Case 4

Presented by Lauren Jamieson
Principal Clinical Scientist
Synnovis, Kings College Hospital

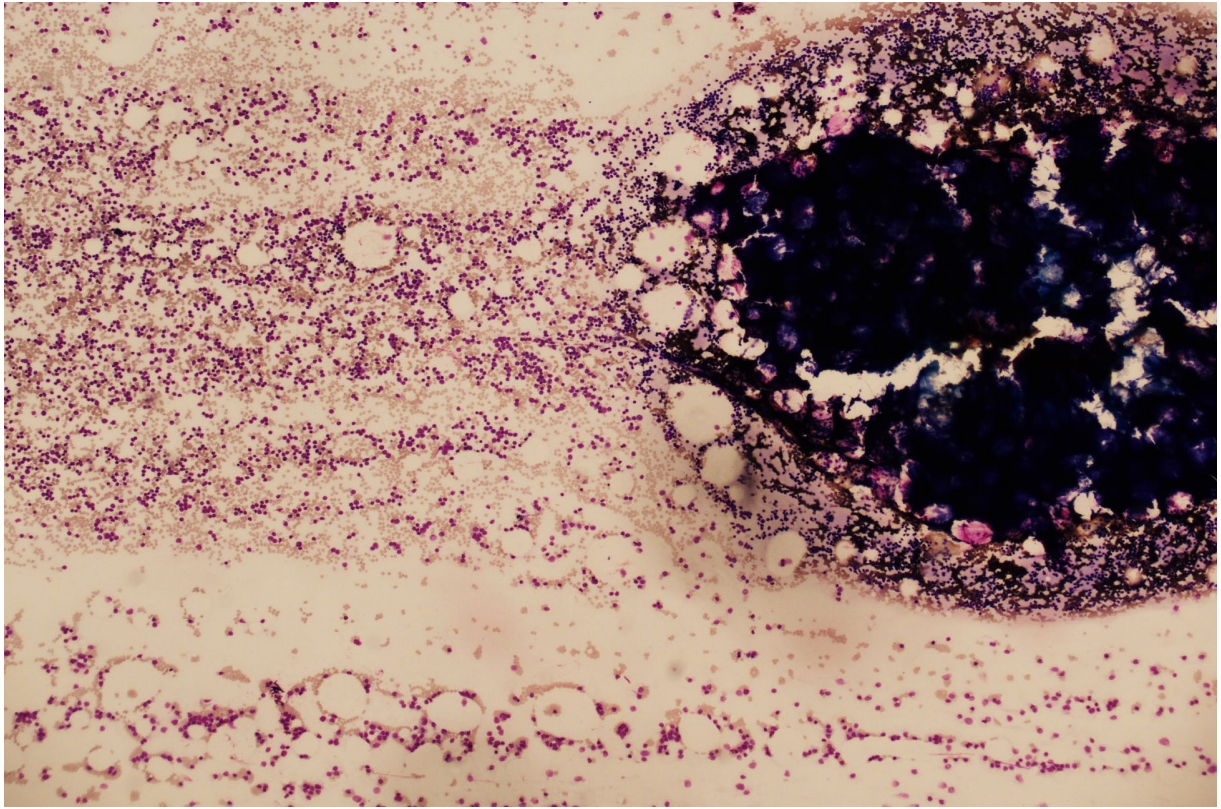
NHS
The Leeds Teaching Hospitals
NHS Trust

British Society for Haematology
Listening • Learning • Leading

Case 4

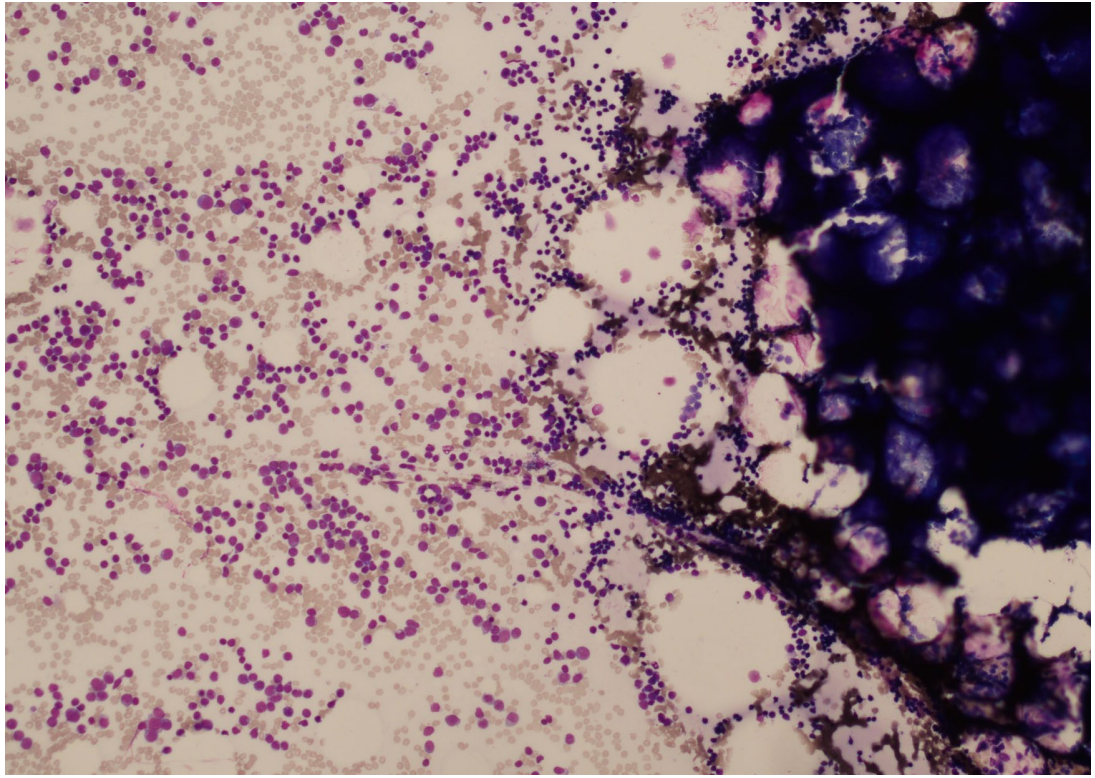
- 75 year old man
- PMH: nil to note
- Presented with pancytopenia: haemoglobin 70 g/L, platelets 30 x 10^9/L and neutrophils 0.6 x 10^9/L
- Suspected abnormal lymphoid population on peripheral blood film; bone marrow aspirate and trephine performed

Bone marrow aspirate x 10



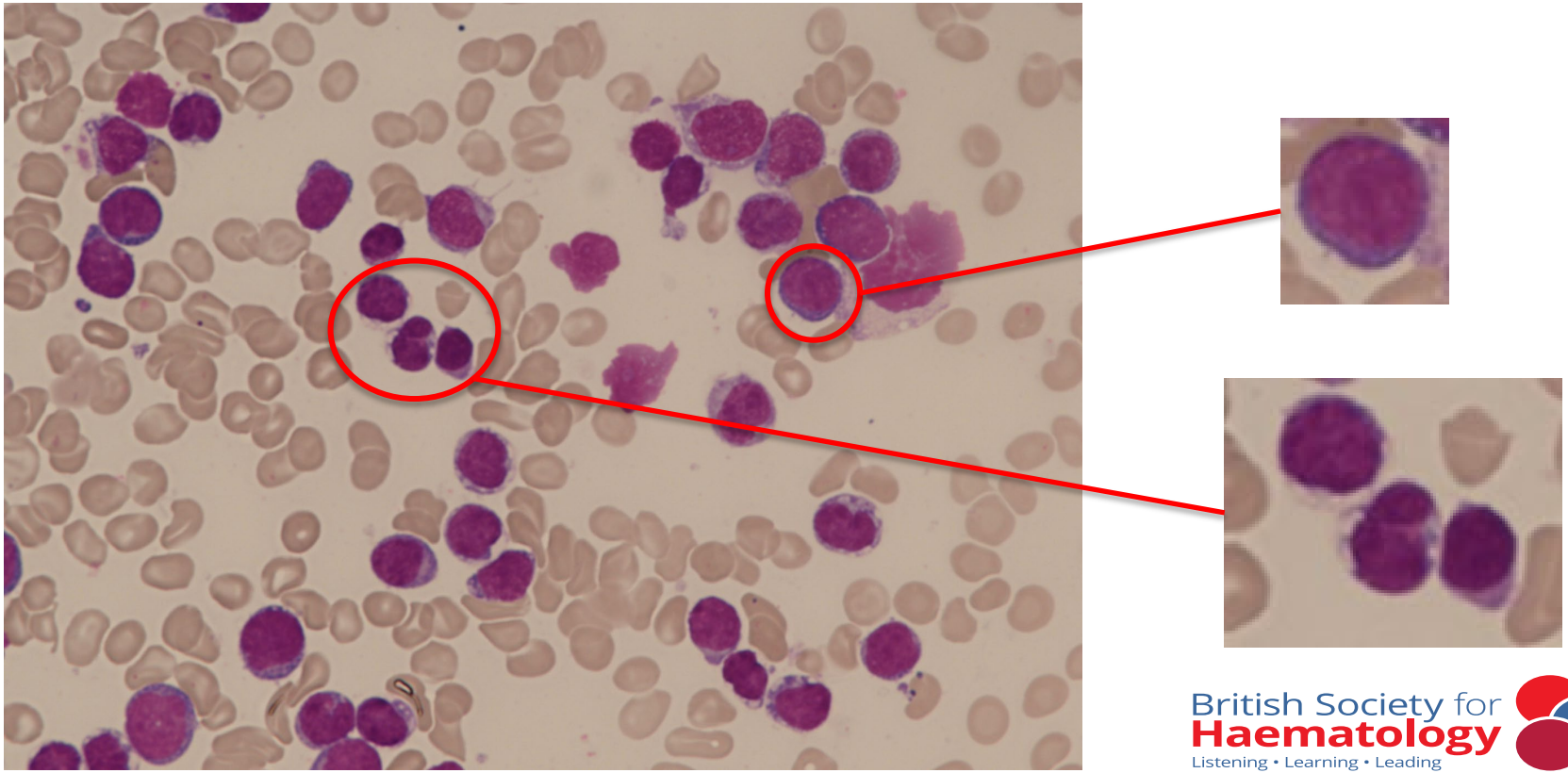
British Society for Haematology
Listening • Learning • Leading

Bone marrow aspirate x 20



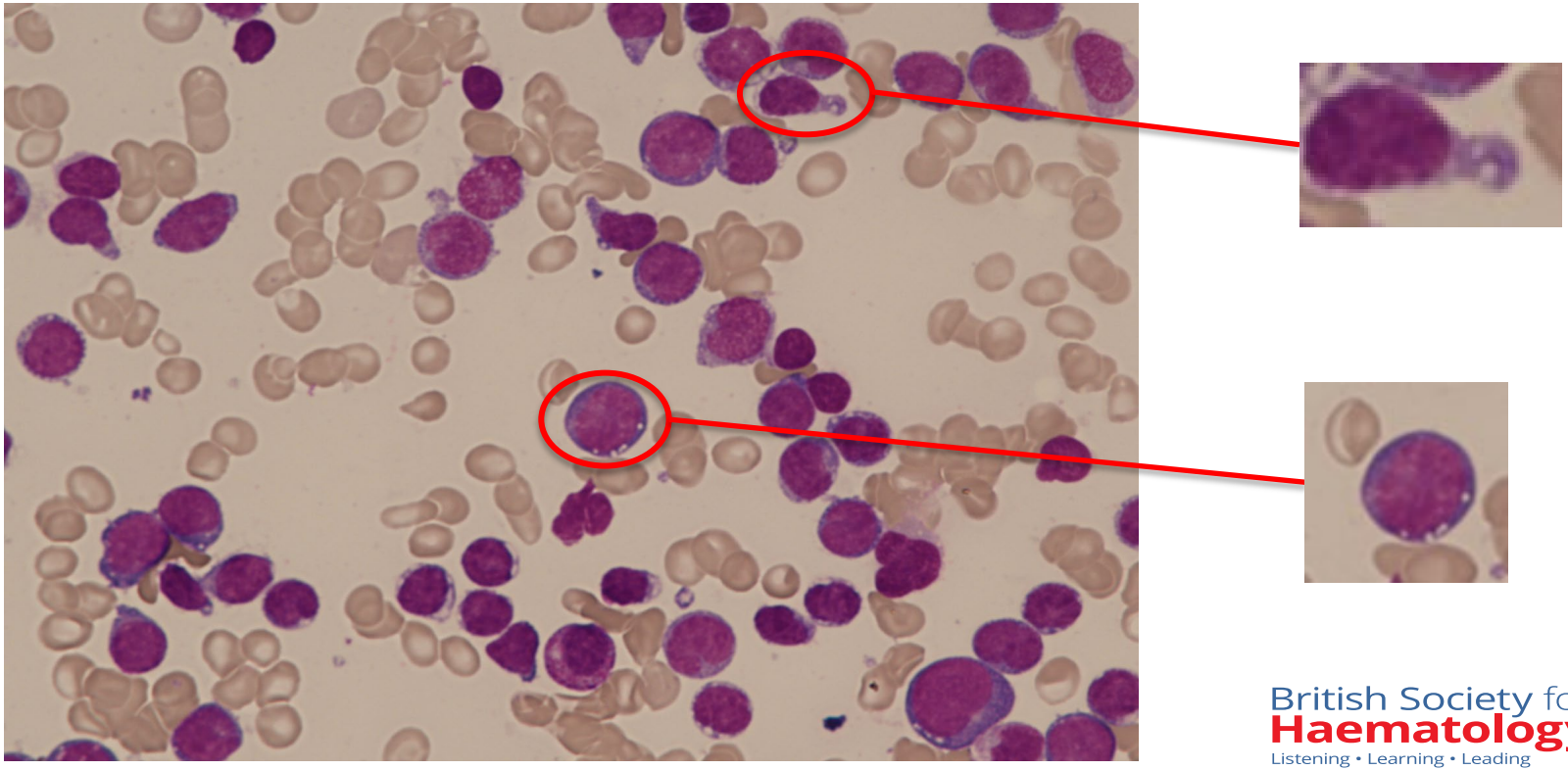
British Society for Haematology
Listening • Learning • Leading

Bone marrow aspirate x 40



British Society for Haematology
Listening • Learning • Leading

Bone marrow aspirate x 60

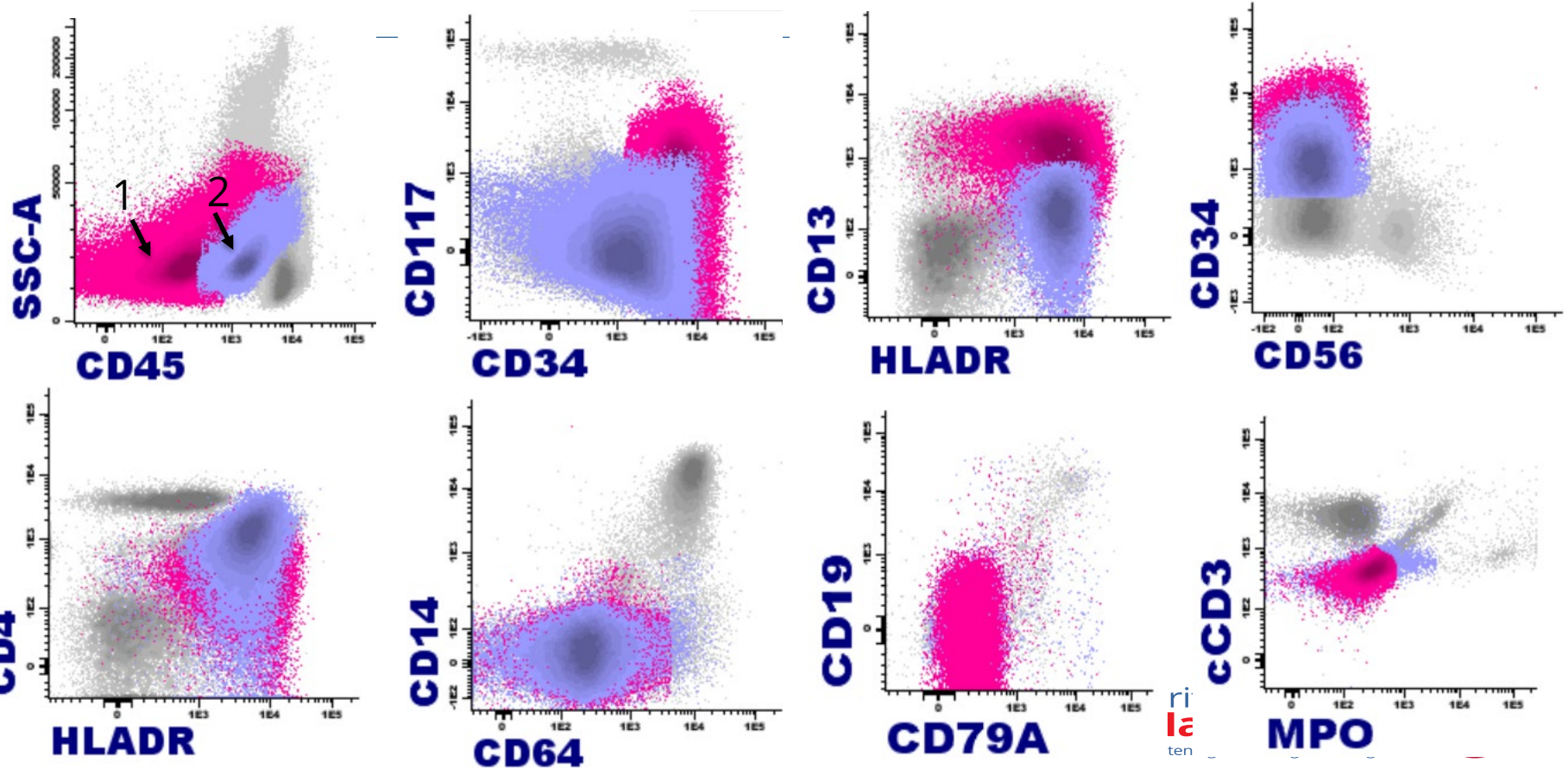


British Society for Haematology
Listening • Learning • Leading

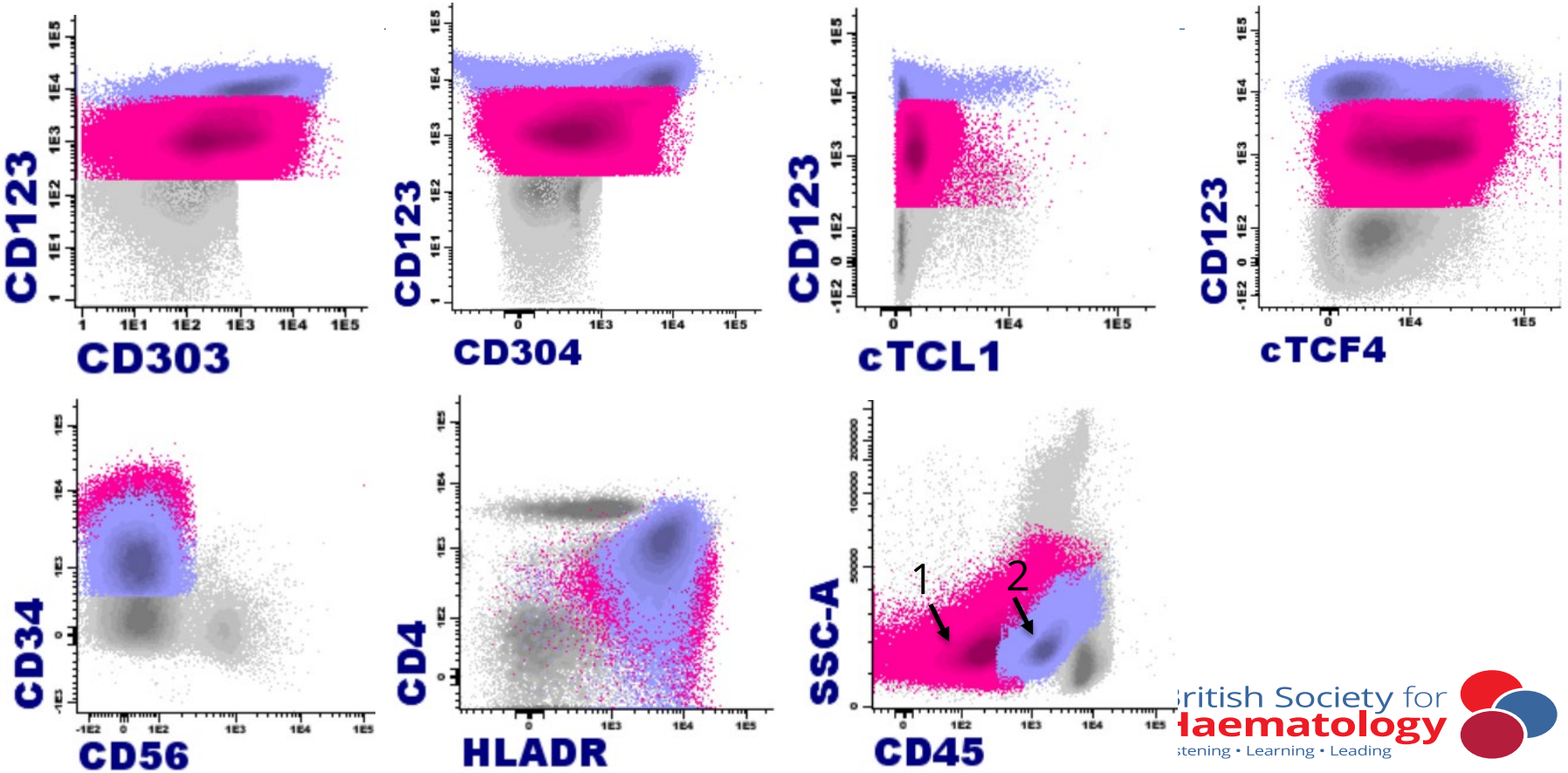
What is the suspected diagnosis?

a) Acute leukaemia
b) High grade transformation of low grade lymphoma
c) Acute leukemia and lymphoproliferative disorder
d) Low grade lymphoproliferative disorder
e) Insufficient information to make a diagnosis

Flow results



Flow results

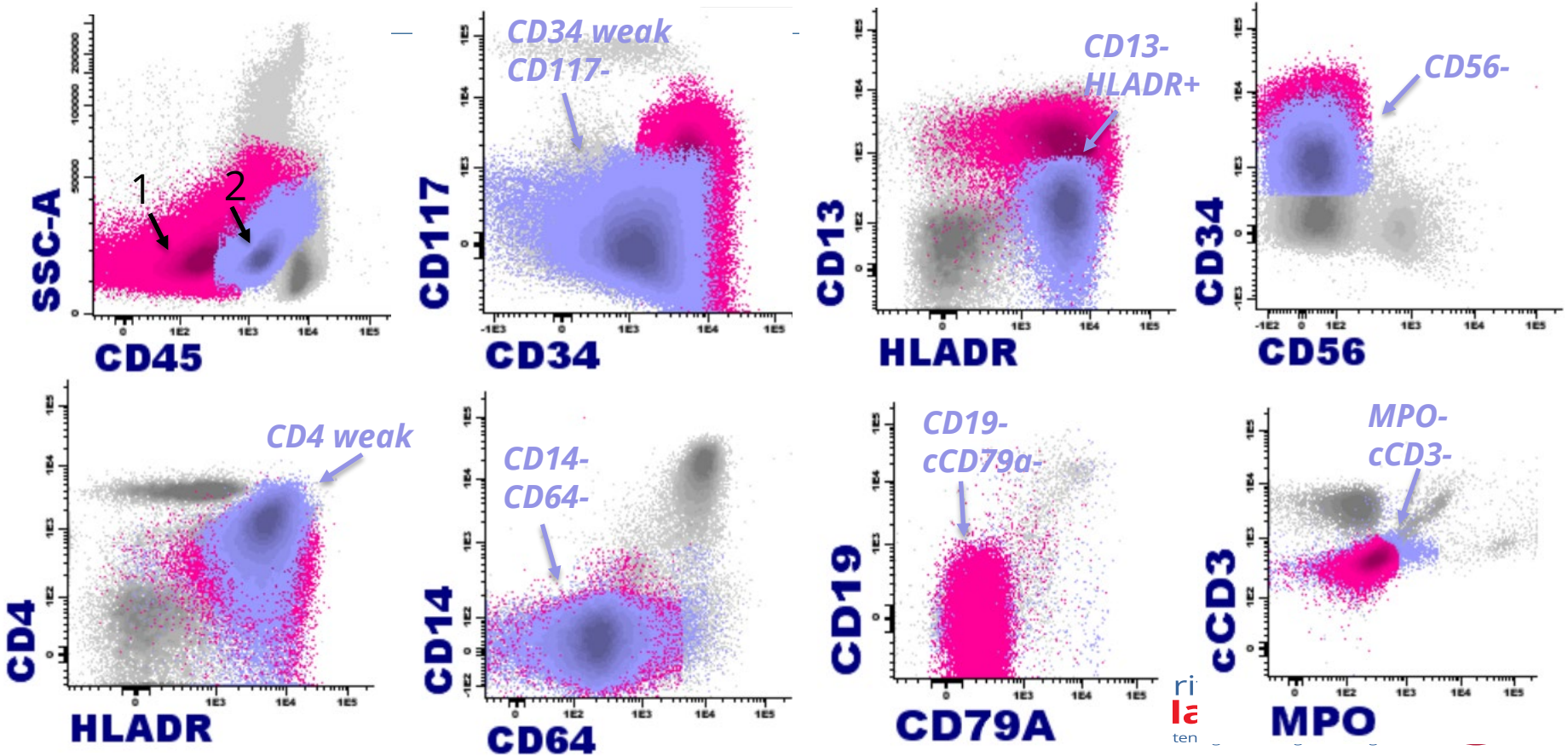


British Society for Haematology
Listening • Learning • Leading

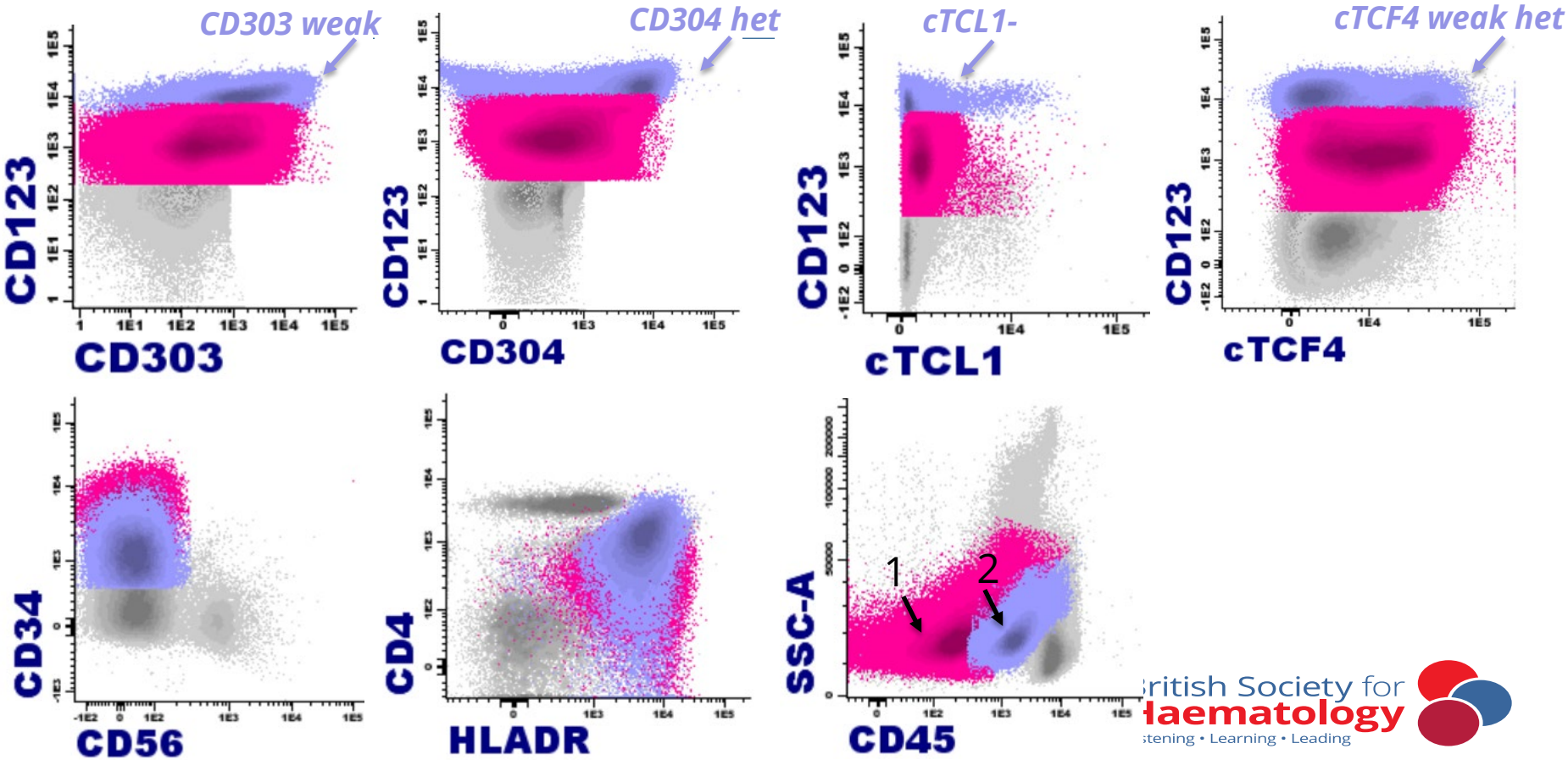
What is population 2 (purple)?

a) Monocytes
b) Myeloid progenitors
c) Plasmacytoid dendritic cells
d) T-cells
e) Basophils

Flow results

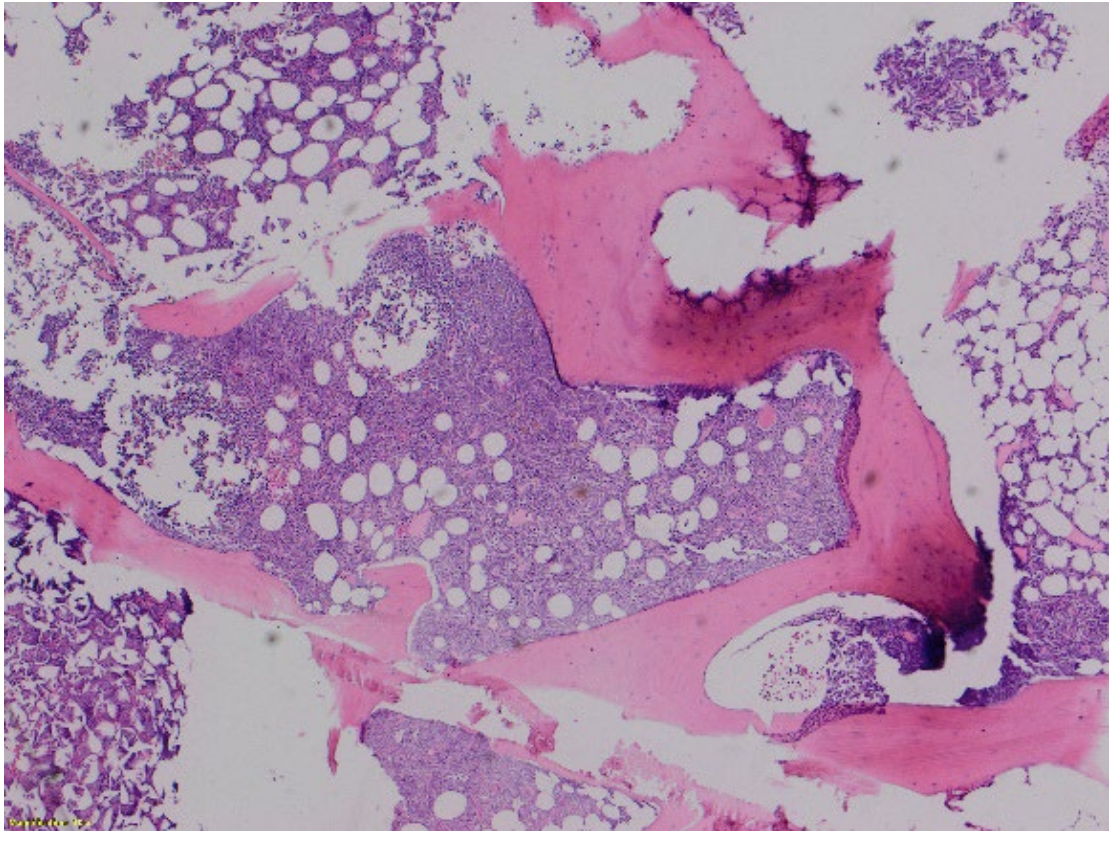


Flow results



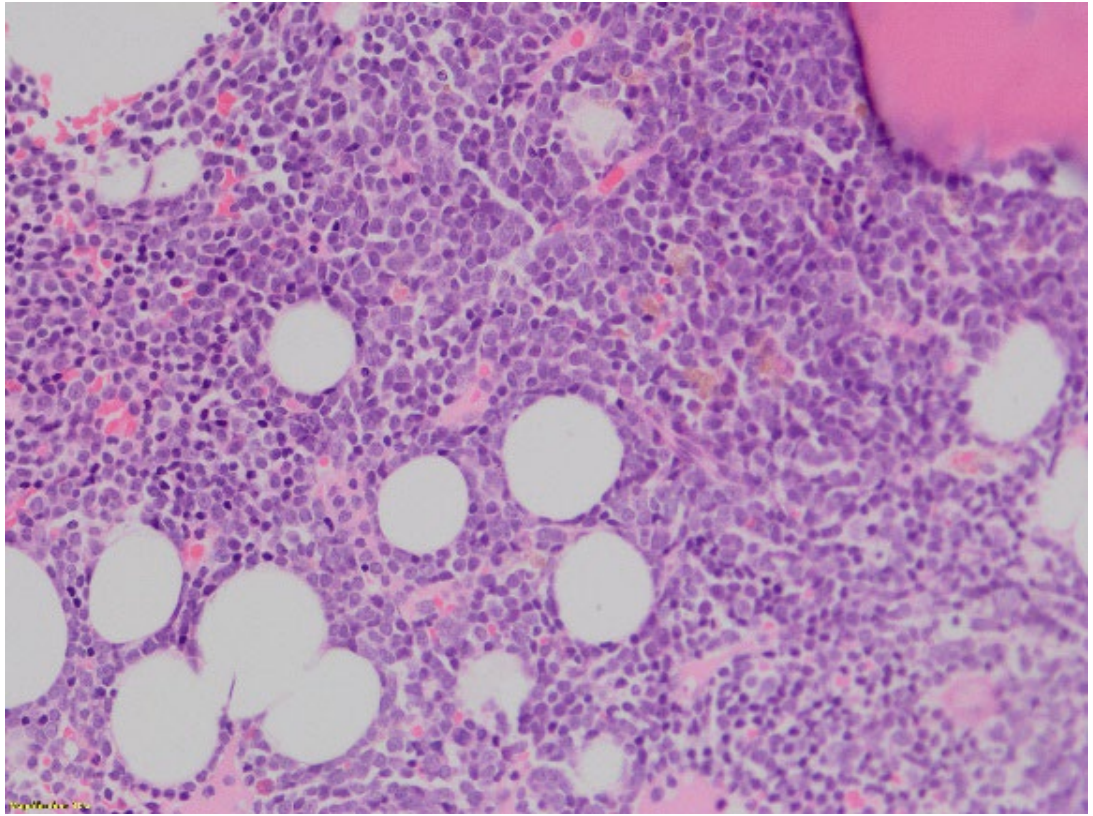
British Society for Haematology
Listening • Learning • Leading

Trephine



Hypercellular

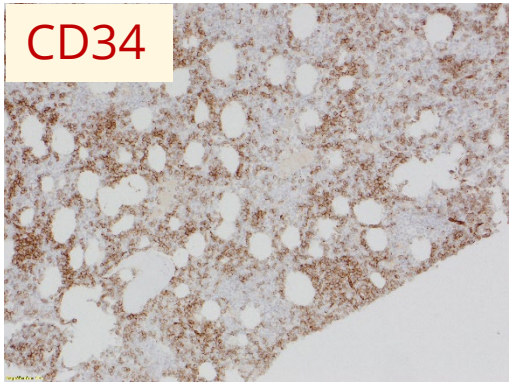
Trephine

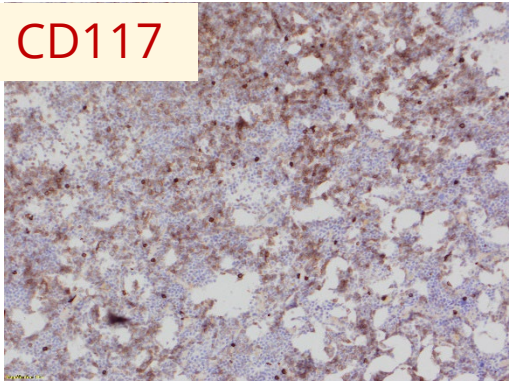


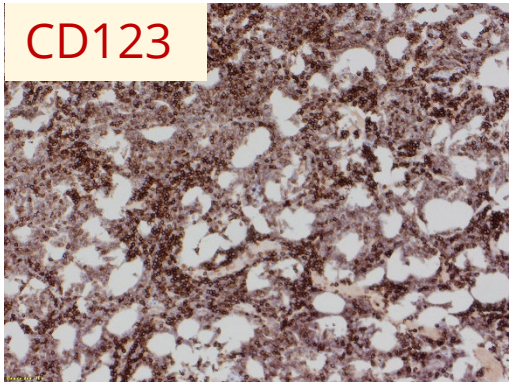
Higher power showing infiltration of the marrow by two populations

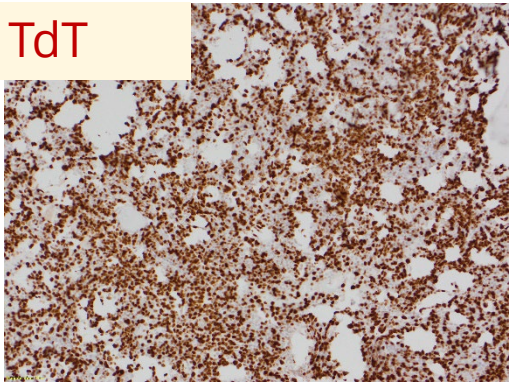
British Society for Haematology
Listening • Learning • Leading

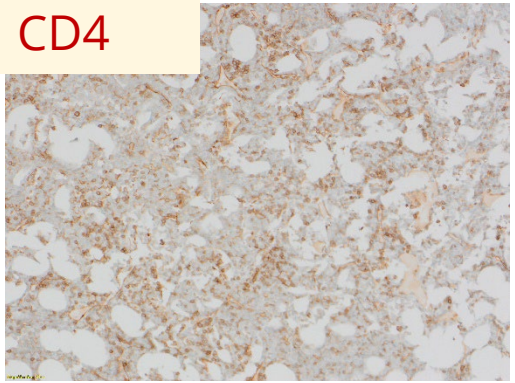
Immunohistochemistry

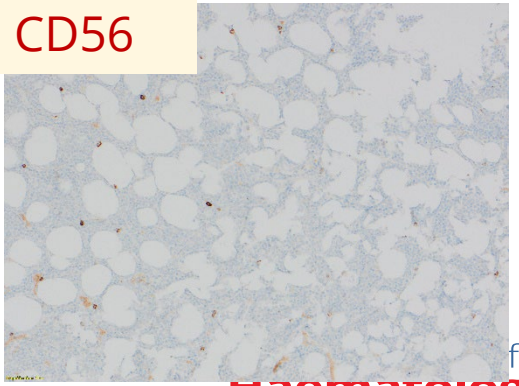




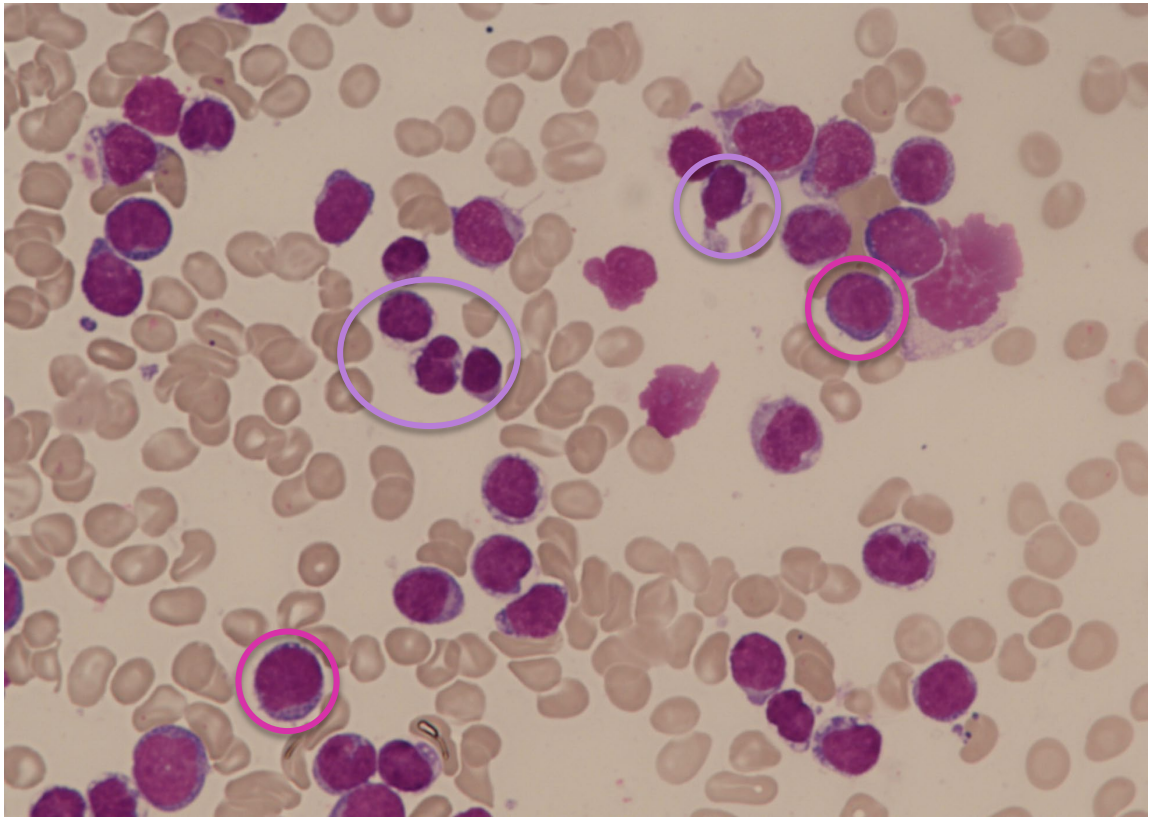








Bone marrow aspirate x 40



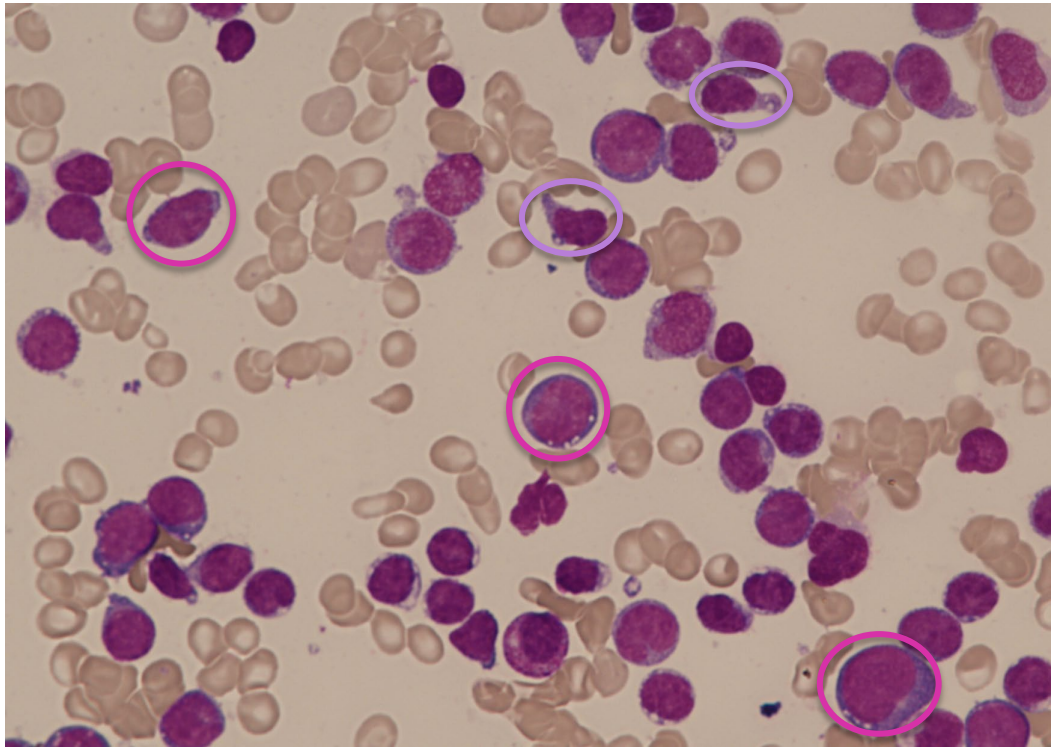
Two predominant populations:

Other cells

Blasts

British Society for Haematology
Listening • Learning • Leading

Bone marrow aspirate x 60



Two predominant populations:

Other cells

Blasts

British Society for Haematology
Listening • Learning • Leading

Genomics

Variants detected in:

- ASXL1
- EZH2 (x2)
- FLT3
- PTPN11
- RUNX1

What is the final diagnosis…?

a) Acute myeloid leukaemia
b) Blastic plasmacytoid dendritic cell neoplasm
c) AML with mature plasmacytoid dendritic cell proliferation
d) Dual diagnosis of acute myeloid leukaemia and blastic plasmacytoid dendritic cell neoplasm

Diagnosis

AML with mature plasmacytoid dendritic cell proliferation (AML-MPDCP)

WHO-HAEM5 Classification

AML with mature plasmacytoid dendritic cell proliferation (AML-MPDCP)

Essential and desirable diagnostic criteria

Essential: an accumulation of mature cells with plasmacytoid morphology and expression of CD123 and/or other pDC markers in the context of a defined myeloid neoplasm. ☑

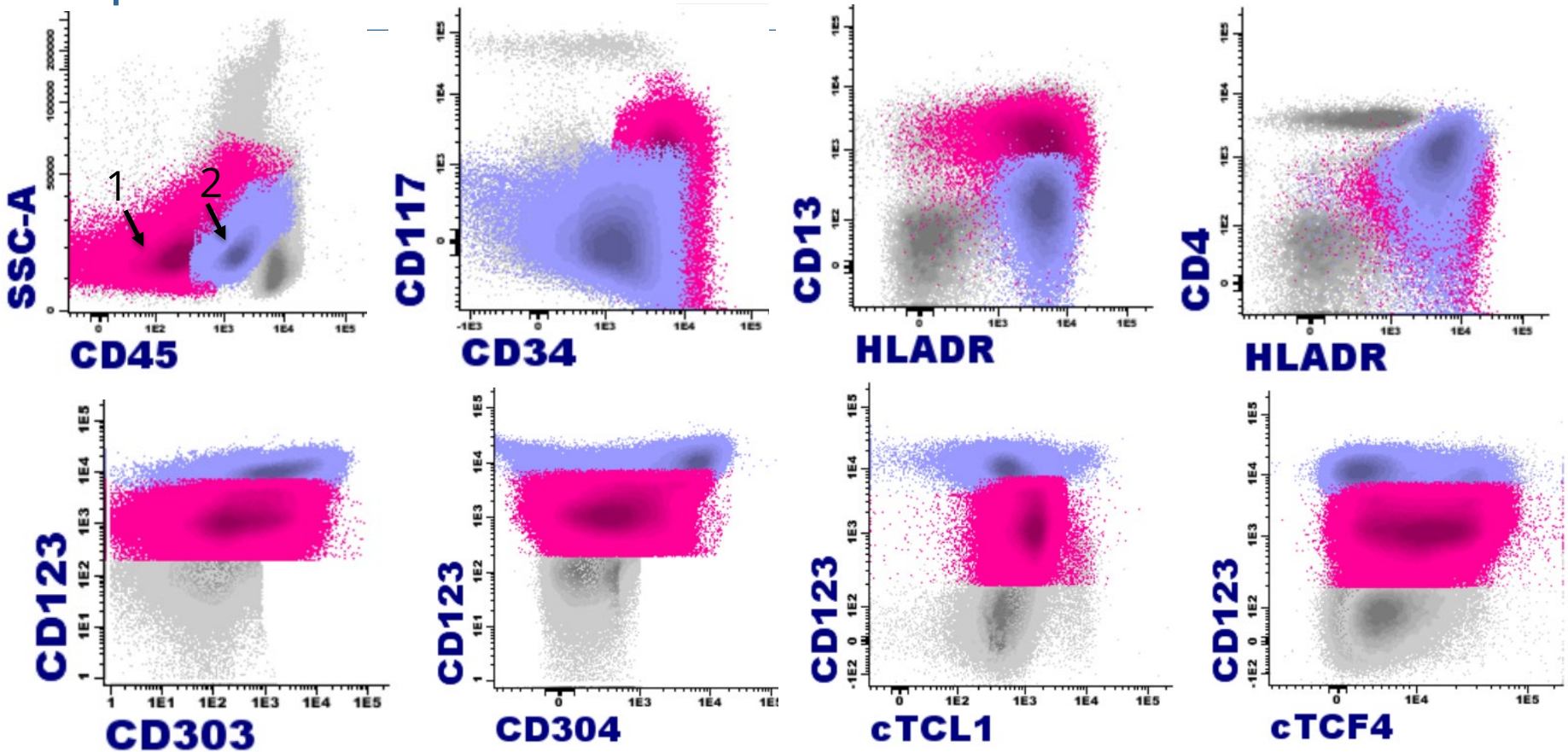
Desirable: an aberrant pDC immunophenotype; absent or low/partial expression of CD56. ☑

British Society for Haematology
Listening • Learning • Leading

Management

- The patient was treated as AML
- Outcome: The patient died during induction treatment

Phenotypic maturity spectrum & overlapping expression



pDC-AML: a distinct entity?

blood Regular Article

MYELOID NEOPLASIA

Plasmacytoid dendritic cell expansion defines a distinct subset of *RUNX1*-mutated acute myeloid leukemia

Wenbin Xiao,[1,2] Alexander Chan,[1] Michael R. Waarts,[2] Tanmay Mishra,[2] Ying Liu,[1] Sheng F. Cai,[2,3] Jinjuan Yao,[4] Qi Gao,[1] Robert L. Bowman,[2] Richard P. Koche,[5] Isabelle S. Csete,[2] Nicole L. DelGaudio,[2] Andriy Derkach,[6] Jeeyeon Baik,[1] Sophia Yanis,[1] Christopher A. Famulare,[7] Minal Patel,[7] Maria E. Arcila,[1,4] Maximilian Stahl,[3] Raajit K. Rampal,[2,3] Martin S. Tallman,[3] Yanming Zhang,[8] Ahmet Dogan,[1] Aaron D. Goldberg,[3] Mikhail Roshal,[1] and Ross L. Levine[2,3,5,7]

[1]Department of Pathology, Hematopathology Service, [2]Human Oncology and Pathogenesis Program, Molecular Cancer Medicine Service, [3]Department of Medicine, Leukemia Service, [4]Department of Pathology, Molecular Diagnostic Laboratory, [5]Center for Epigenetics Research, [6]Department of Epidemiology-Biostatistics, [7]Center for Hematologic Malignancies, and [8]Department of Pathology, Cytogenetics Laboratory, Memorial Sloan Kettering Cancer Center, New York, NY

KEY POINTS

- pDC-AML is characterized by a high frequency of *RUNX1* mutations and increased expression of a pDC transcriptional program.
- CD123 targeting represents a potential treatment approach for pDC-AML.

Plasmacytoid dendritic cells (pDCs) are the principal natural type I interferon–producing dendritic cells. Neoplastic expansion of pDCs and pDC precursors leads to blastic plasmacytoid dendritic cell neoplasm (BPDCN), and clonal expansion of mature pDCs has been described in chronic myelomonocytic leukemia. The role of pDC expansion in acute myeloid leukemia (AML) is poorly studied. Here, we characterize patients with AML with pDC expansion (pDC-AML), which we observe in ~5% of AML cases. pDC-AMLs often possess cross-lineage antigen expression and have adverse risk stratification with poor outcome. *RUNX1* mutations are the most common somatic alterations in pDC-AML (>70%) and are much more common than in AML without pDC expansion and BPDCN. We demonstrate that pDCs are clonally related to, as well as originate from, leukemic blasts in pDC-AML. We further demonstrate that leukemic blasts from *RUNX1*-mutated AML upregulate a pDC transcriptional program, poising the cells toward pDC differentiation and expansion. Finally, tagraxofusp, a targeted therapy directed to CD123, reduces leukemic burden and eliminates pDCs in a patient-derived xenograft model. In conclusion, pDC-AML is characterized by a high frequency of *RUNX1* mutations and increased expression of a pDC transcriptional program. CD123 targeting represents a potential treatment approach for pDC-AML. (*Blood*. 2021;137(10):1377-1391)

- *"It is recognised that in some cases of AML there might be a continuous phenotypical spectrum between the mature pDCs present and dominant AML".* WHO-HAEM5

British Society for Haematology
Listening • Learning • Leading

Acknowledgments

- Dr Guy Hannah
- Dr Liron Barnea-Slonim
- Kate Jones
- Lab & clinical teams, SE-HMDS
- Support from IAF A016