

Measurable Residual Disease in Acute Myeloid Leukemia

Detection of Leukemia Stem Cells

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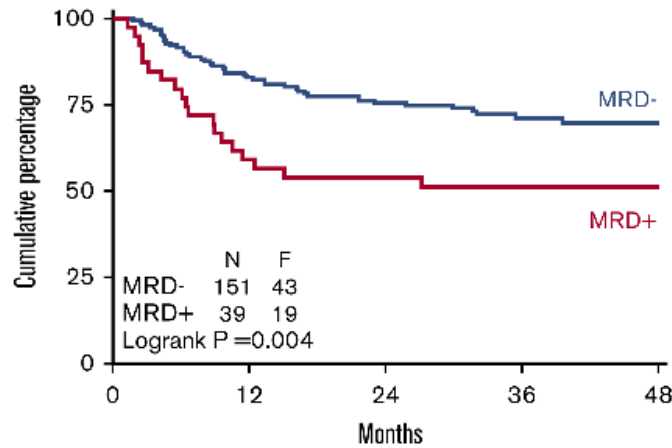
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MRD negative patients relapse

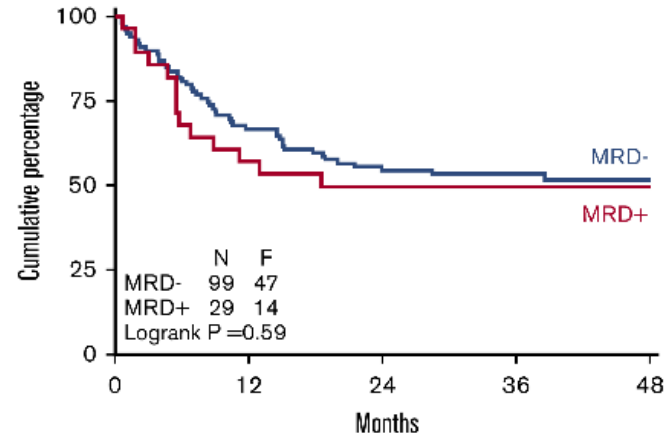
A Relapse-free survival from date MRD sample after cycle 2
Favorable ELN 2017 risk group



At risk:		0	12	24	36	48
MRD-	151	124	110	62	19	
MRD+	39	23	21	9	2	

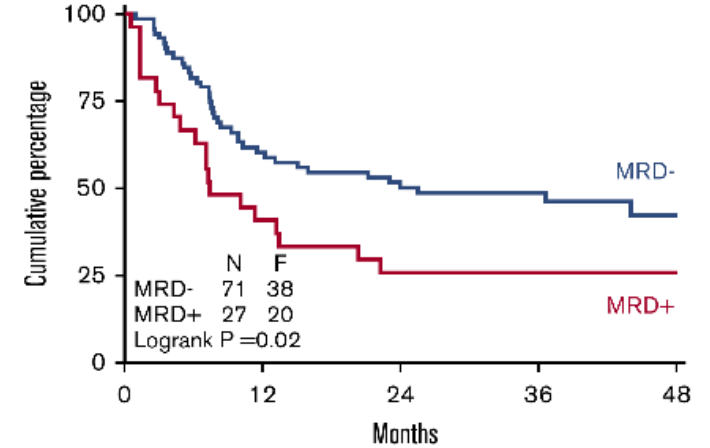
25% of MRD- favorable patients relapse

B Relapse-free survival from date MRD sample after cycle 2
Intermediate ELN 2017 risk group



At risk:		0	12	24	36	48
MRD-	99	66	54	32	10	
MRD+	29	16	12	12	5	

C Relapse-free survival from date MRD sample after cycle 2
Adverse ELN 2017 risk group



At risk:		0	12	24	36	48
MRD-	71	42	35	21	4	
MRD+	27	11	7	5	4	

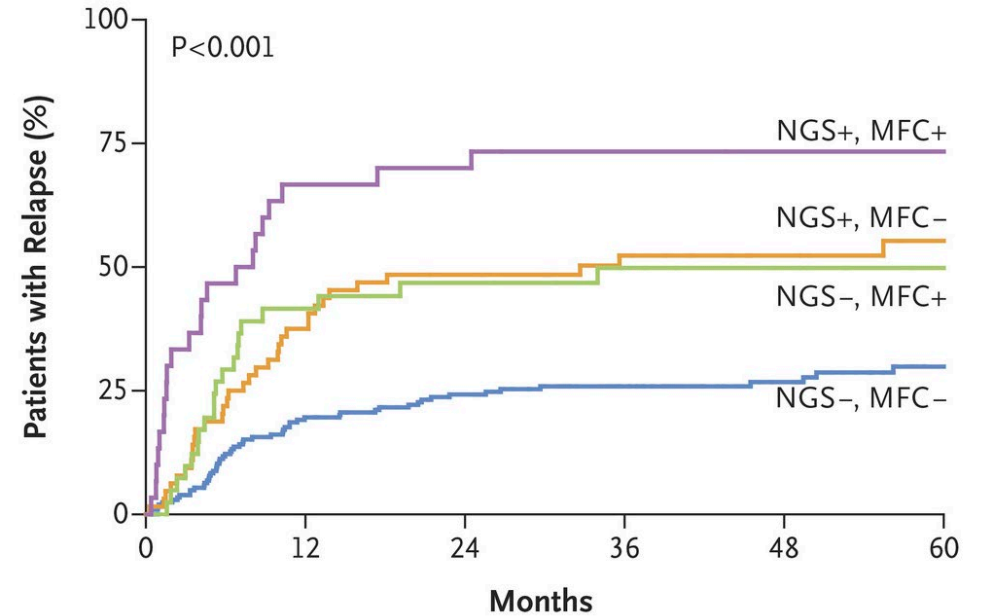
50% of MRD- adverse patients relapse

Prognostic value lost due to therapy guidance



Strategies to improve MRD assessment

- Molecular MRD
- Sequential MRD monitoring
- Incorporation of Leukemia Stem Cells

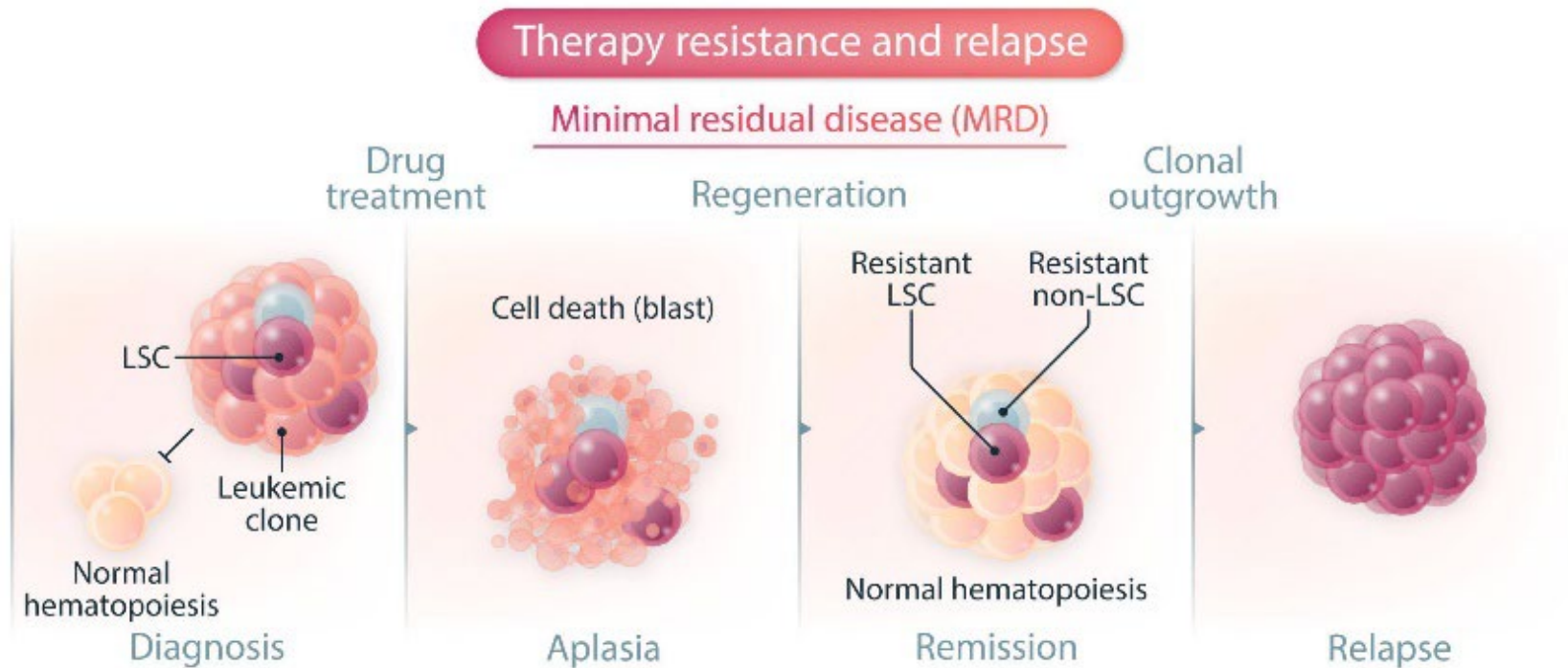


No. at Risk							
NGS+, MFC+	30	8	7	5	4	4	
NGS-, MFC+	41	22	18	14	11	7	
NGS+, MFC-	64	39	30	22	15	11	
NGS-, MFC-	205	153	130	101	69	42	



Leukemia Stem Cell concept

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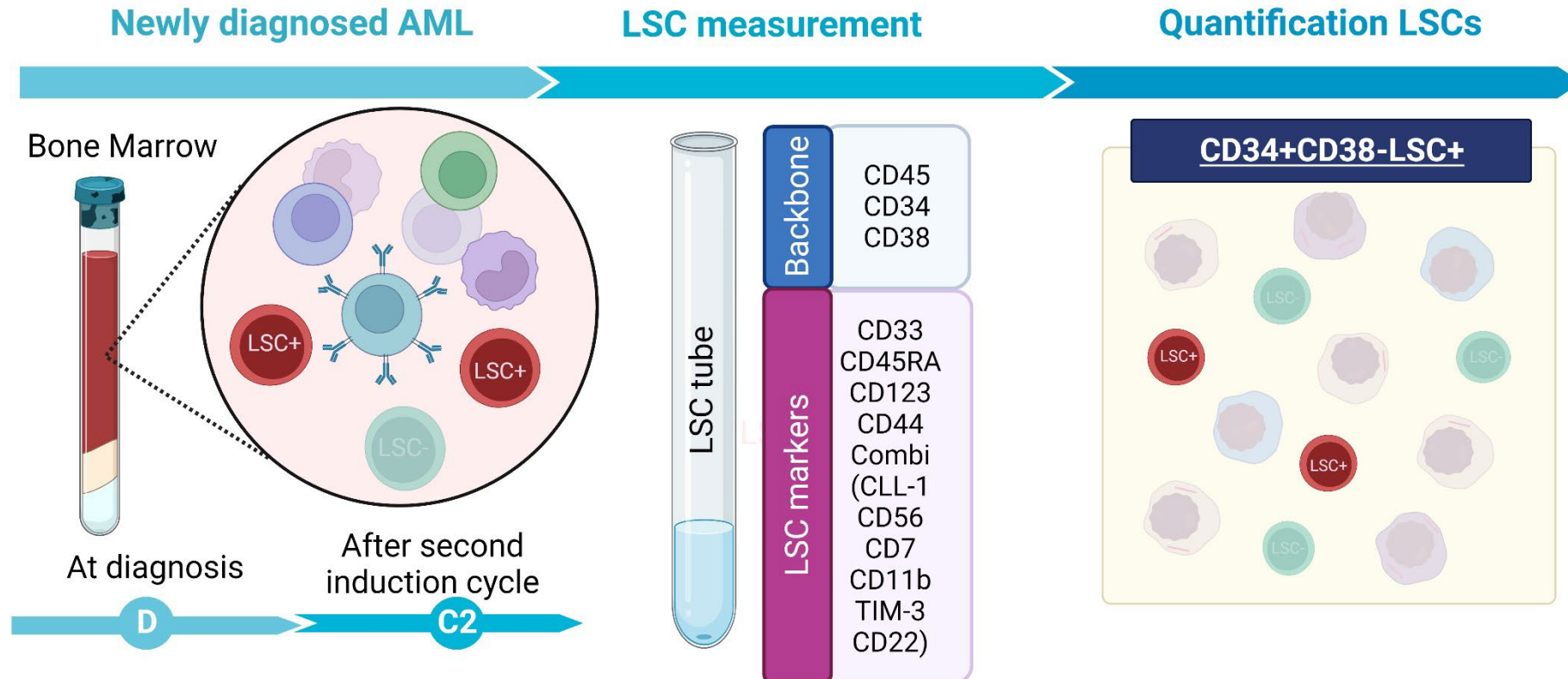


Leukemia Stem Cell concept

- Immunophenotype
 - LSC: CD45dimCD34+CD38-LSC+
 - Aberrant LSC marker positive
 - HSC: CD45dimCD34+CD38-LSC-



One tube LSC assay



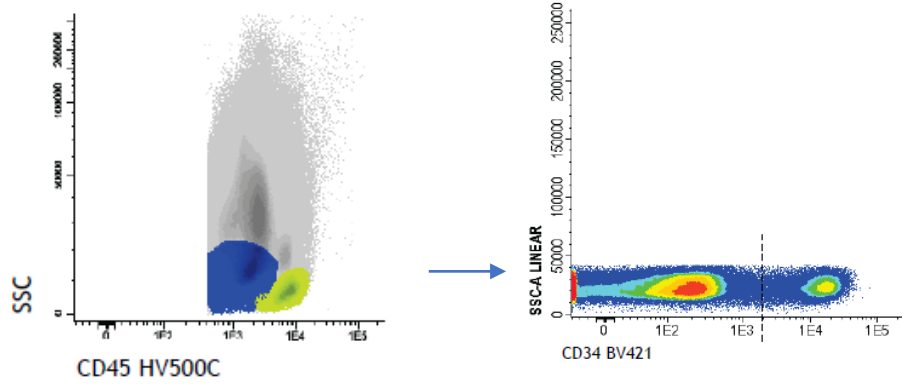


Challenges one tube LSC assay

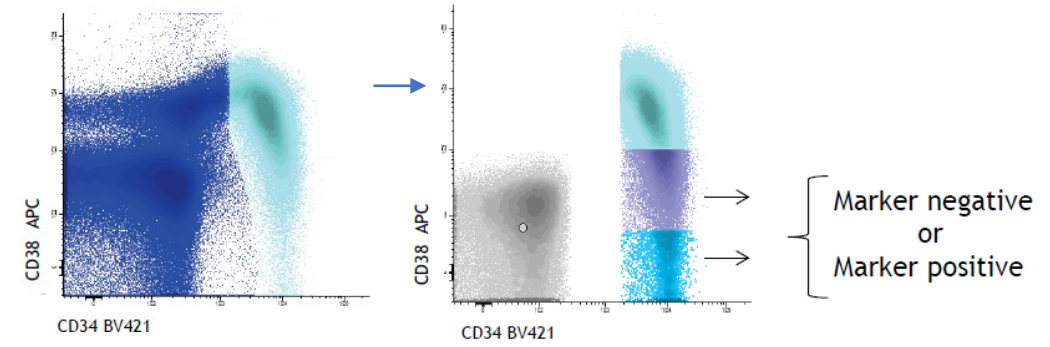
Tube	FITC	PE	PerCP-CY5.5	PeCy7	APC	APC-H7	BV421	HV500C
1	CD45RA	CLL-1 TIM-3 CD7 CD11b CD22 CD56	CD123	CD33	CD38	CD44	CD34	CD45

- No universal LSC marker to detect LSCs
- Diagnosis cut-off: 0.03%
- Follow up cut-off: 0.0000%
- Acquisition of 4,000,000 cells, thus BM material is limiting factor
- Needs validation
- Requires standardization and harmonization
- CD34-negative AML

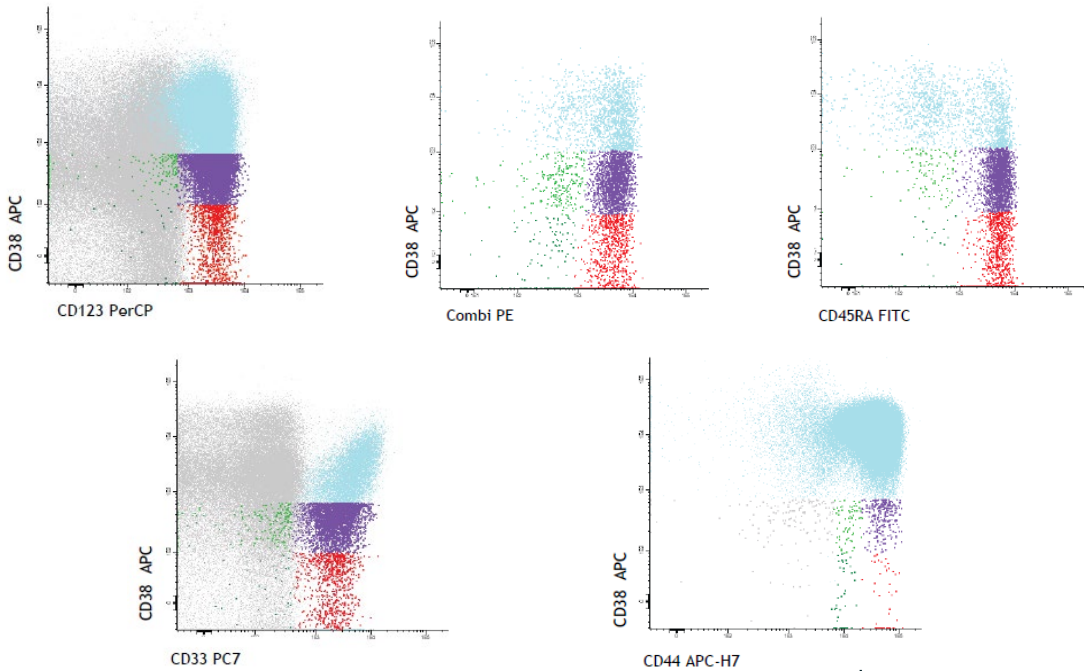
Gating CD45dim cells + CD34+ blasts



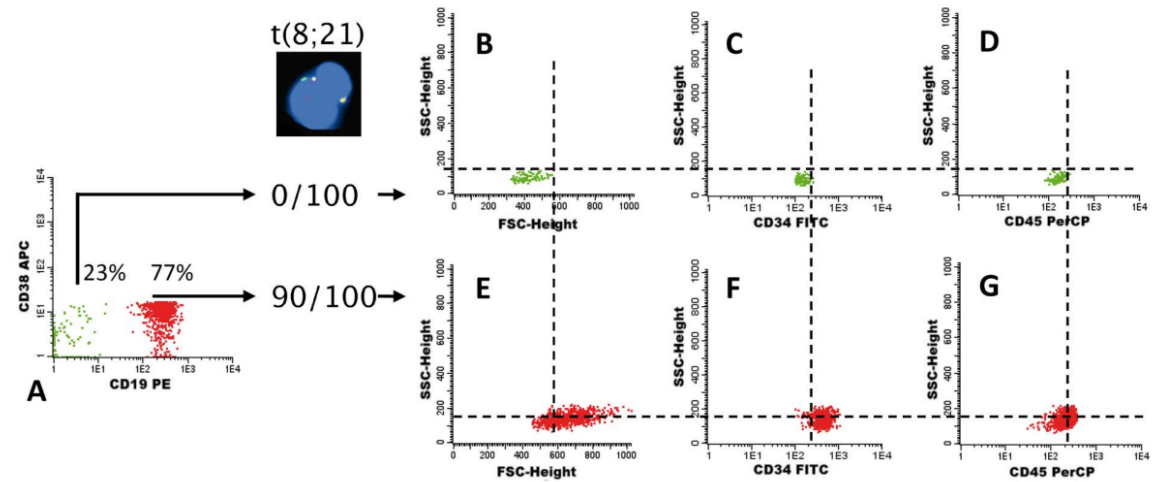
Gating CD38



Gating LSC

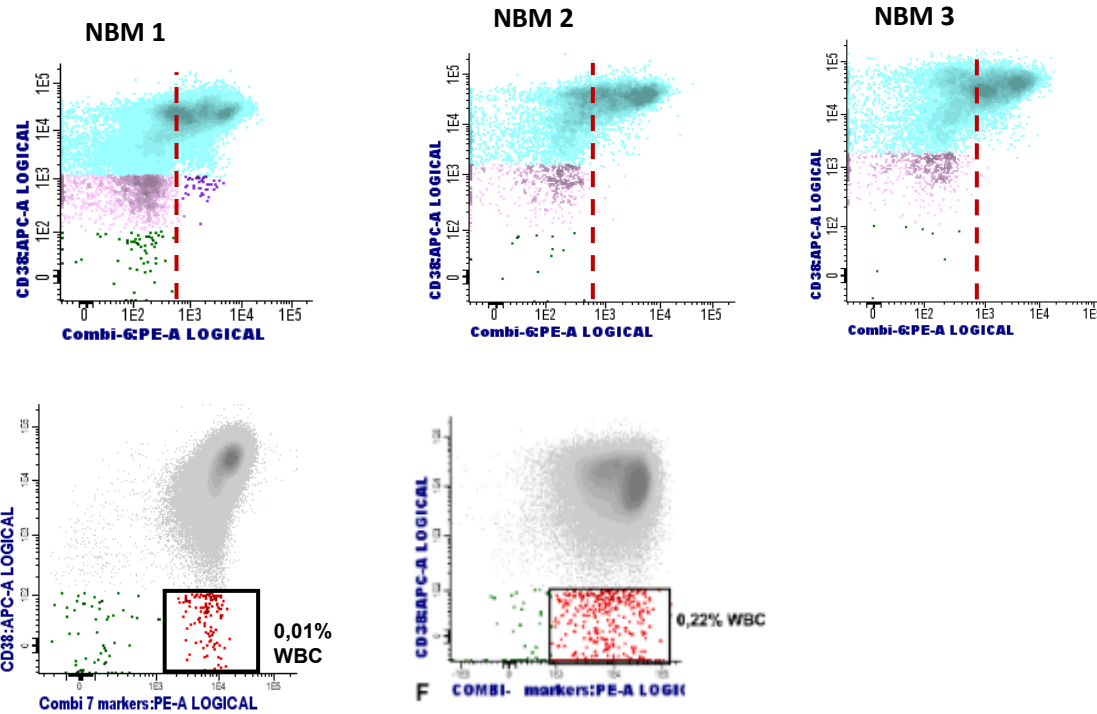


Backgating based on physical properties



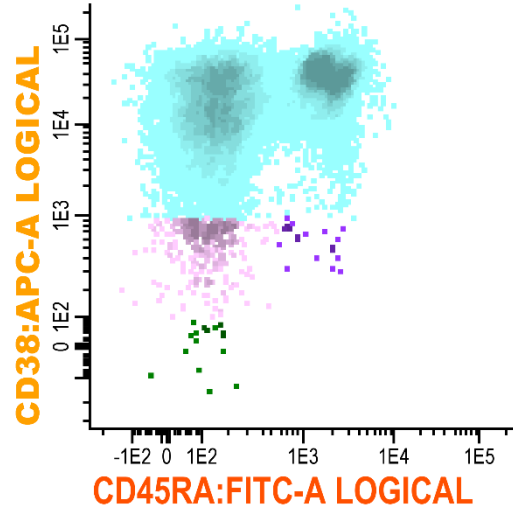


One tube LSC assay

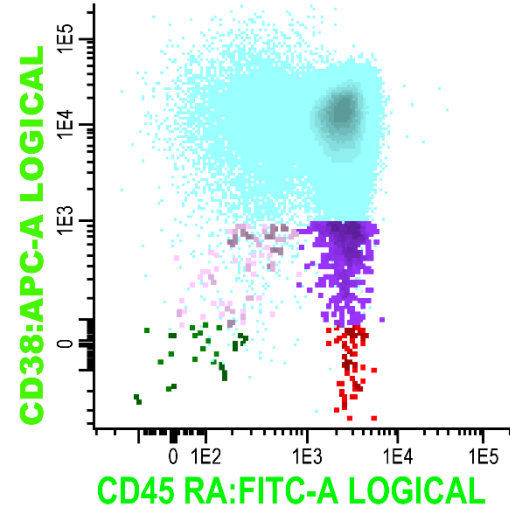




One tube LSC assay



Normal bone marrow

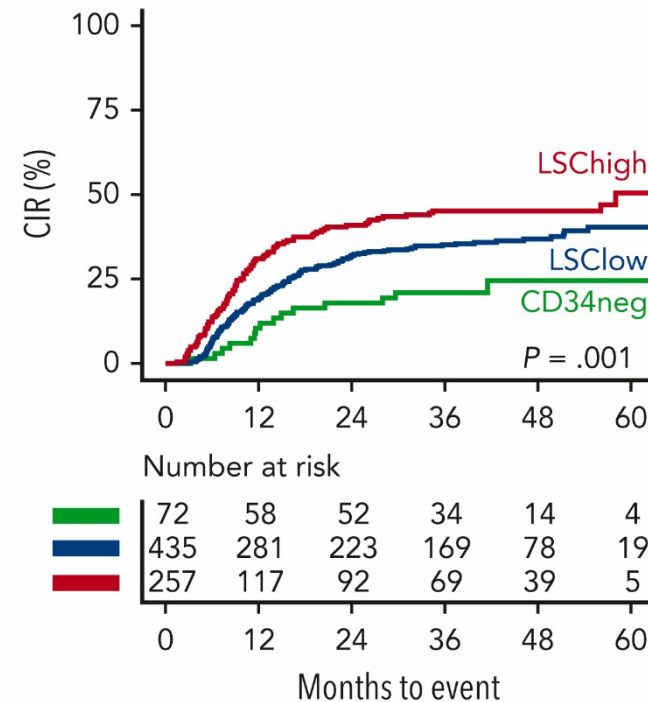
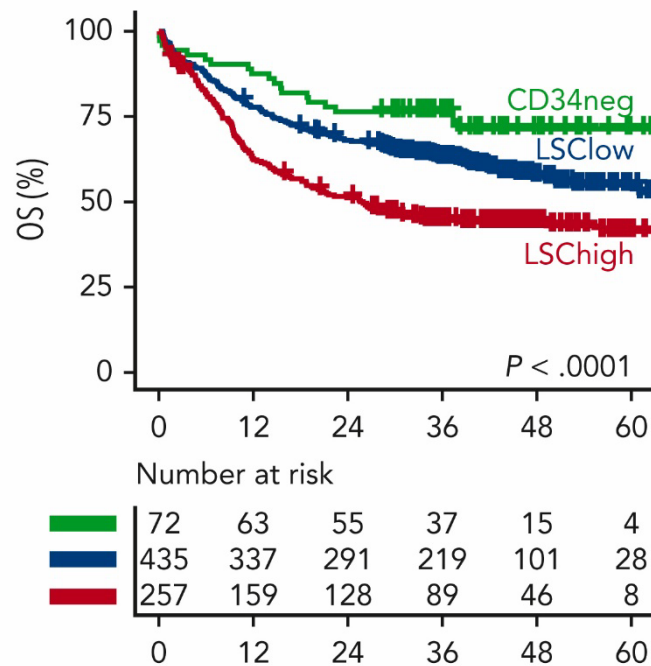


AML



Relevance of LSC measurement

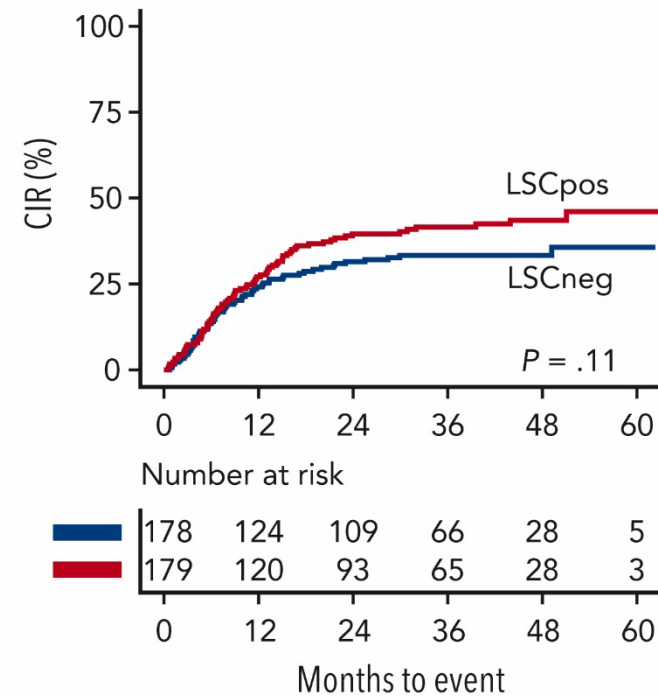
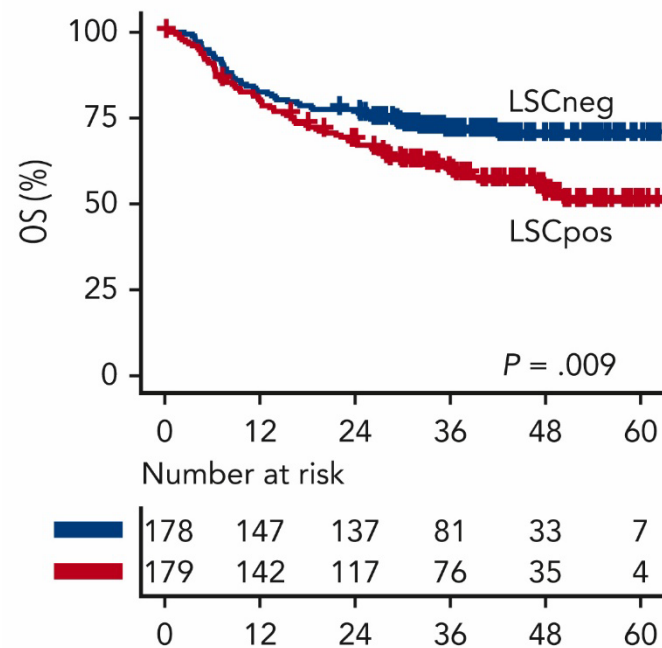
- Prognostic value at diagnosis and after two cycles of chemotherapy





Relevance of LSC measurement

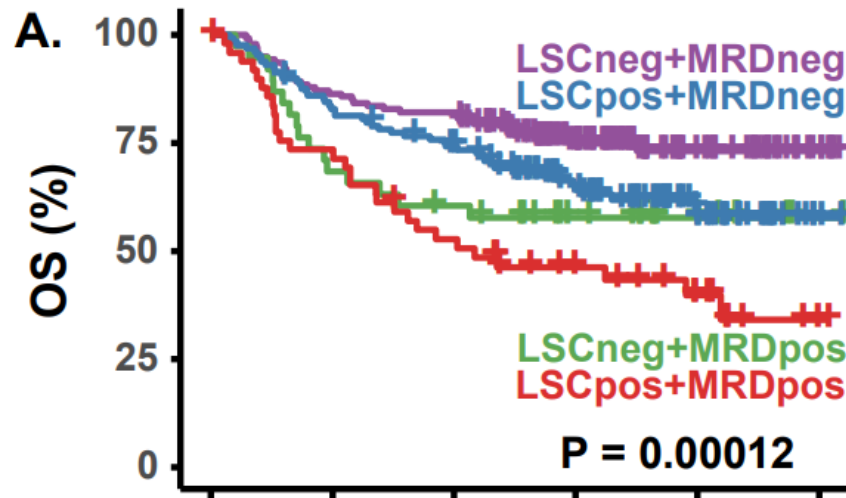
- Prognostic value at diagnosis and after two cycles of chemotherapy





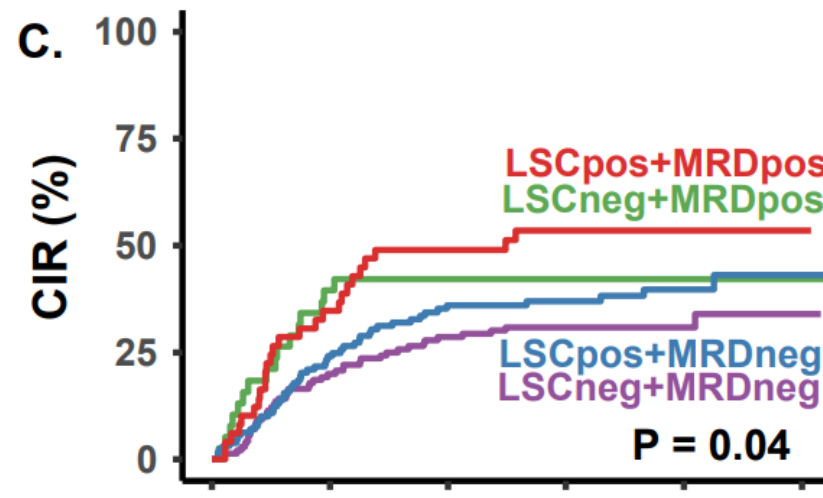
Combination with MRD

- Prognostic value at diagnosis and after two cycles of chemotherapy



Number at risk

■	140	121	115	67	26	6
■	38	26	22	14	7	1
■	129	106	92	60	26	3
■	50	36	25	16	9	1
	0	12	24	36	48	60



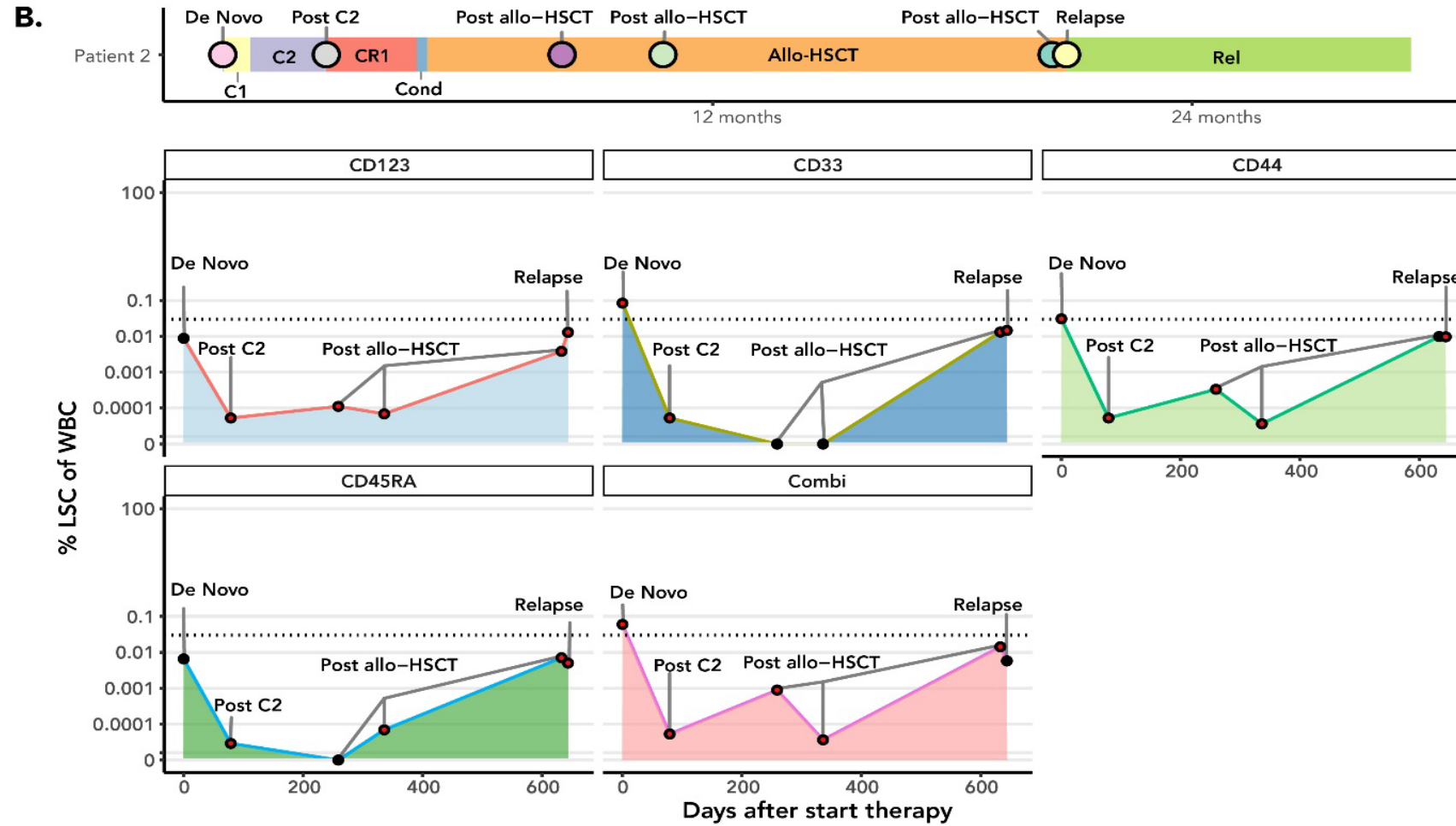
Number at risk

■	140	104	92	54	22	4
■	38	20	17	12	6	1
■	129	92	74	53	21	2
■	50	28	19	12	7	1
	0	12	24	36	48	60

Months to event



Monitoring





Conclusions

- LSC assessment reveals a poor prognostic patient group within the MRD-negative group
- Combining MRD, LSC, molecular MRD and different from normal analysis helps to identify more patient in the MRD-negative group that might relapse



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Monitoring

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