Hematologic malignancies in children

Denmark 1980 – 91,British Columbia 1982 – 96, and UK 1990-99

Leukemia 1995; 9: 1569, BJH 1999; 106: 1027, BJH 2003;121:758

incidence/million children/year

	DK+BC	UK
AML	5.4	5.8
MDS	1.8	0.8
ML of DS	0.9	0.6
JMML	1.2	0.6
CML	0.6	0.5

Pediatric Aspects of MDS

Down Syndrome Disease

Transient abnormal myelopoiesis (TAM)

Myeloid leukemia of DS

Myelodysplastic Syndrome	PB blasts (%)	BM blasts (%)
Refractory Cytopenia (RC)	< 2	< 5
Refractory anemia excess blasts (RAEB)	2 - 19	5 - 19
RAEB in transformation (RAEB-T)	20 - 29	20 – 29

Juvenile myelomonocytic Leukemia (JMML)

Splenomegaly

Leukocytosis, monocytosis

Increased Hb F

Monosomy 7

Hasle et al.: Leukemia 2003;17(2):277

Pediatric Aspects of the WHO Classification

Secondary MDS Prior chemo- or radiation therapy

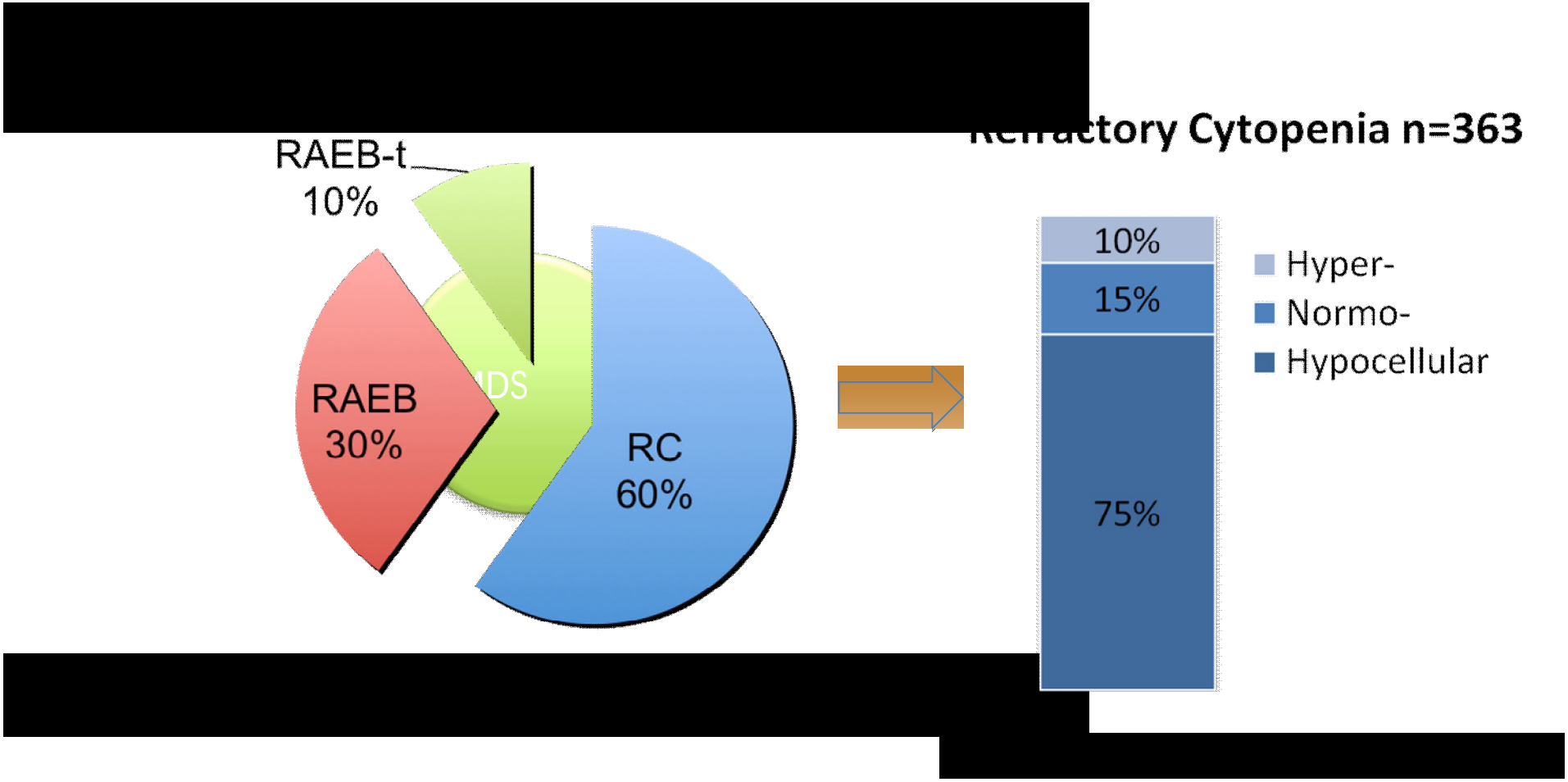
Prior acquired aplastic anemia

In congenital bone marrow failure disorder

In familial disease (first degree relative)

Primary MDS All other

Primary MDS


RAEB-t
10%
RAEB
30%
MDS
RC
60%
Refractory Cytopenia n=363
10%
15%
75%
Hyper-
Normo-
Hypocellular

Down Syndrome (DS), Transient abnormal myelopoiesis (TAM) and MDS/AML

(Wechsler , Nature Genetics 2002,32,148,Klusman, Blood, 2008,Kanezaki, Blood, 2010)

- 10% DS have TAM
- 20-25% recur with MDS/AML
- Risk of MDS/AML x 700 in DS
- TAM and MDS/AML both associated to GATA 1 mutations
- Risk of progression of TAM related to GATA 1 expression
- preventive effect of AraC on progression to MDS/AML

Molecular biology in JMML

GM-CSF-mediated RAS/MAP kinase pathway signaling involved in 75% of JMML patients

- RAS mutations found in 15-20%
- NF1 mutations found in 30%

- *PTPN11* mutations found in 33%

+CBL mutations

Traitement des SMD de l'enfant

Allogreffe ++++++

- Dans les LMMJ,AREB, AREBt
- Dans les cytopénies réfractaires avec anomalies chromosomiques ou cytopénies importantes

Therapy for Refractory cytopenia: Current Approach of EWOG-MDS