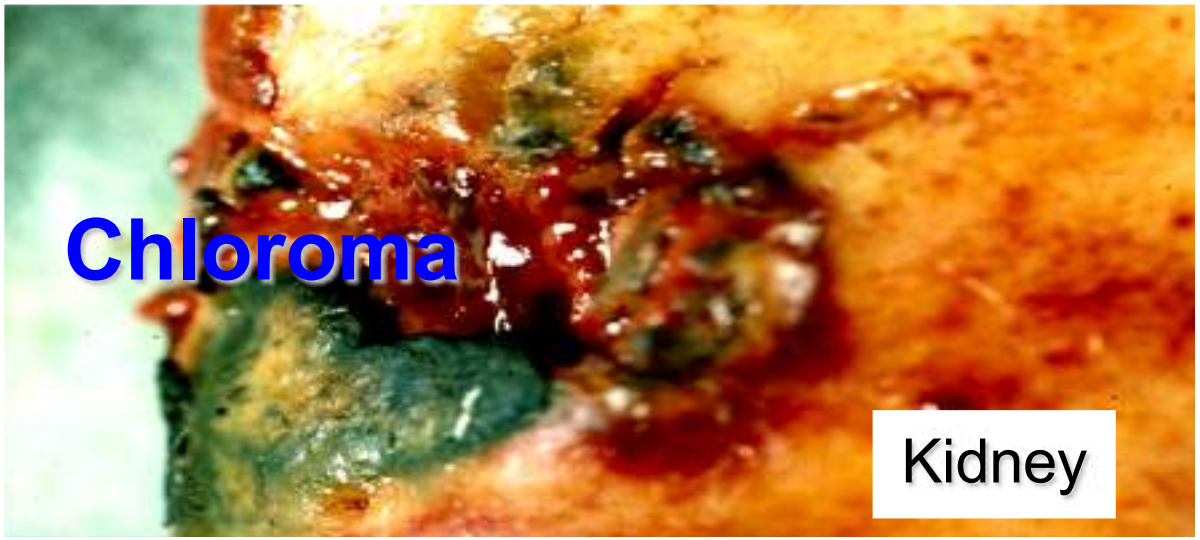

CD117

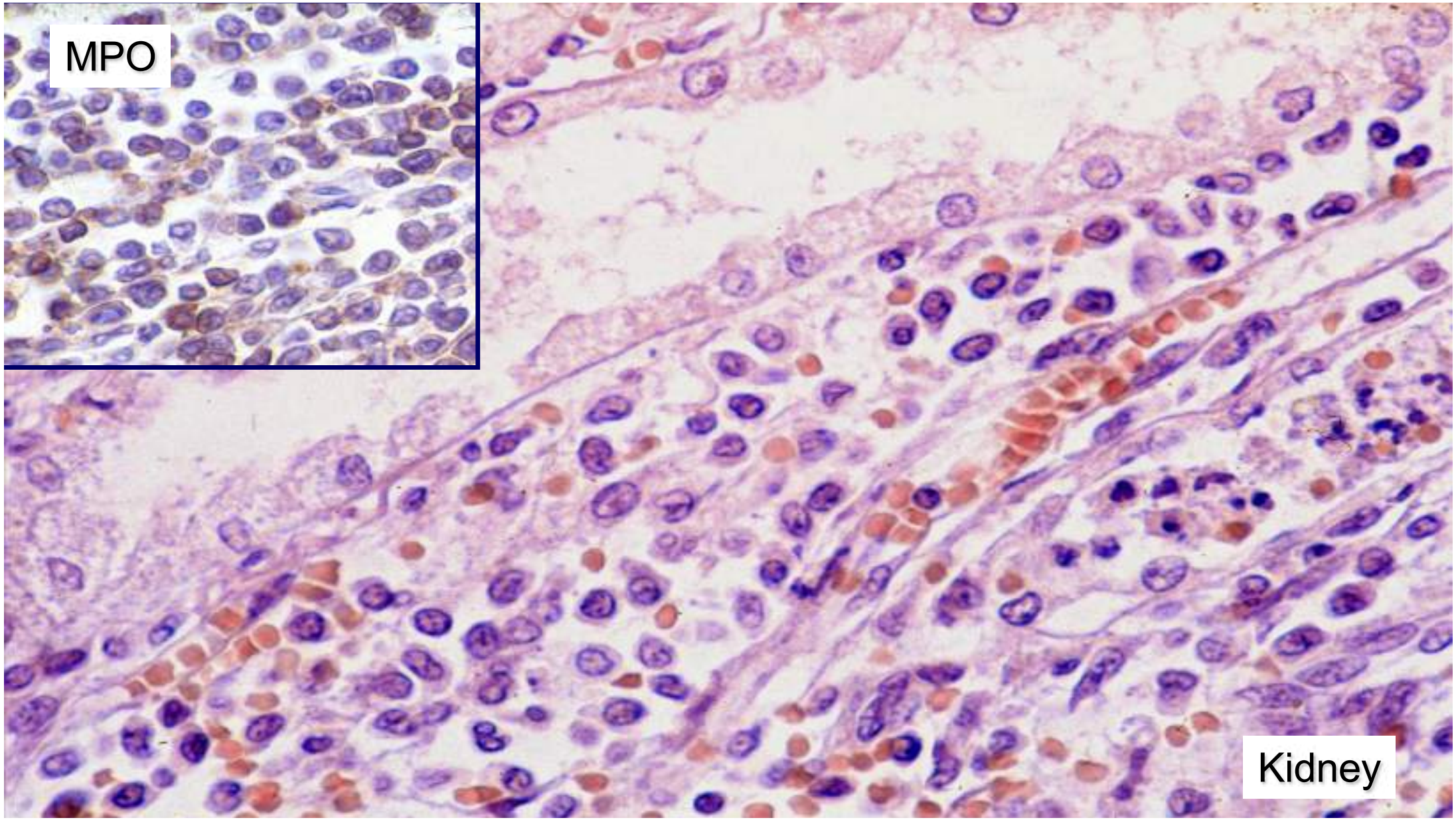

TDT

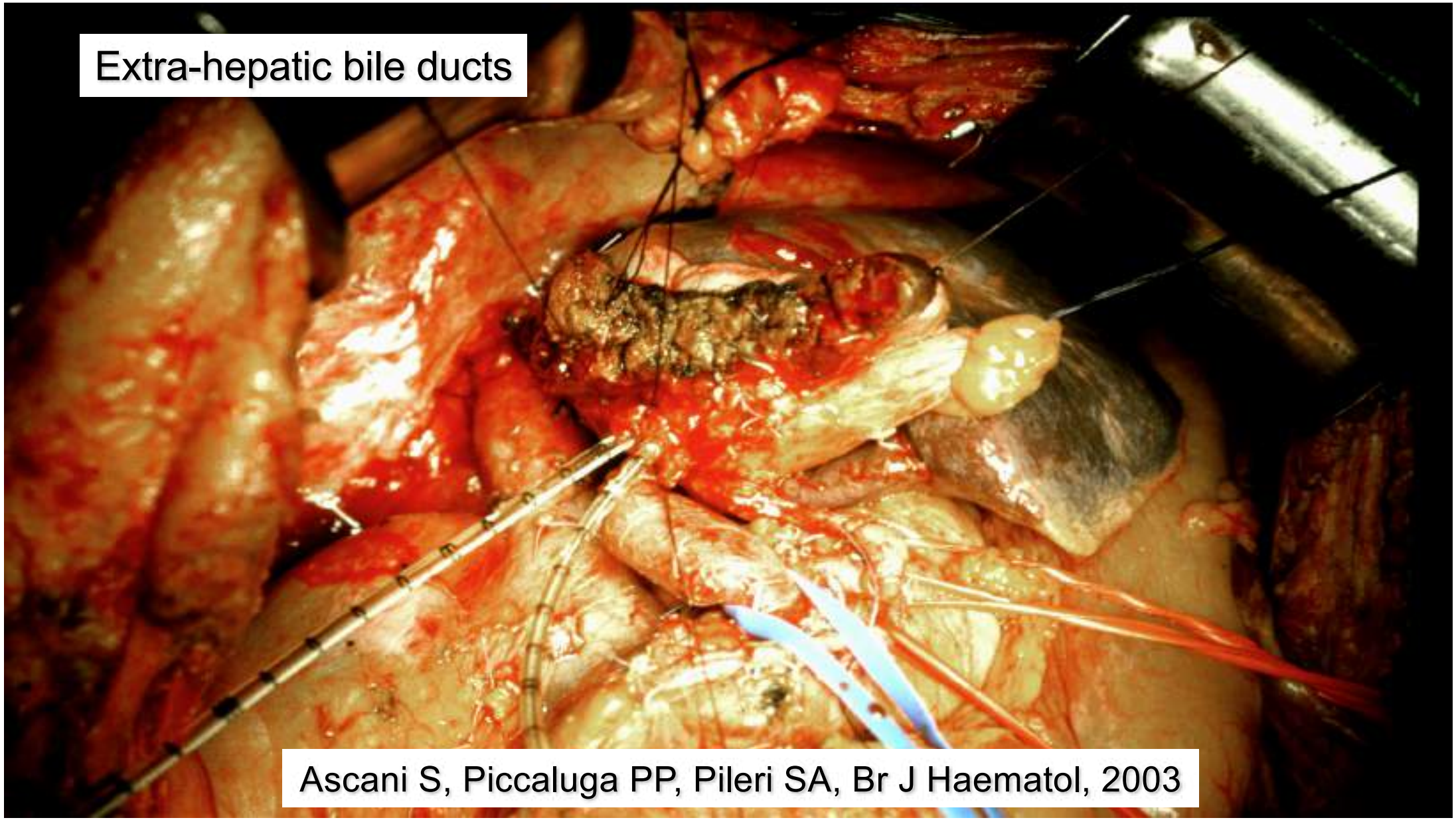

CD34



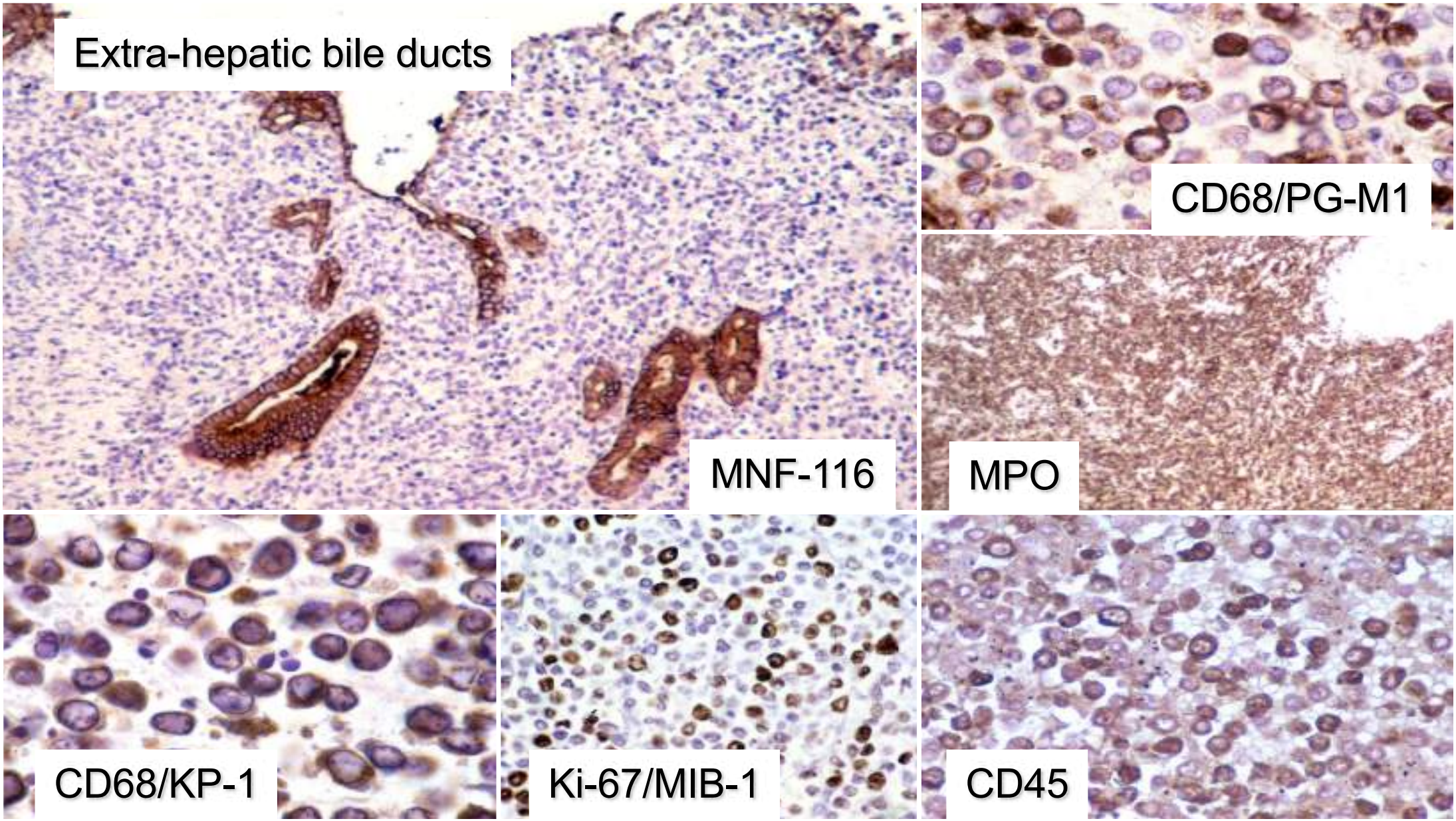


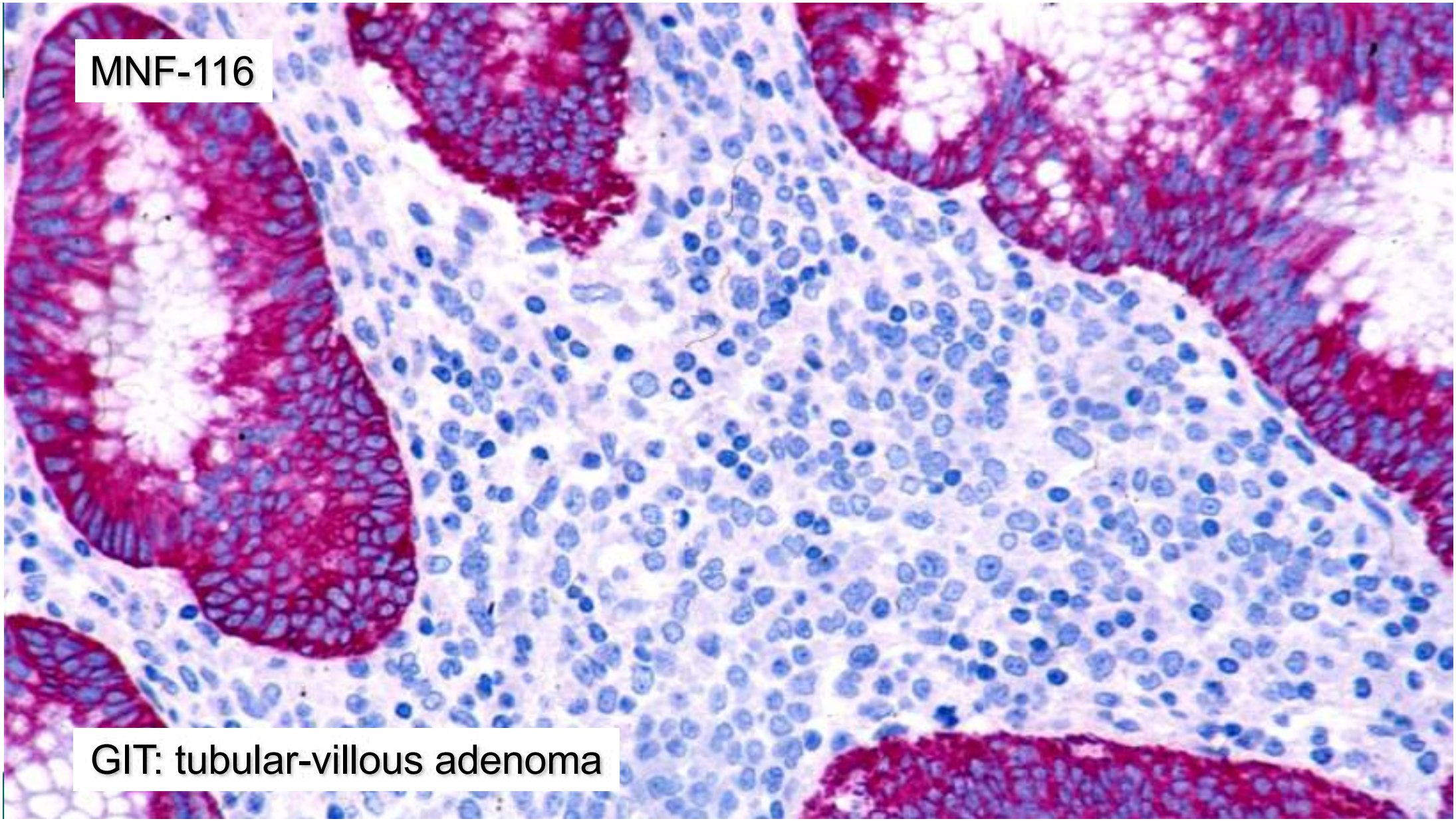

Chloroma
Kidney


MPO
Kidney


Extra-hepatic bile ducts
Ascani S, Piccaluga PP, Pileri SA, Br J Haematol, 2003

Extra-hepatic bile ducts

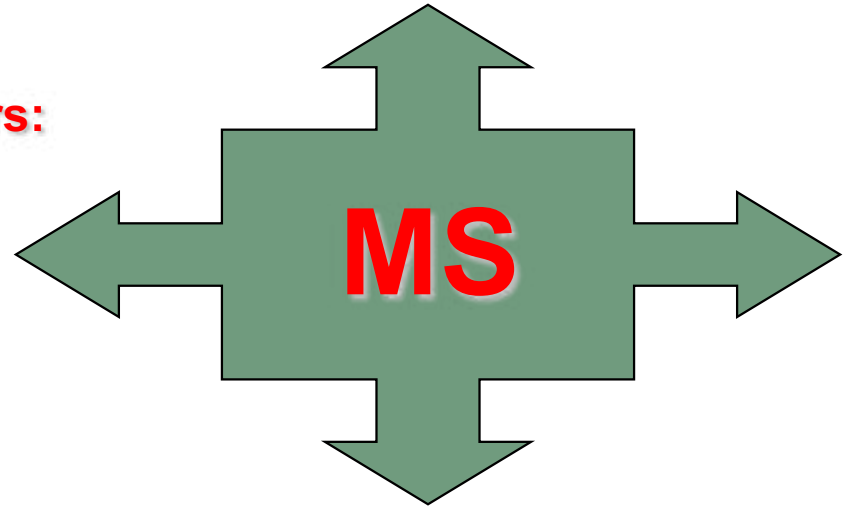

Extra-hepatic bile ducts
MNF-116
CD68/PG-M1
MPO
CD68/KP-1
Ki-67/MIB-1
CD45


MNF-116
GIT: tubular-villous adenoma

Differential diagnosis

Aggressive lymphomas

Non-haematopoietic tumours:
neuroblastoma,
rhabdomyosarcoma,
Ewing's/PNET,
medulloblastoma,
others



BPDCT

Extra-medullary haematopoiesis

Phenotypic profile

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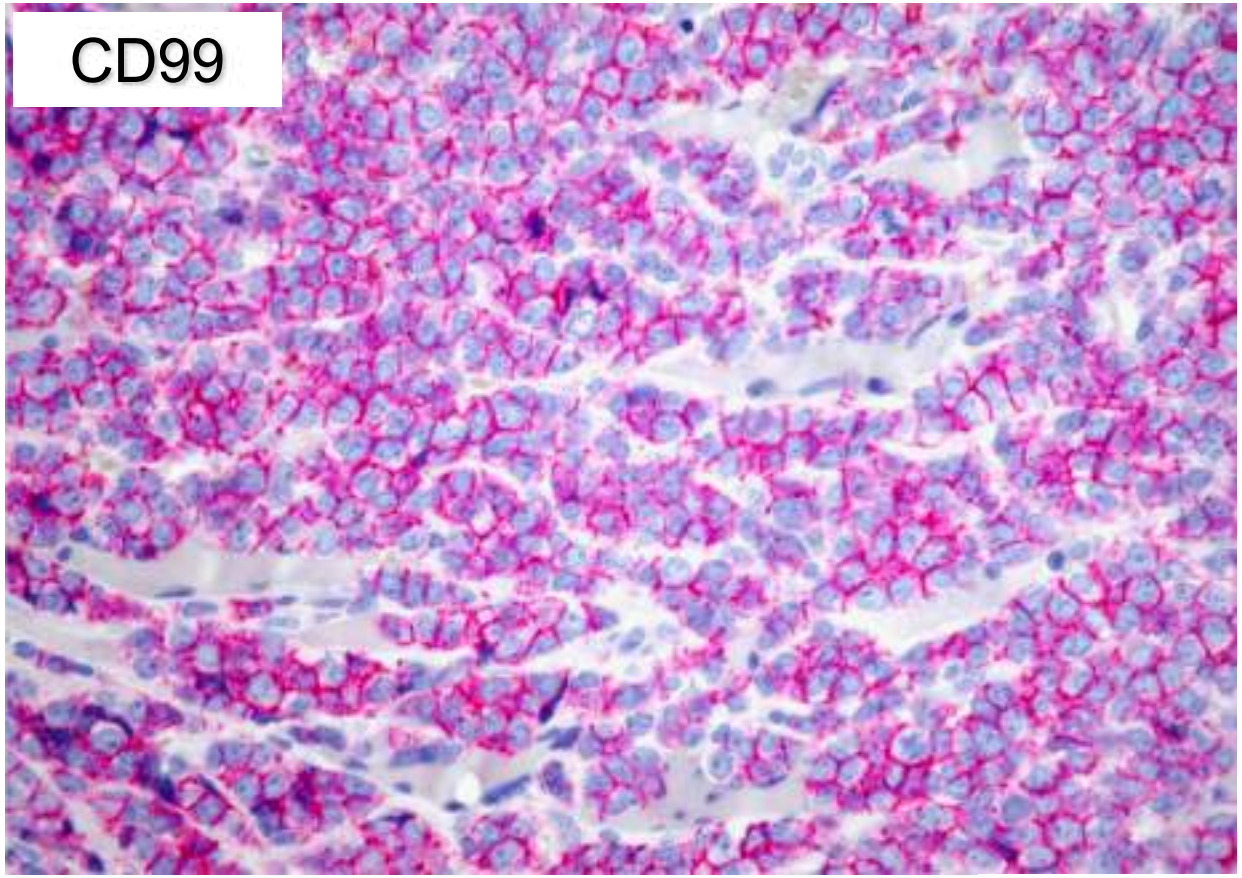
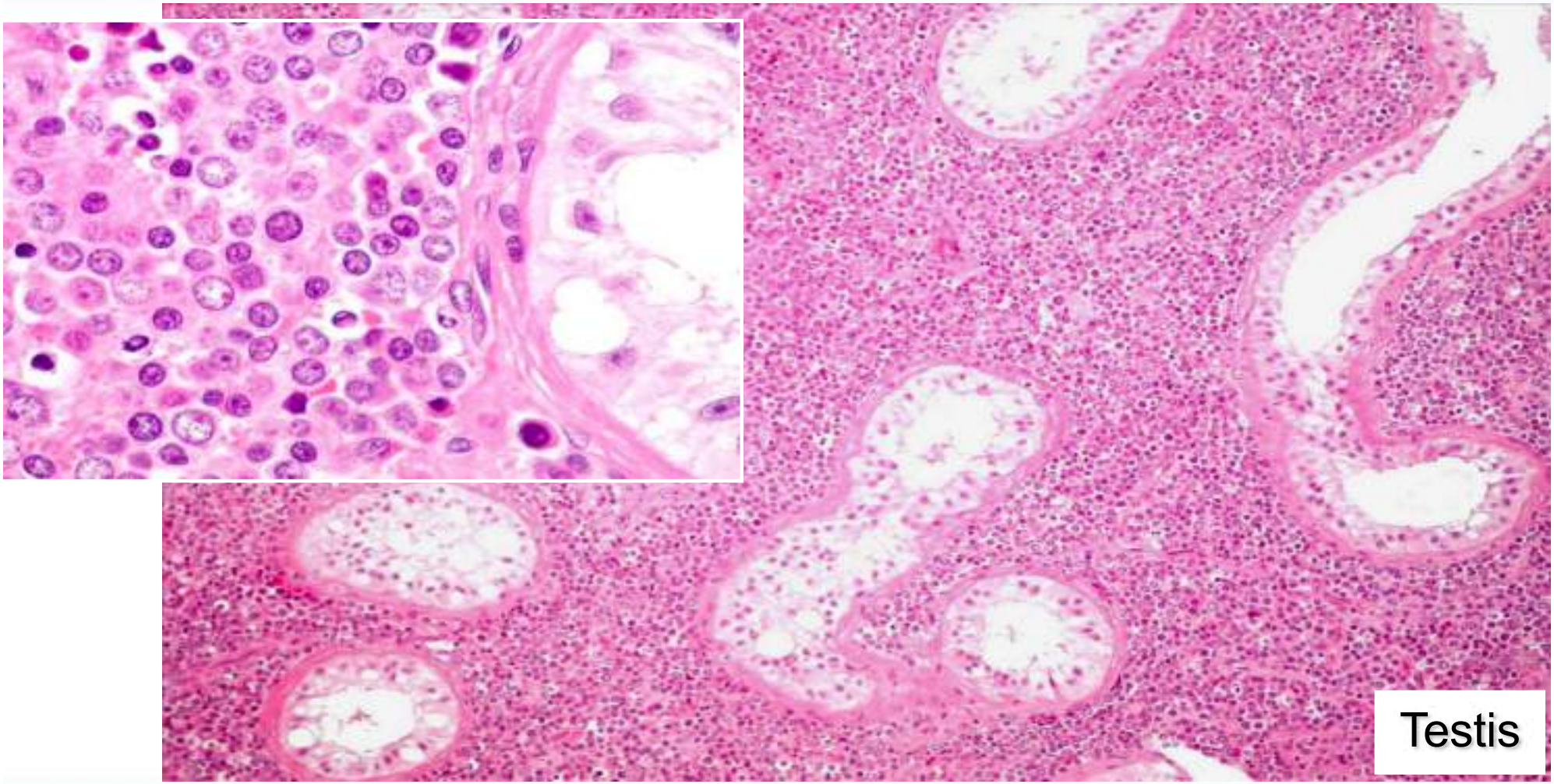
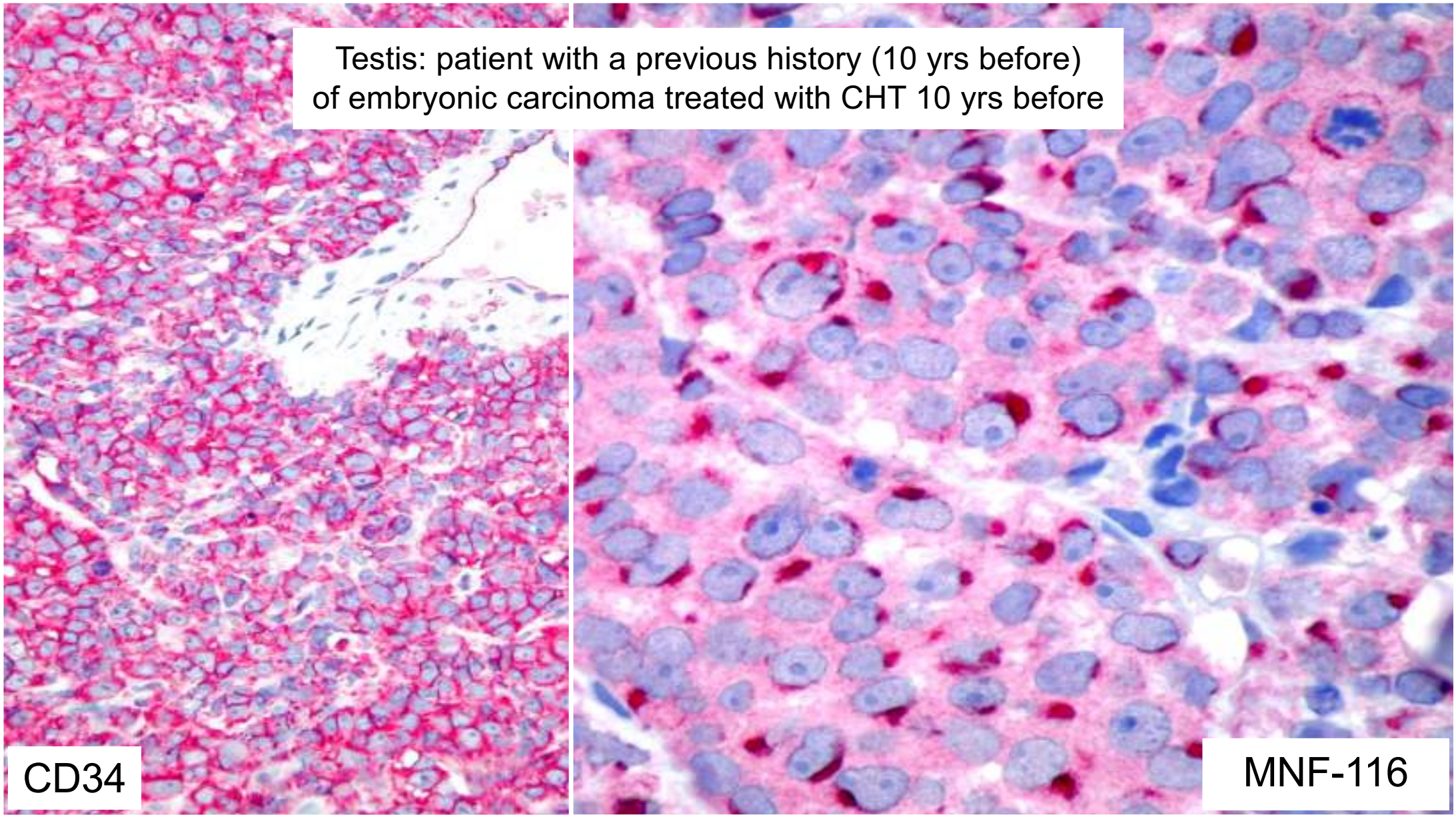
Pileri et al Leukemia 2007 21, 340-350



Zhang PJ et al. Mod Pathol 2000, 13:452-8.



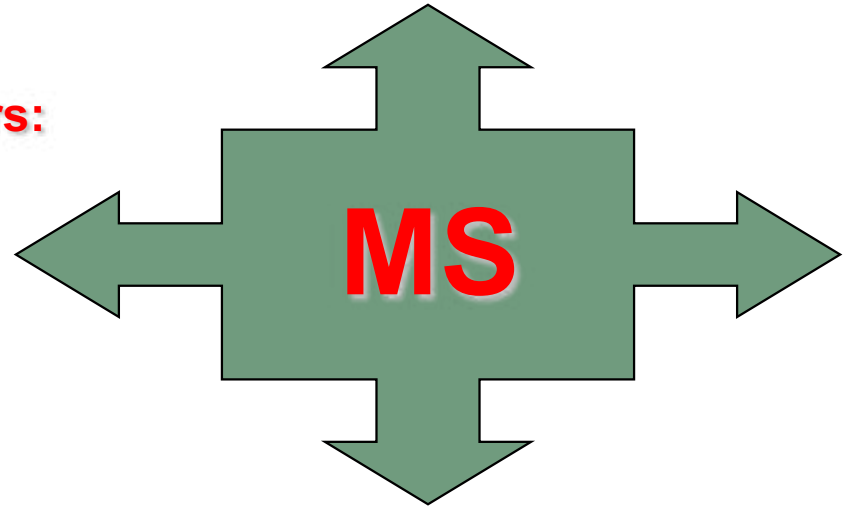
Testis


Testis: patient with a previous history (10 yrs before)
of embryonic carcinoma treated with CHT 10 yrs before
CD34
MNF-116

Differential diagnosis

Aggressive lymphomas

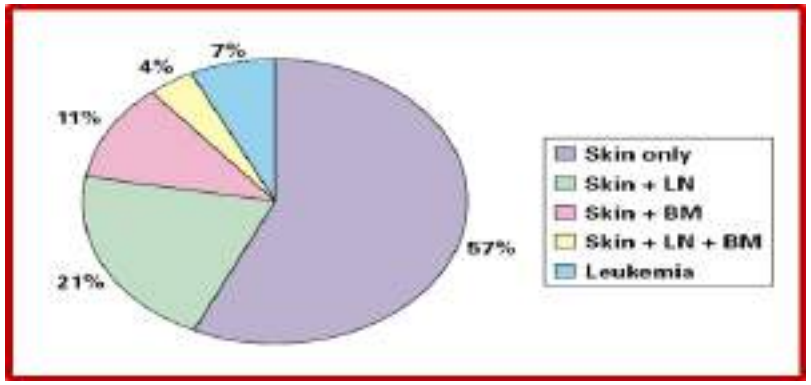
Non-haematopoietic tumours:
neuroblastoma,
rhabdomyosarcoma,
Ewing's/PNET,
medulloblastoma,
others

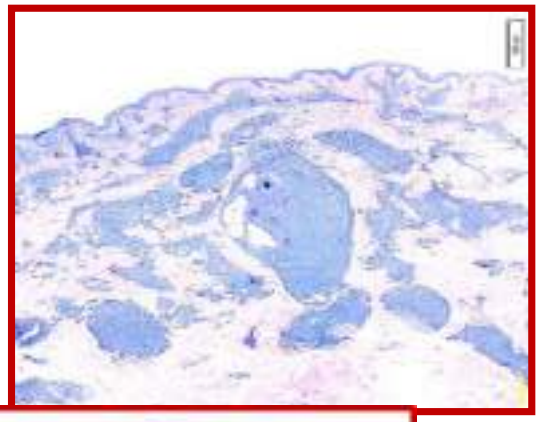


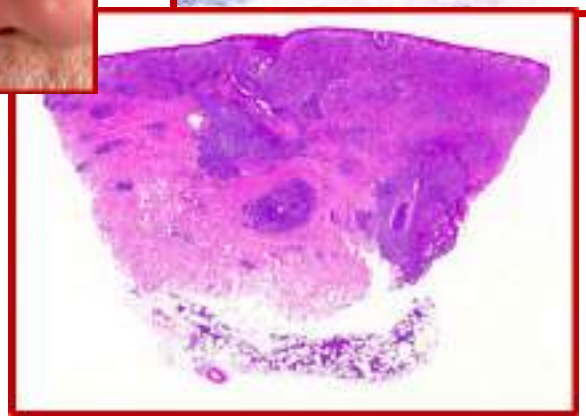
BPDCT

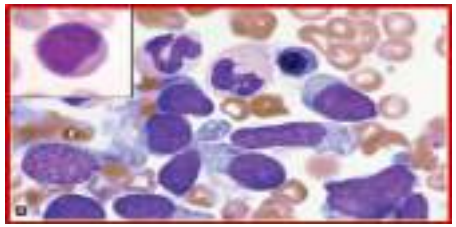
Extra-medullary haematopoiesis

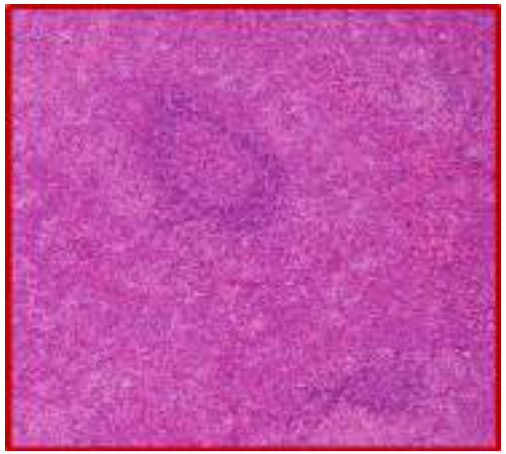
Blastic plasmacytoid dendritic cell neoplasm

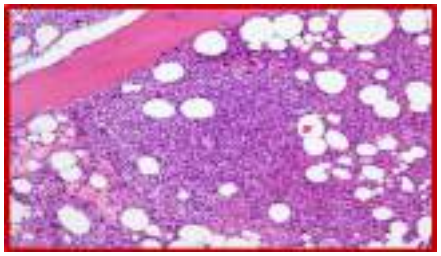




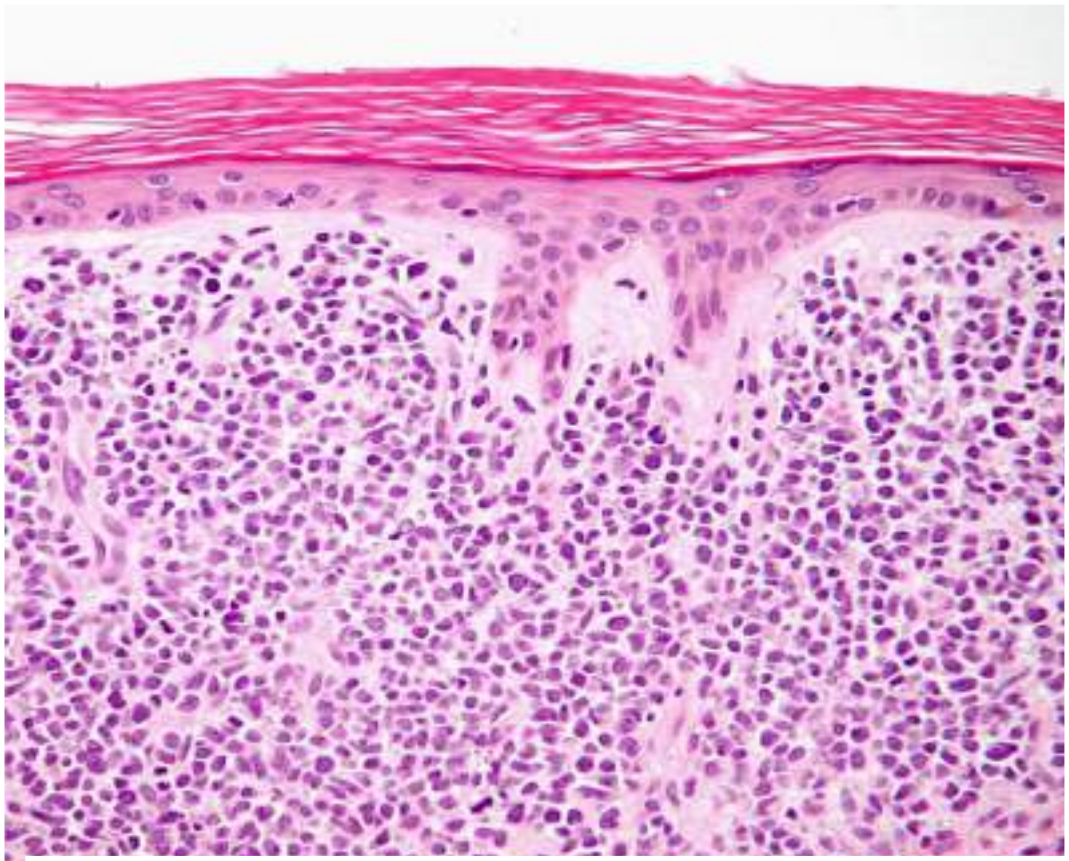


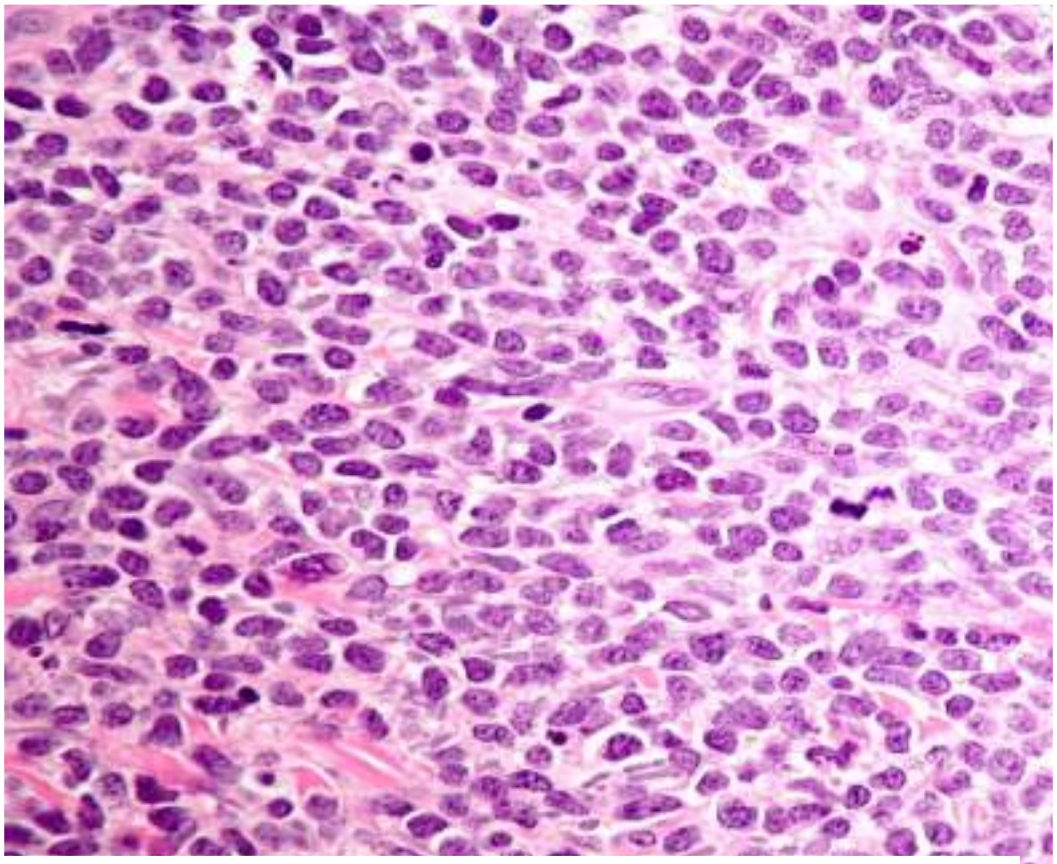






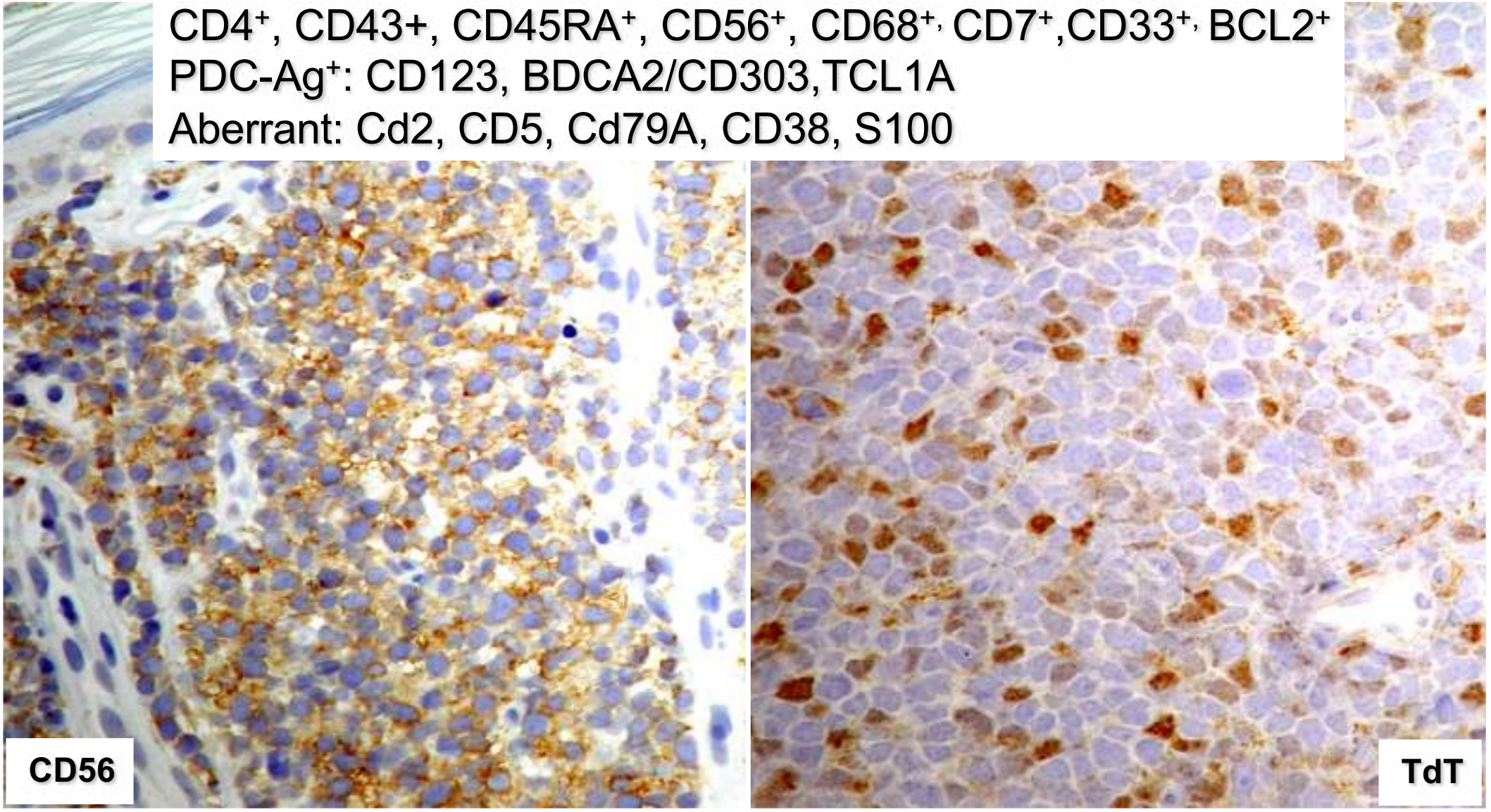
Dendritic cell precursor tumour

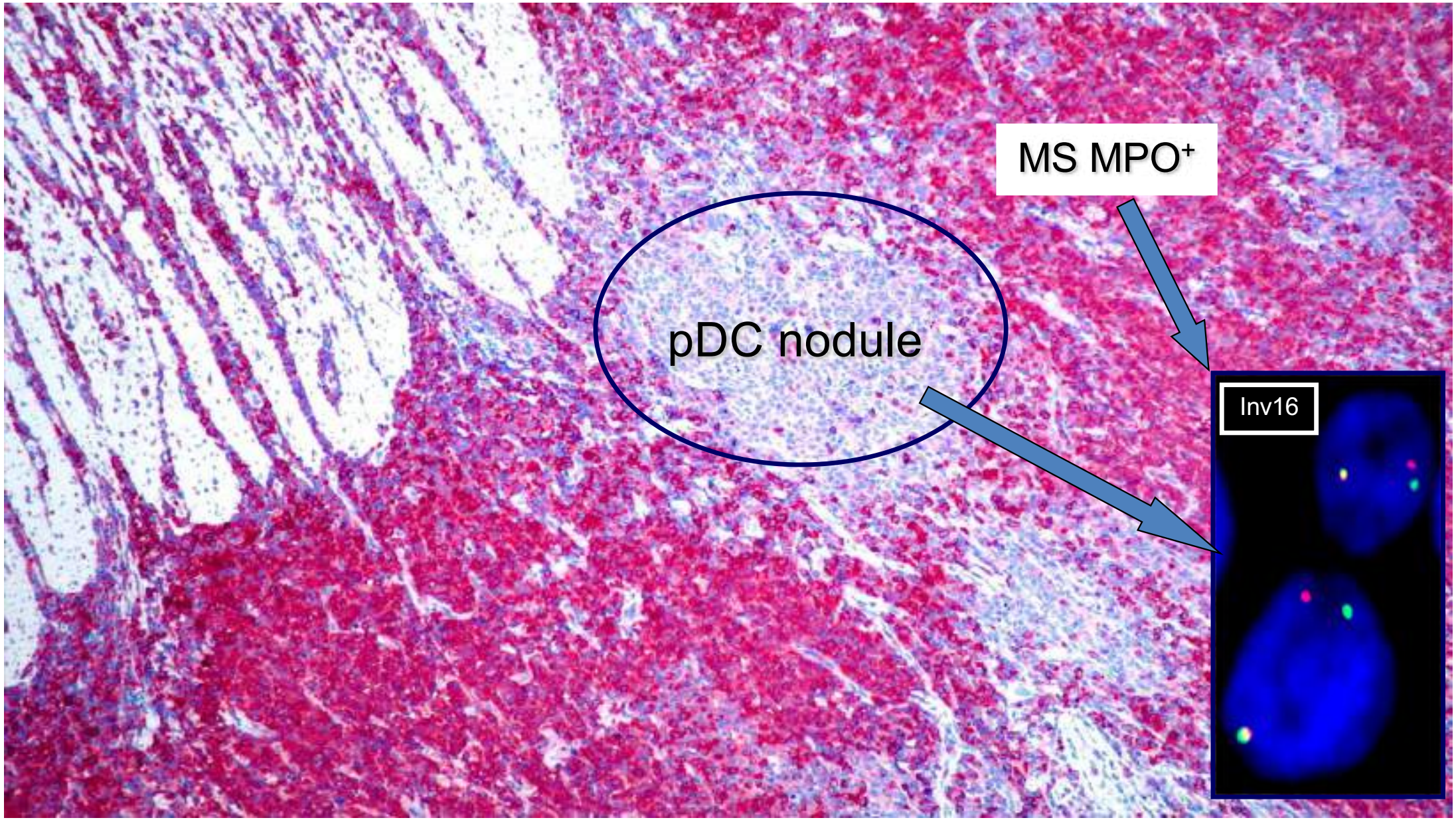




Mostly adult-elderly people, predominantly males. Skin, bone marrow & blood, lymph nodes, … disseminated. Rarely myeloid leukemia associated. Very aggressive

CD4^{+}, CD43+, CD45RA^{+}, CD56^{+}, CD68^{+}, CD7^{+},CD33^{+}, BCL2^{+}
PDC-Ag^{+}: CD123, BDCA2/CD303,TCL1A
Aberrant: Cd2, CD5, Cd79A, CD38, S100

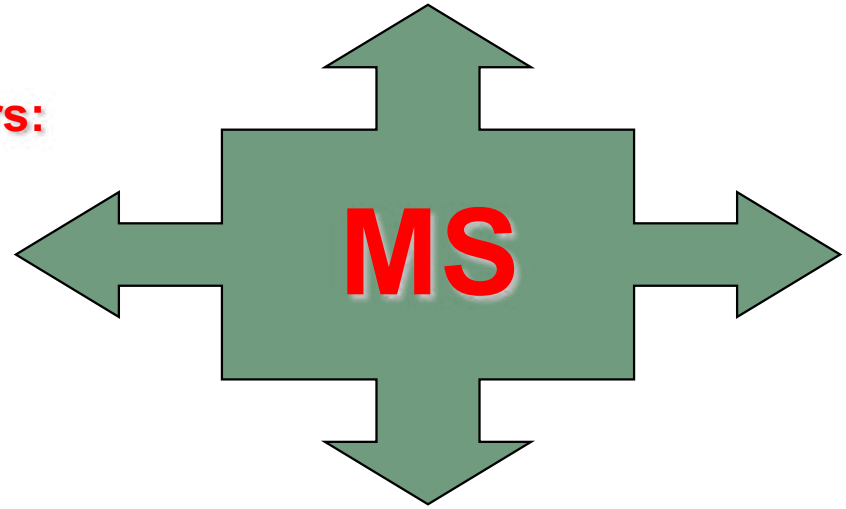



MS MPO+
pDC nodule
Inv16

Differential diagnosis

Aggressive lymphomas

Non-haematopoietic tumours:
neuroblastoma,
rhabdomyosarcoma,
Ewing's/PNET,
medulloblastoma,
others

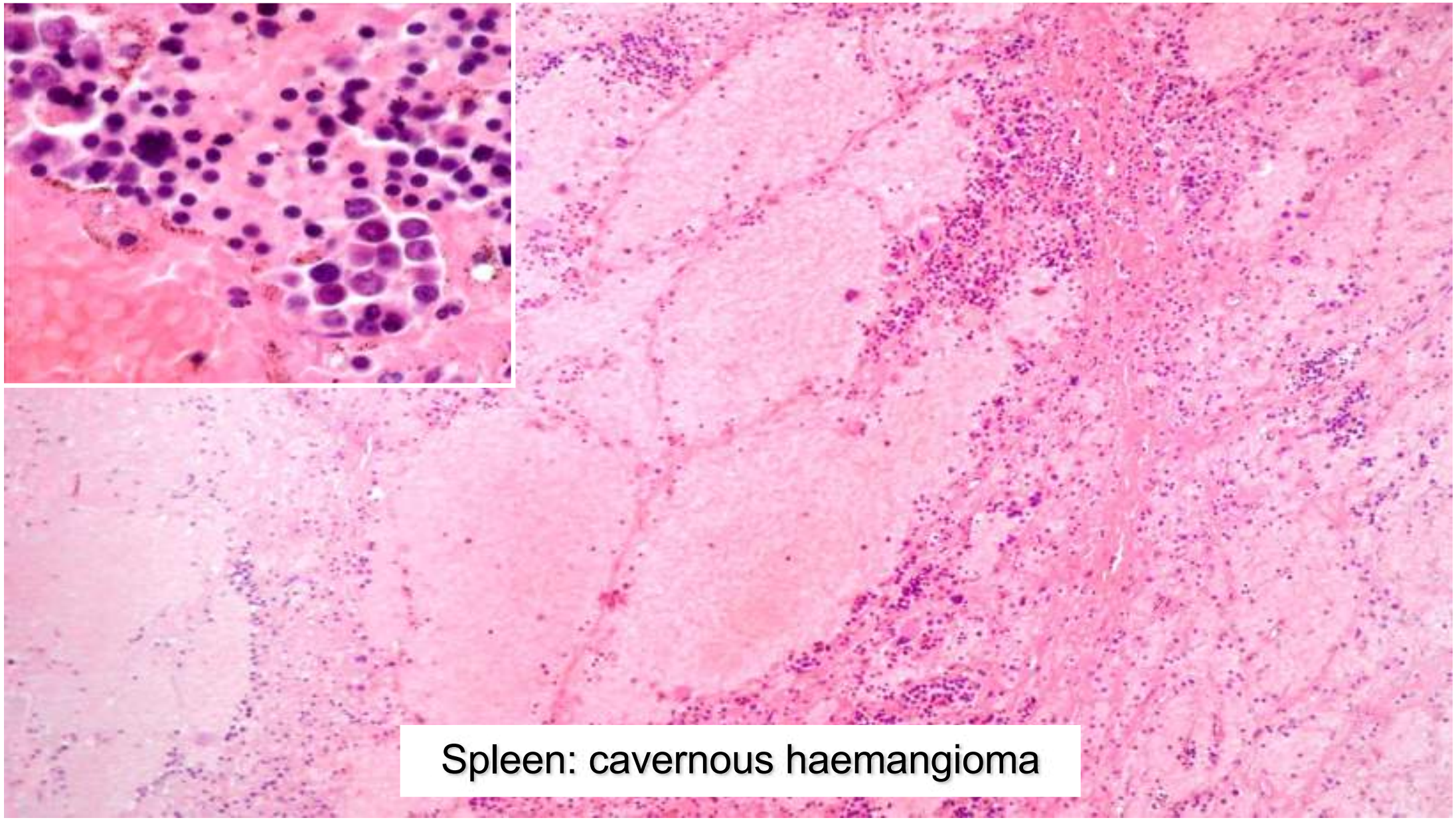


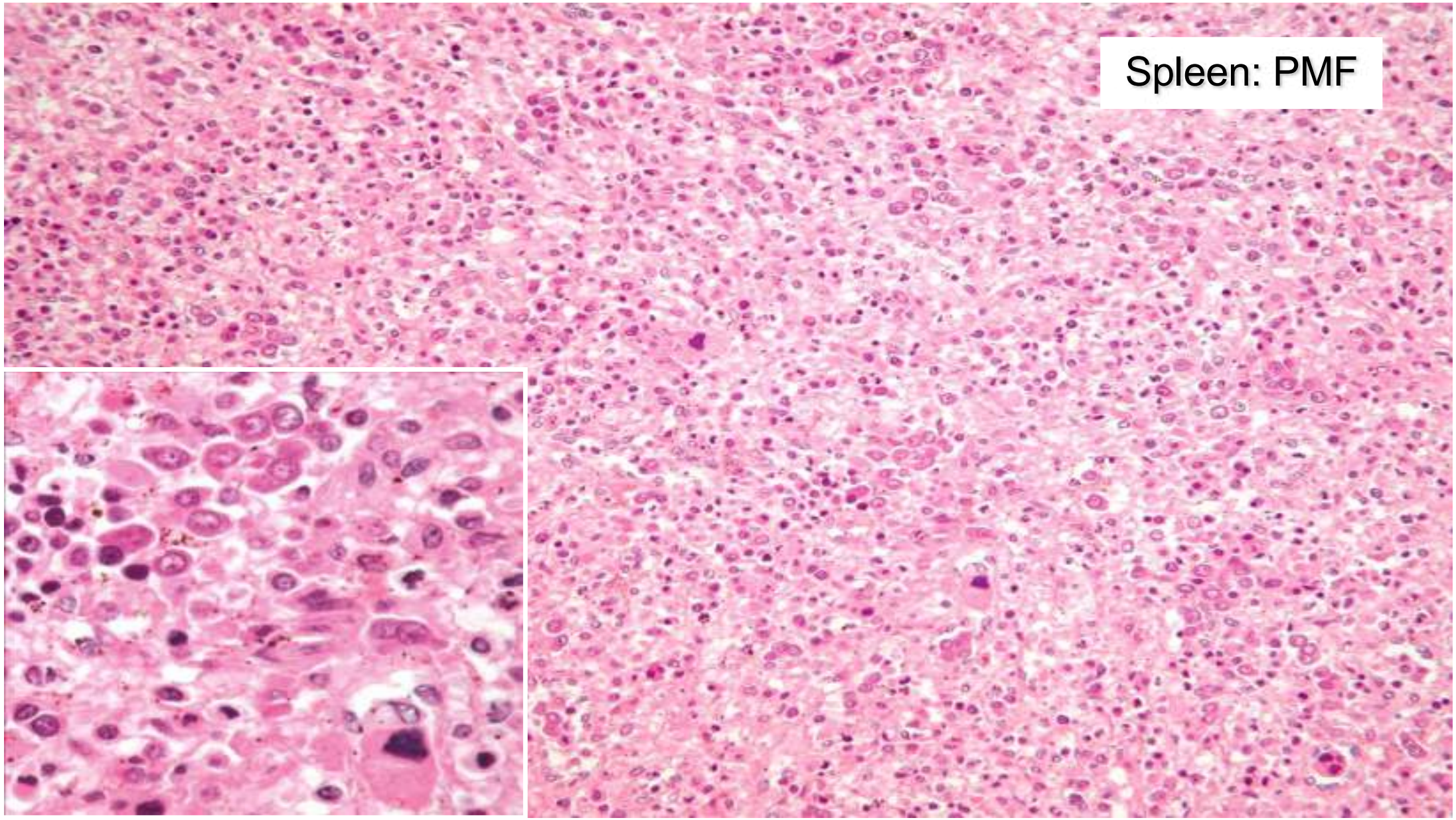
BPDCT

Extra-medullary haematopoiesis

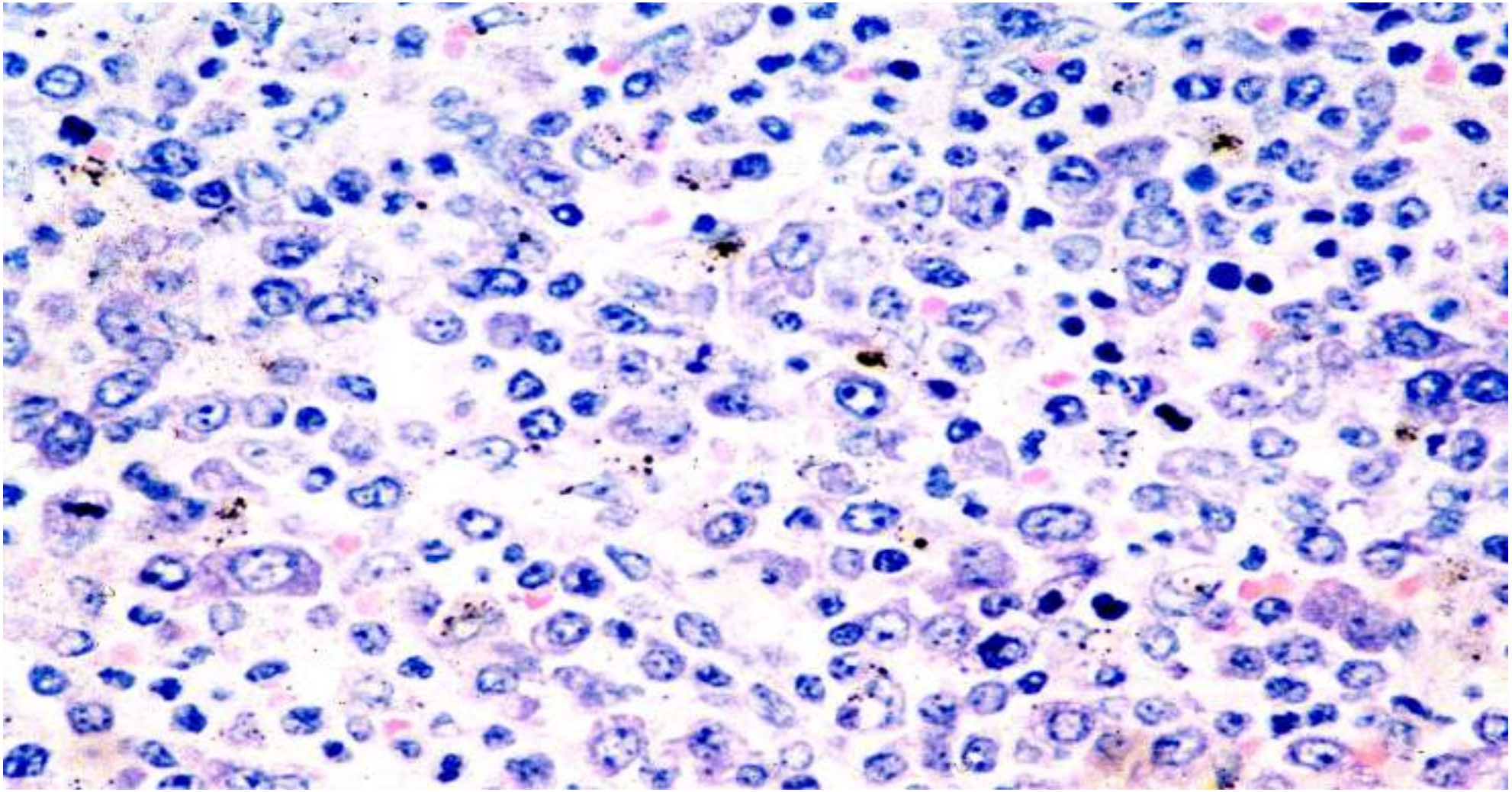
Extra-medullary haematopoiesis

- Haemoglobinopathies (ß-thalassaemia)
- Haemolytic anaemia
- Splenic cavernous haemangioma
- PMF
- G-CSF prolonged administration (Friedman HD et al, Ann Hematol 1998)


Spleen: cavernous haemangioma

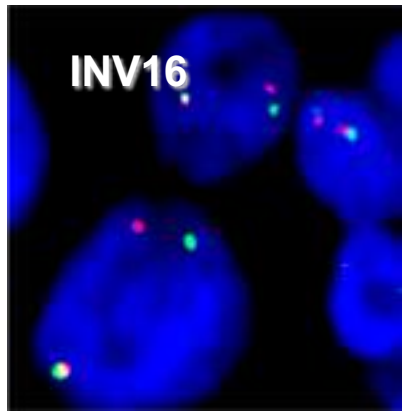

Spleen: PMF

Extra-medullary haematopoietic mass following prolonged G-CSF administration



Genetic profile

» 55% of cases chrmosomal aberrations (> by FISH analysis):
t(8,21) (q22;q22), inv(16), 11q23, t(9;11), t(8;17), t(8;16), t(8;17), t(1;11), trisomies of chr 4, 8, 11, monosomy 7, and del of chr 5q, 16q, and 20q



» Complex cytogenetics in17% pts with de novo MS,
39% in pts with MS arising in setting of AML

» some abnormalities are associated with particular sites
Inv(16), ampl CBFB: breast, uterus, small intestine
Trisomy 8 and KMT2A-MLLT3 fusion: skin, breast
t(8,21): orbital MS in paediatric

conventional cytogenetic analysis is rarely performed for MS, as it is frequently mistaken for a solid tumour at the time of Diagnosis (karyotyping from corresponding bone marrow, if involved)

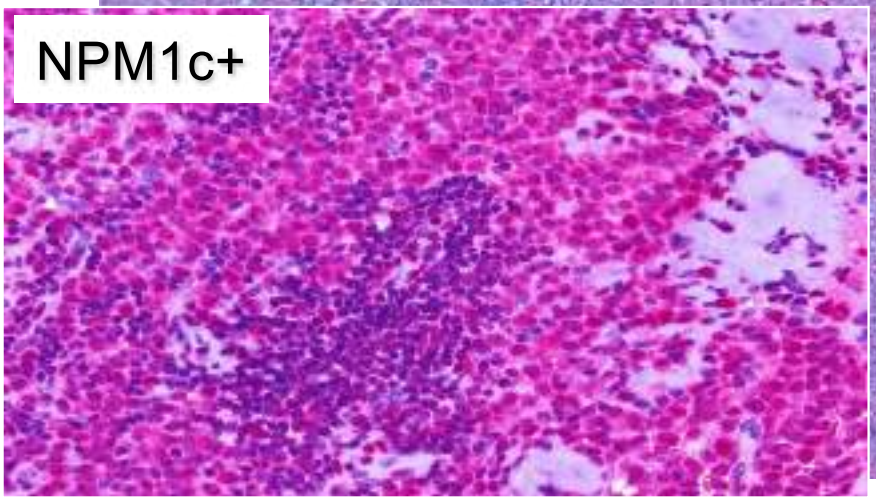
Genetic profile: NGS (FFPE)

Mutation	%
NPM1	15-28
FLT3-ITD	15
IDH2	7-11
RTK-RAS (NRAS, KRAS, CBL, PTPN11)	56
TP53	56-85
DNMT3A	21
RUNX1	7-11
KIT	14-15.4
TET2	16-21

Myeoid Sarcoma: lymph node

Cytoplasmic nucleophosmin is not detected in blastic plasmacytoid dendritic cell neoplasm

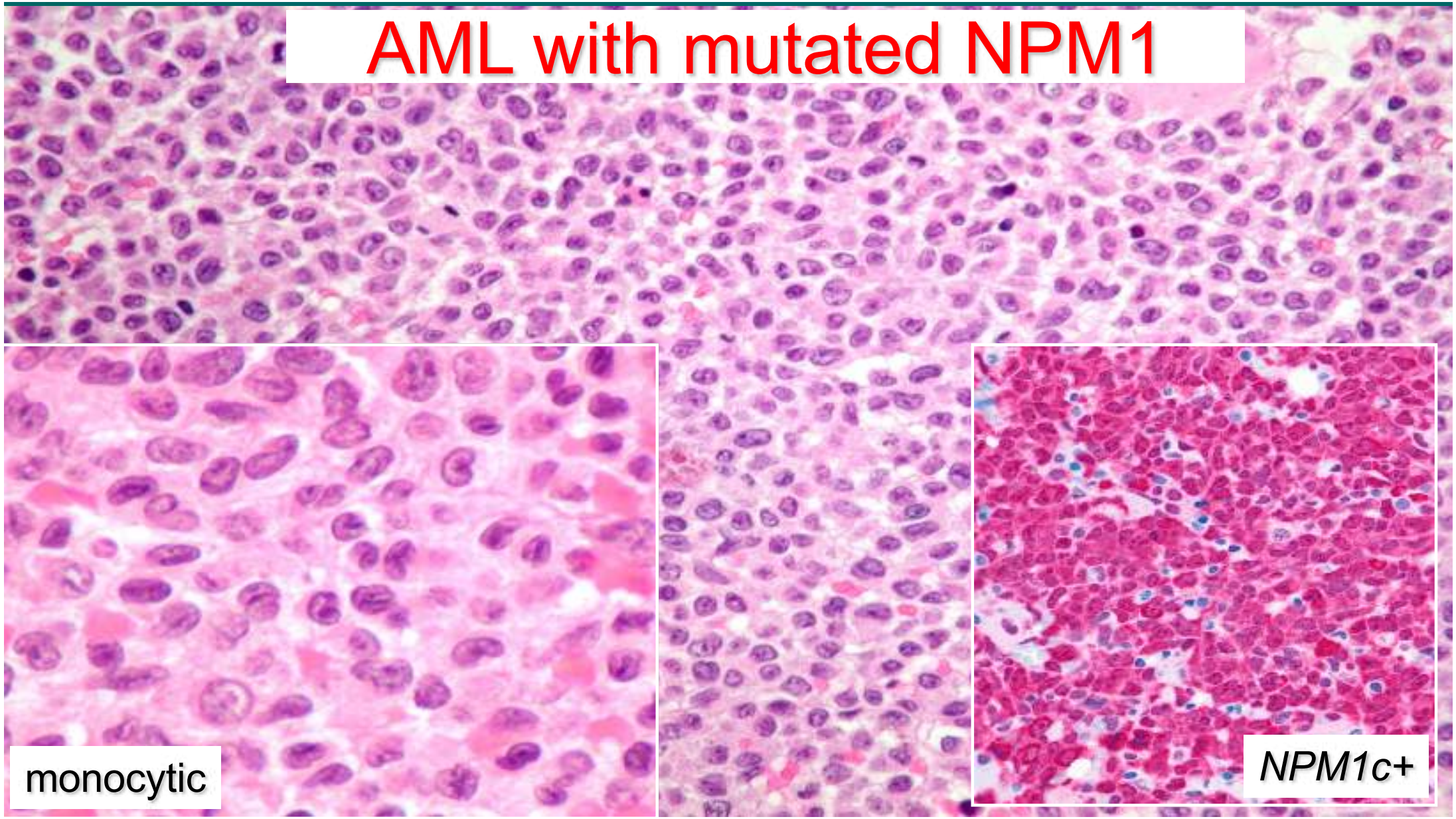
Fabio Facchetti,[1] Stefano A. Pileri,[2] Claudio Agostinelli,[2] Maria Paola Martelli,[3] Marco Paulli,[4] Adriano Venditti,[5] Massimo F Martelli,[3] and Brunangelo Falini[3]



NPM1c+

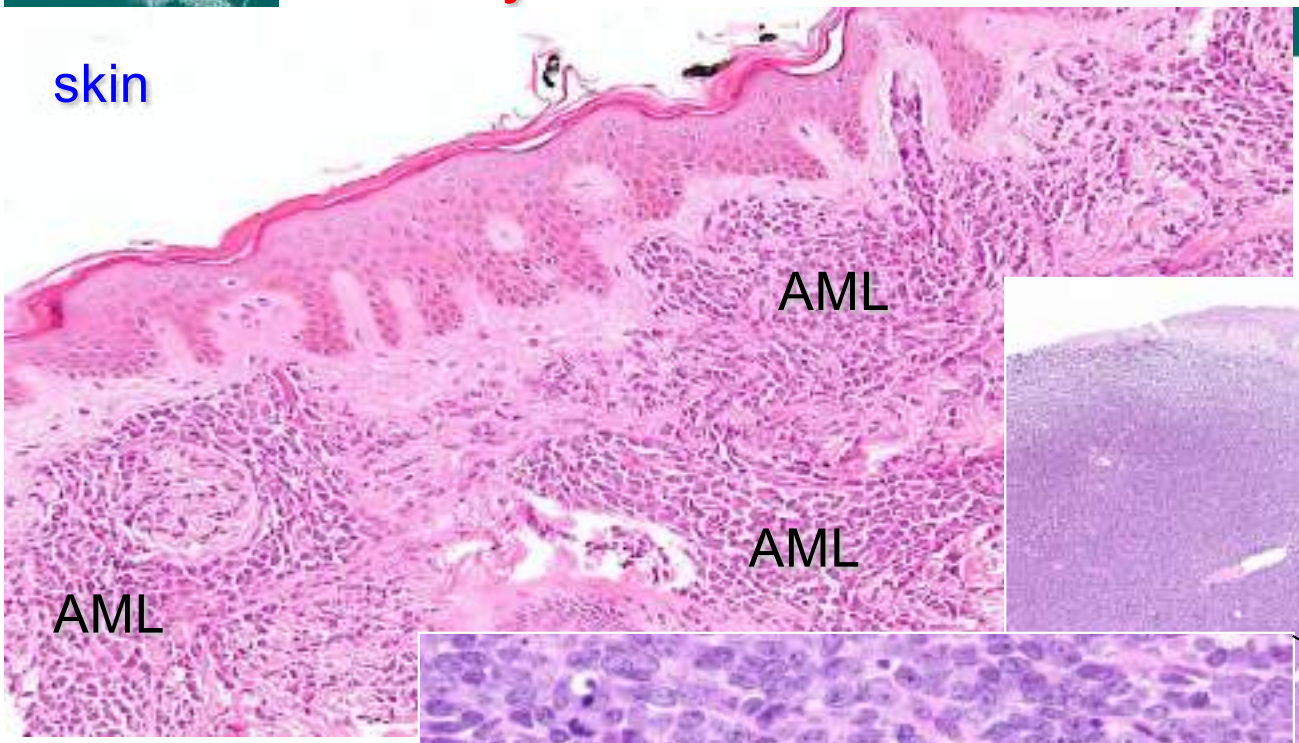
CD68PGM1+

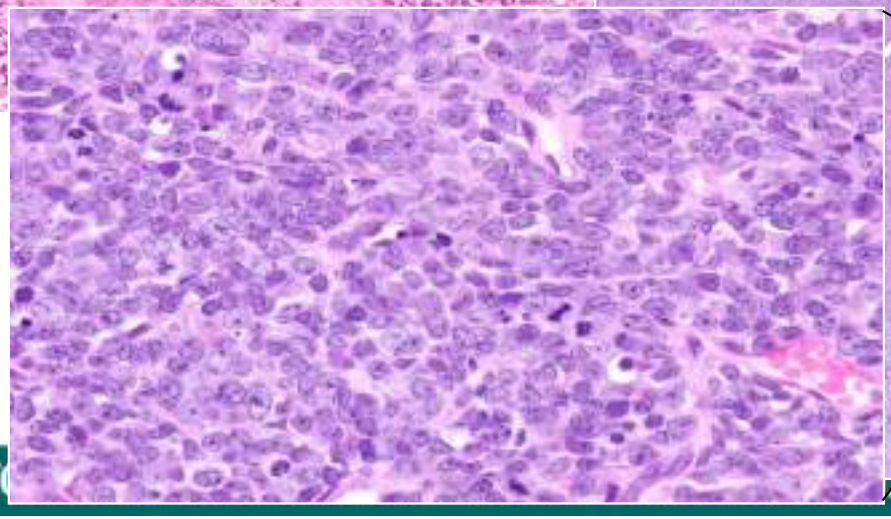
AML with mutated NPM1

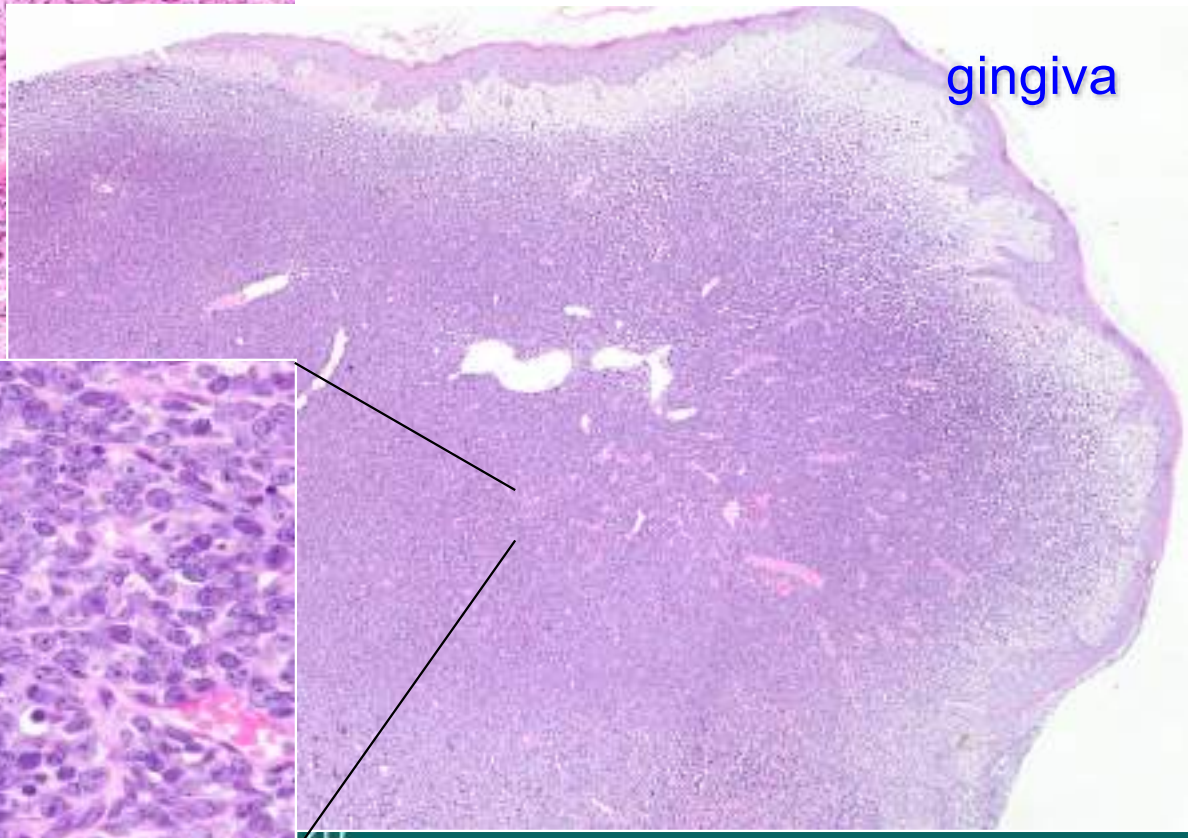


Many cases shows extramedullary involvement

skin







Genetic profile: NGS (FFPE)

Mutation	%
NPM1	15-28
FLT3-ITD	15
IDH2	7-11
RTK-RAS (NRAS, KRAS, CBL, PTPN11)	56
TP53	56-85
DNMT3A	21
RUNX1	7-11
KIT	14-15.4
TET2	16-21