LAM MRD FLOW &LSC – APPORT DANS LA PRISE EN CHARGE DES PATIENTS ALLOGREFFES POUR LAM

Adriana PLESA , CHU Lyon , France

SFGM-TC SFH

Paris, 9 Septembre 2021

Hôpitaux de Lyon

Centre Hospitalier Régional Universitaire de Lille

Review Article

blood

BLOOD, 26 JANUARY 2017 • VOLUME 129, NUMBER 4

Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel

Hartmut Döhner,[1] Elihu Estey,[2] David Grimwade,[3] Sergio Amadori,[4] Frederick R. Appelbaum,[2] Thomas [illegible]ner,[5] Hervé Dombret,[6] Benjamin L. Ebert,[7] Pierre Fenaux,[8] Richard A. Larson,[9] Ross L. Levine,[10] Francesco [illegible]-Coco,[4] Tomoki Naoe,[11] Dietger Niederwieser,[12] Gert J. Ossenkoppele,[13] Miguel Sanz,[14] Jorge Sierra,[15] Martin S. Tallman,[10] Hwei-Fang Tien,[16] Andrew H. Wei,[17,18] Bob Löwenberg,[19] and Clara D. Bloomfield[20]

Monitoring of MRD. Two approaches can be used to detect MRD, that is, multiparameter flow cytometry (MFC) and molecular techniques, including real-time quantitative PCR (RT-qPCR), digital PCR, and next-generation sequencing–based technologies. Standardized RT-qPCR assays are now available to detect AML-associated genetic lesions (Table 4). Each methodology

2021 Update on Measurable Residual Disease (MRD) in Acute Myeloid Leukemia (AML): A Consensus Document from the European LeukemiaNet MRD Working Party

Michael Heuser[1], Sylvie D. Freeman[2], Gert J. Ossenkoppele[3], Francesco Buccisano[4], Christopher S. Hourigan[5], Lok Lam Ngai[3], Jesse Tettero[3], Costa Bachas[3], Constance Baer[6], Marie-Christine Béné[7], Veit Bücklein[8], Anna Czyz[9], Barbara Denys[10], Richard Dillon[11], Michaela Feuring-Buske[12], Monica L. Guzman[13], Torsten Haferlach[6], Lina Han[14], Julia Herzig[8], Jeffrey Jorgensen[15], Wolfgang Kern[6], Marina Konopleva[14], Francis Lacombe[16], Marta Libura[17], Agata Majchrzak[18], Luca Maurillo[4], Yishai Ofran[19], Jan Philippe[10], Adriana Plesa[20], Claude Preudhomme[21], Farhad Ravandi[14], Christophe Roumier[21], Marion Subklewe[8], Felicitas Thol[1], Arjan A. van de Loosdrecht[3], Bert van der Reijden[23], Adriano Venditti[4], Agnieszka Wierzbowska[24], Peter Valk[25], Brent Wood[26], Roland B. Walter[27], Christian Thiede[22,28], Konstanze Döhner[12], Gail J. Roboz[13], Jacqueline Cloos[3]

ELN MRD 2021

Mesurable Residual Disease

Applicability — **Sensitivity** — **Applicability** — **Sensitivity**

10^{-3} ➡ 5.10^{-4}

Flow AND Biomol

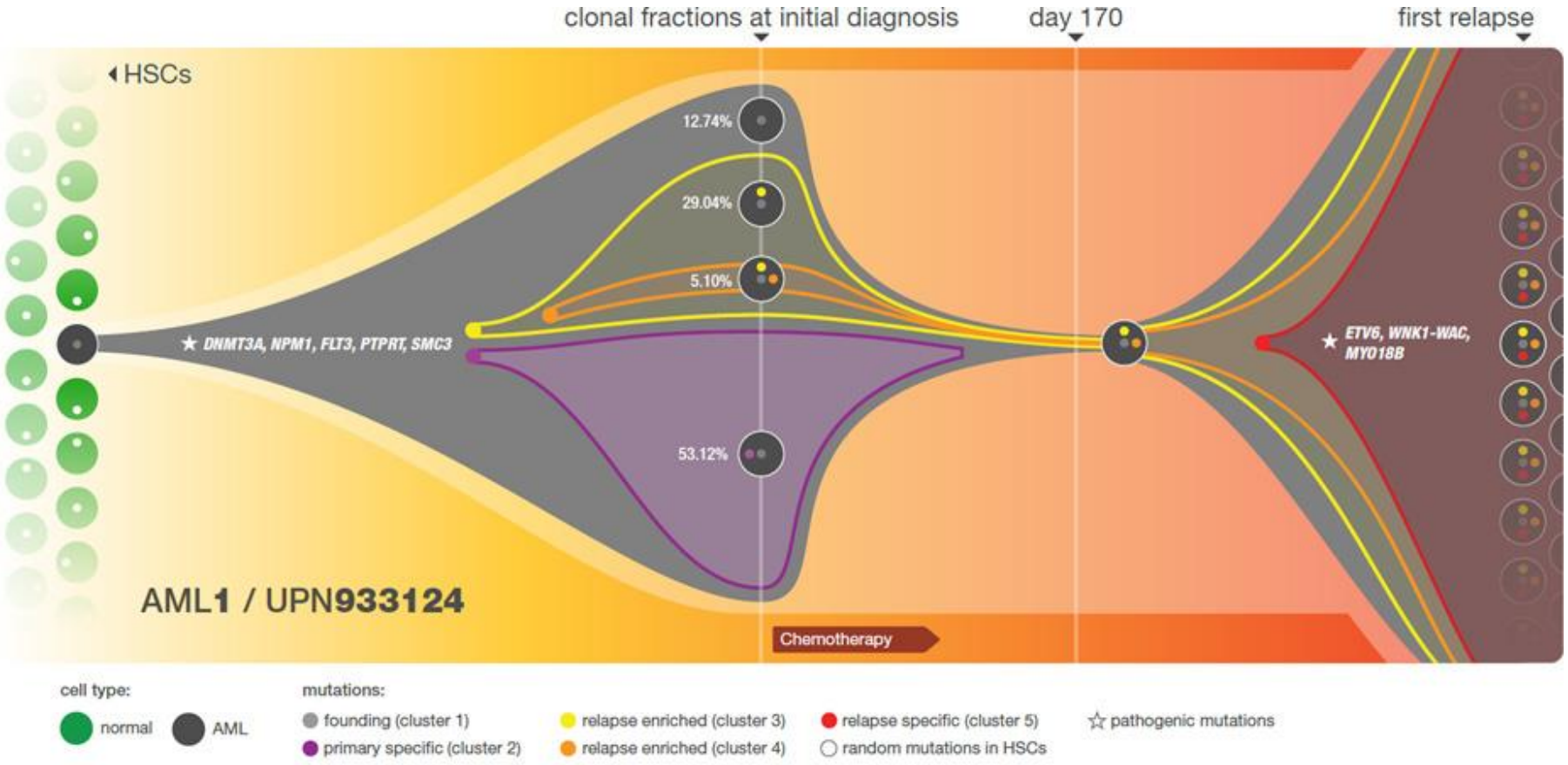
10^{-4} ➡ 10^{-5}

Table 6. Response criteria in AML

Category	Definition	Comment
Response		
CR without minimal residual disease (CR_{MRD-})	If studied pretreatment, CR with negativity for a genetic marker by RT-qPCR, or CR with negativity by MFC	Sensitivities vary by marker tested, and by method used; therefore, test used and sensitivity of the assay should be reported; analyses should be done in experienced laboratories (centralized diagnostics)

AML clonal heterogeneity

génomique & phénotypique & fonctionnelle



L Ding *et al*. *Nature* **000**, 1-5 (2012) doi:10.1038/nature10738

Educational book ASH 2019, Sylvie Freeman

(A Plesa/C Roumier) Coordonnateurs MRDflow French Flow ALFA Intergroup

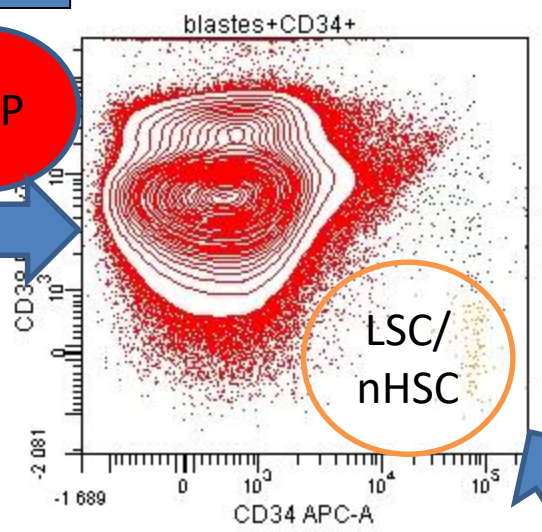
AML dg

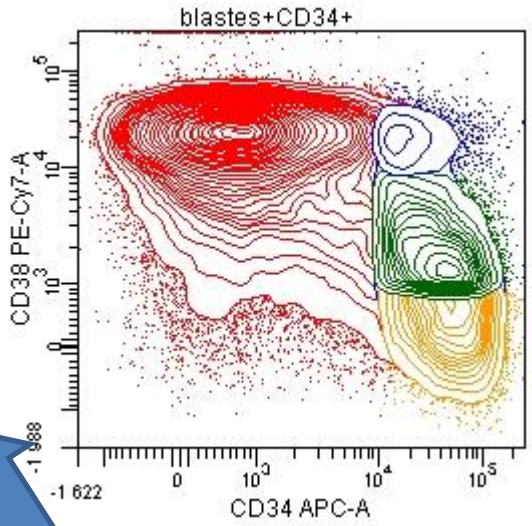
CN, NPM1+FLT3ITD-

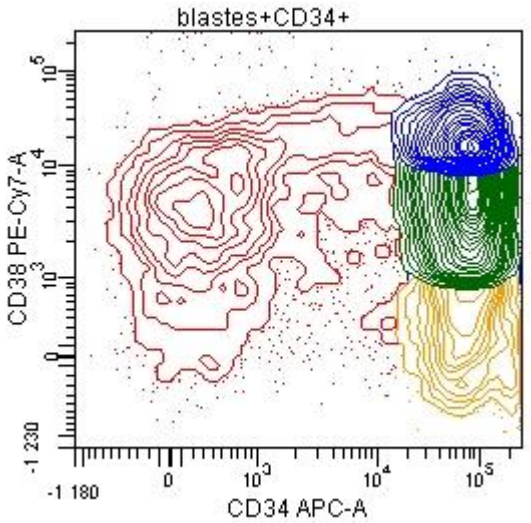
CN, NPM1+FLT3ITD+

+8, del20q-,NPM1-FLT3ITD+

LAIP



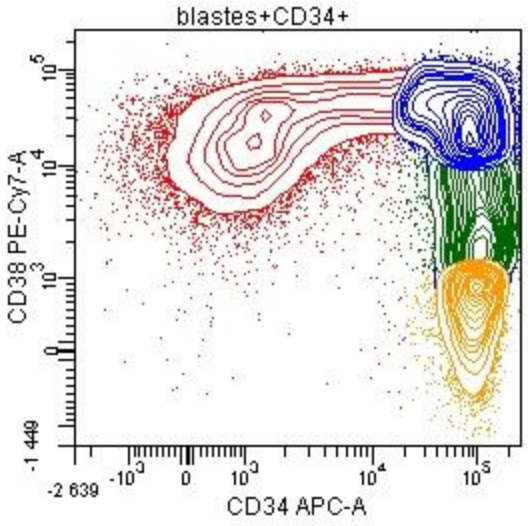


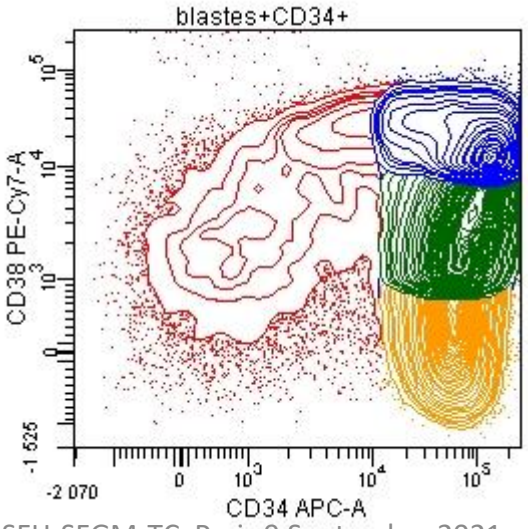


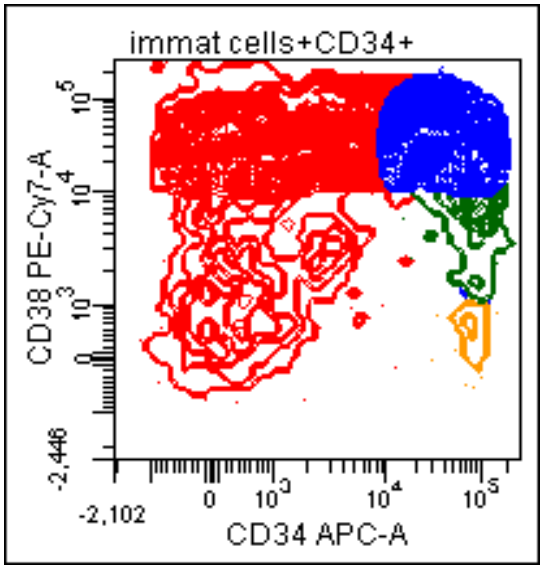
Caryotype CX>5, WT1+, dupMLL

EVI1+, del7q

nBM







Définition MRD de type LAIP vs DFN vs LSC (Panel ALFA Intergroup (coordination A Plesa/C Roumier selon ELN)

Patient au diagnostic
LAIP + DFN + LSC

	FL1	FL2	FL3	FL4	FL5	FL6	FL7	FL8
T 1	CD7+CD56	CD13	CD33	CD34	CD38	CD117	CD19	CD45
T 2	CD90	MIX LSC: TIM3+CLL1+CD97	CD123	CD34	CD38	CD117	CD45RA	CD45
T3 option	CD36	CD11b	CD33	CD34	HLA-DR	CD117	CD4	CD45

Ex dg LAIP: CD7+CD56+CD19+…
Ex dg LSC: CD34+CD38-CD45RA+MIX+CD33++

MRDflow (avec panel fait au dg)
LAIP+DFN+LSC

	FL1	FL2	FL3	FL4	FL5	FL6	FL7	FL8
T 1	CD7+CD56	CD13	CD33	CD34	CD38	CD117	CD19	CD45
T 2	CD90	MIX LSC: TIM3+CLL1+CD97	CD123	CD34	CD38	CD117	CD45RA	CD45
T3 option	CD36	CD11b	CD33	CD34	HLA-DR	CD117	CD4	CD45

MRD LAIP: CD7+CD56+CD19+…
MRD LSC: CD34+CD38-CD45RA+MIX+CD33++

Patient sans Panel MRD au dg

MRDflow (sans panel fait au dg)
LAIP+DFN+LSC

	FL1	FL2	FL3	FL4	FL5	FL6	FL7	FL8
T 1	CD7+CD56	CD13	CD33	CD34	CD38	CD117	CD19	CD45
T 2	CD90	MIX LSC: TIM3+CLL1+CD97	CD123	CD34	CD38	CD117	CD45RA	CD45
T3 option	CD36	CD11b	CD33	CD34	HLA-DR	CD117	CD4	CD45

MRD DFN: CD7+CD56+CD19+…
MRD LSC: CD34+CD38-CD45RA+MIX+CD33++

MRD possible évaluable mais parfois moins de sensibilité/spécificité --- panel dg NECESSAIRE!!!

MRD evaluation of AML in clinical practice: are we there yet?

Sylvie D. Freeman[1] and Christopher S. Hourigan[2]

[1]Clinical Immunology Service, Institute of Immunology and Immunotherapy, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; and [2]Laboratory of Myeloid Malignancies, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD

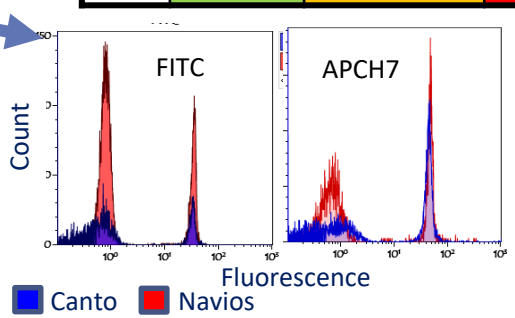
Educational book ASH 2019, Sylvie Freeman (A Plesa/C Roumier) Coordonnateurs MRDflow French Flow ALFA Intergroup

HARMONISATION OF PRE-ANALYTICAL SAMPLE PROCESSING
Bulk Lysis / Staining/Wash/
Acquisition of minimum 500,000 cells

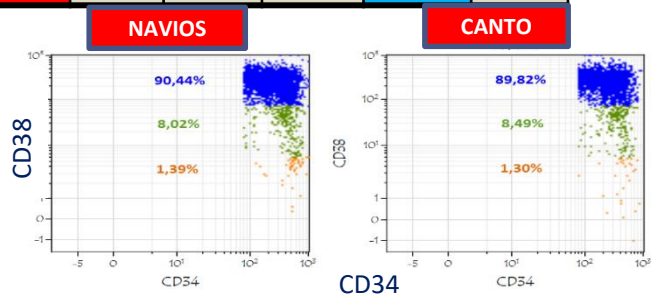
PANEL CONSTRUCTION **[1]**

	FL1	FL2	FL3	FL4	FL5	FL6	FL7	FL8
T 1	CD7+CD56	CD13	CD33	CD34	CD38	CD117	CD19	CD45
T 2	CD90	MIX LSC: TIM3+CLL1+CD97	CD123	CD34	CD38	CD117	CD45RA	CD45
T3 option	CD36	CD11b	CD33	CD34	HLA-DR	CD117	CD4	CD45

HARMONISATION OF CYTOMETER SETTINGS
to achieve comparable fluorescent profiles **[2]**
Canto cytometers used by 12 Laboratories
Navios cytometers used by 10 Laboratories



Harmonised Calibration Target MFI Peaks



Comparable Antibody Fluorescent Profiles between Cytometer Platforms

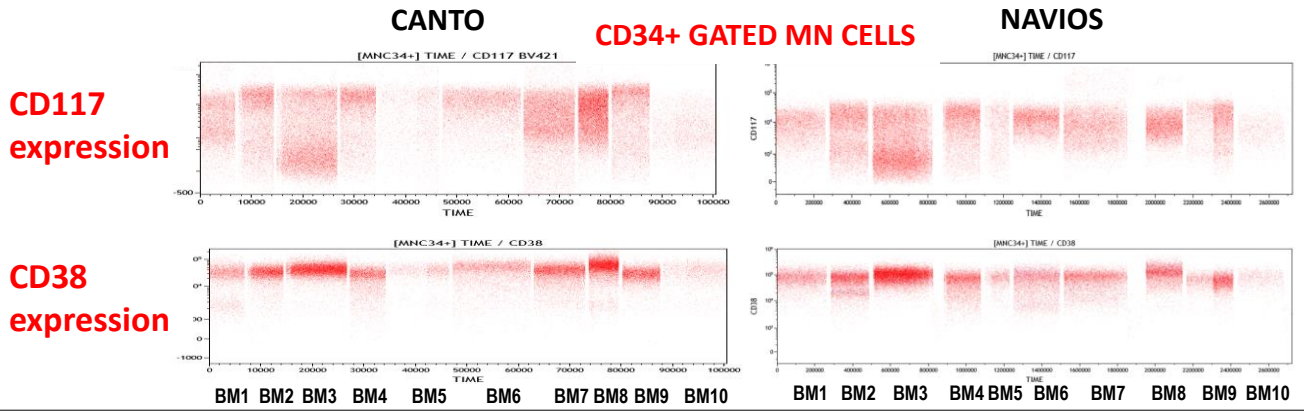
HARMONISATION OF GATING STRATEGY
to achieve reproducibility in detection of low frequency immunophenotypic aberrant profiles

INTER-LABORATORY COMPARISONS FOR QUALITY ASSESSMENT OF FLUORESCENT PROFILES AND GATING

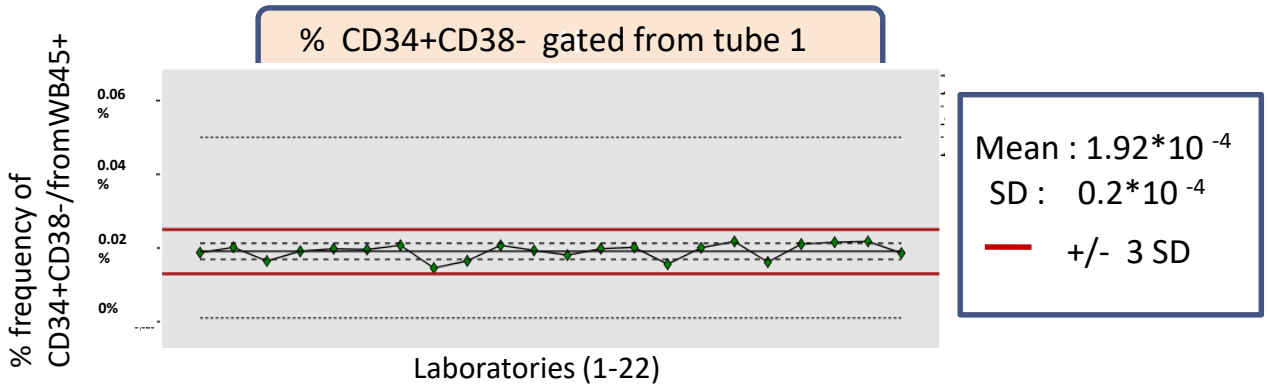
A Schema of a Flow Cytometric AML MRD multi-center Harmonisation Strategy

B Examples of Inter-Laboratory Quality Assessments

QA of marker expression profiles for 10 shared normal bone marrow samples **[3]**

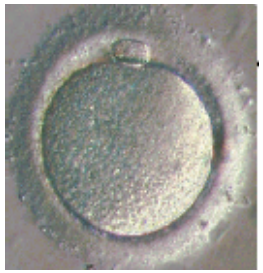


QA from normal BM sample shared among 22 centers **[4]**



Minimal information should be given in **Clinical FlowReport**:

- Quality of BM (dilution)
- Strategy of identification of MRD: LAIP/DFN/LSC
- Description of the LAIP used
- LOD based on nBM
- Thresholds < 10-3 for LAIP or <10-4 for LSC
- Interpretation of the result:
  - MRD+
  - MRD- with LOD value
  - MRD detectable but nonquantifiable

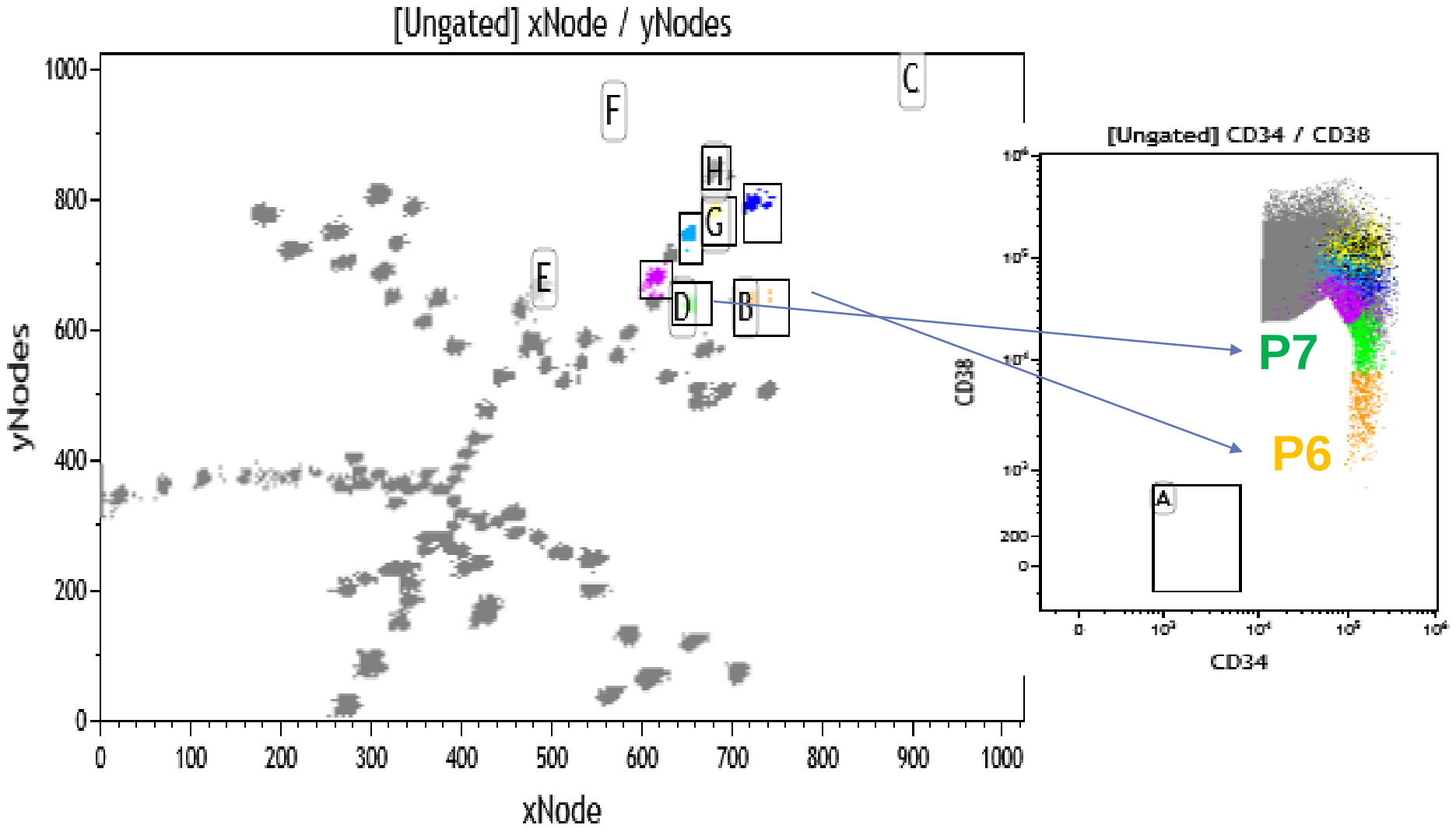
nHSC		LSC
1963 Till & Mc Culloch		1997 John Dick & D Bonnet
CD34+ CD38-		**CD34+ CD38-**
HLADR- CD90+CD45RA- CD13+/CD33lo, CD117+	**Marqueurs fonctionnels Side Population (SP) Hoechst 33342 ALDH Quiescence G0/G1 5-FU Rhod123 Xenograft, PDX**	**HLADR- CD90-CD45RA+ CD13+/CD33lo/++CD117-/lo**
CD123-/lo CD44+ VLA4+ CXCR4+ CD47+ CD49f+		**CD123++ CD44++ VLA4++ CXCR4++ CD47++ CD49f++**

CLL-1-, TIM3-, CD97-
CD96-, GPR56+,EPCR+,CD93+lo, CD81, CD200

CLL-1+, TIM3+,CD97+
CD96++,GPR56-/+, EPCR++CD93++

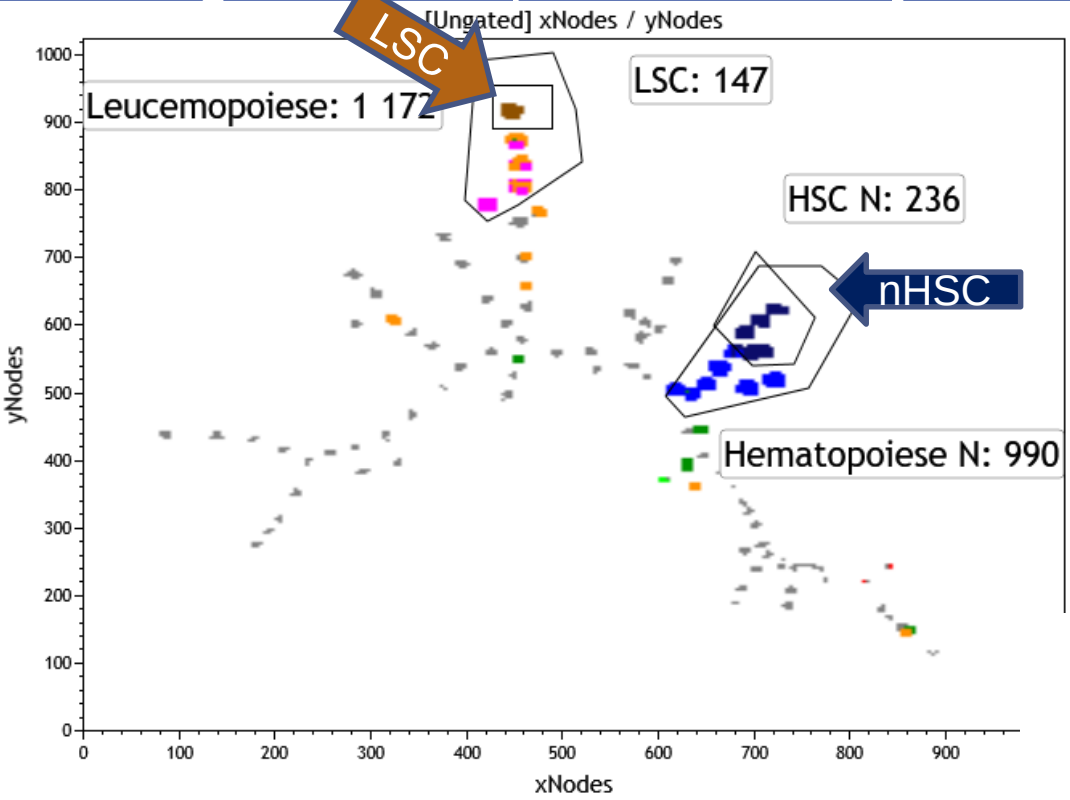
Space 34+38+/- P6/P7/P8 Flow SOM (Self Organizing Map)

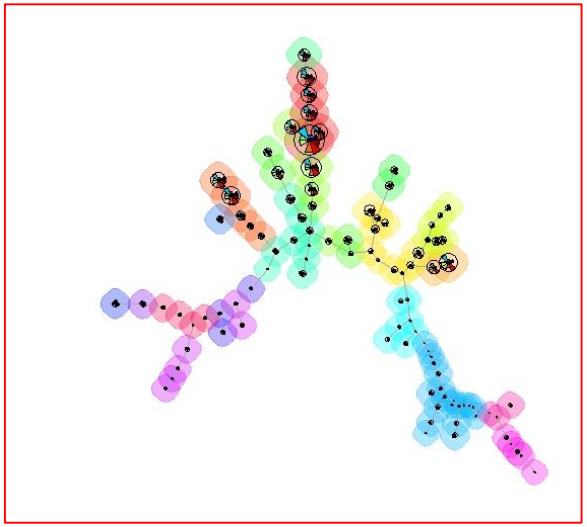
C Roumier/F Dumezy (CHU Lille) & A Plesa (CHU Lyon)

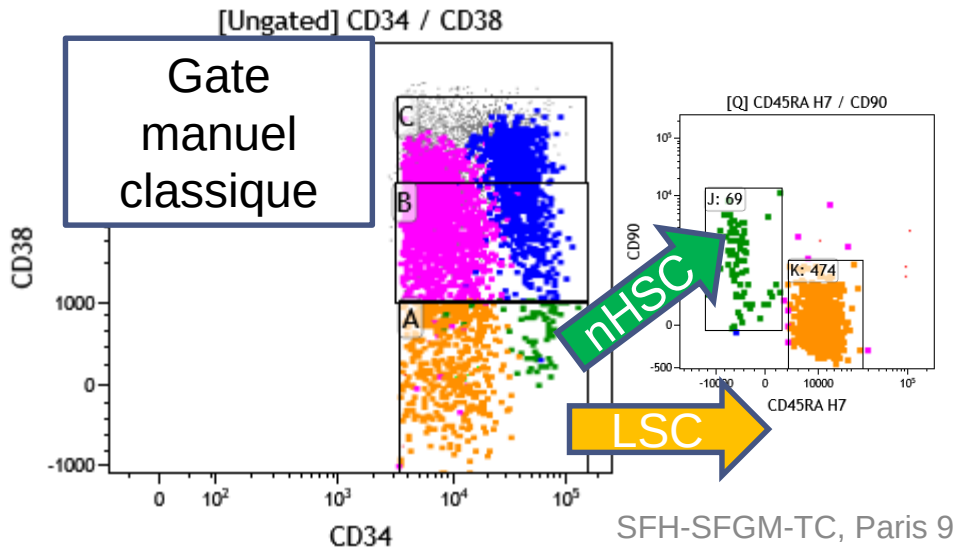


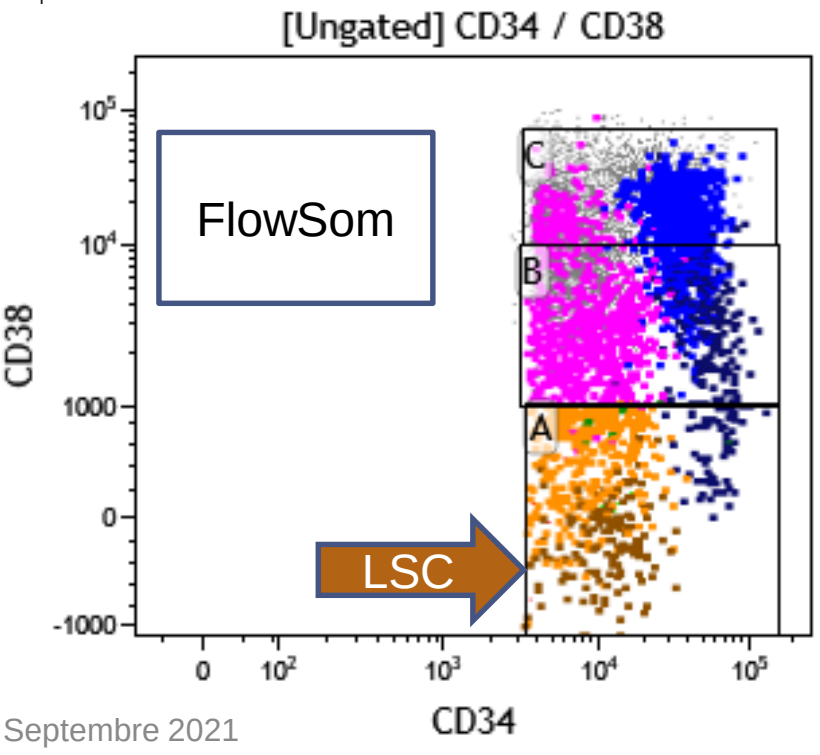
Van Gassen S, Callebaut B and Saeys Y (2017). *FlowSOM: Using self-organizing maps for visualization and interpretation of cytometry data*. http://www.r-project.org, http://dambi.ugent.be.

Integrate Unsupervised analyse in AML-LAIP&LSCflow









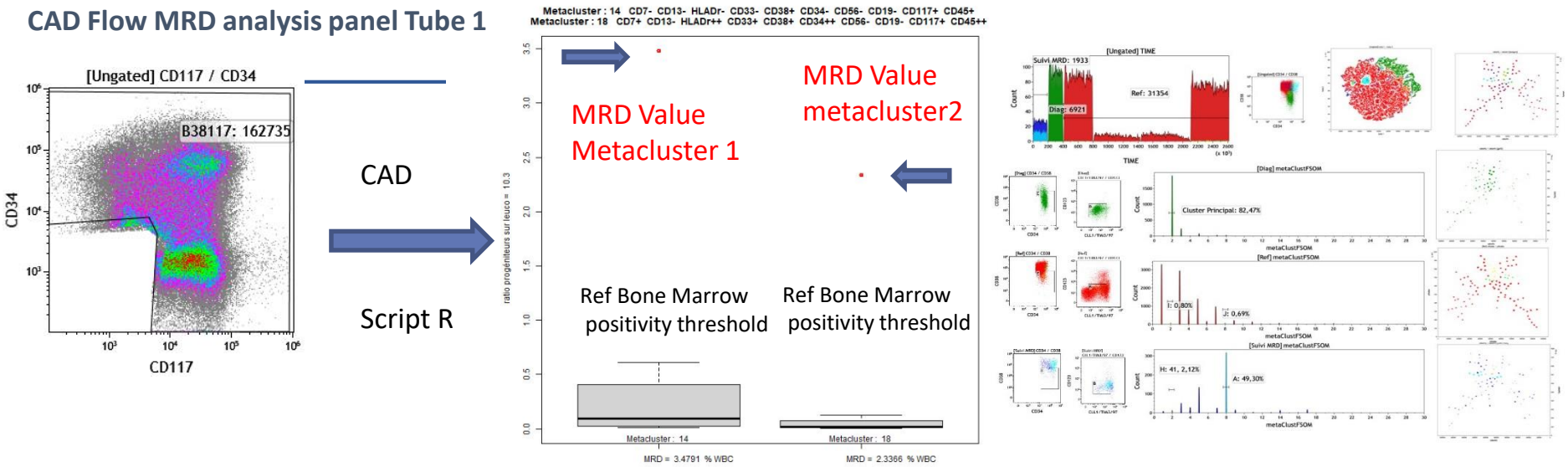
Computer aided design (CAD) flow in assessment of AML MRD flow -ALFA French Flow AML MRD Group

Florent Dumezy, Christophe Roumier, Joris Gutrin, Xavier Thomas, Celine Berthon, Hervé Dombret, Claude Preudhomme, Adriana Plesa

[1]Laboratory of Hematology and Flow cytometry, Lyon-Sud Hospital, HCL-CHU Lyon, France
[2]Laboratory of Hematology and Flow cytometry, CHU-Lille, France
[3]Department of Hematology, Saint Louis Hospital, AP-HP, Paris, France

Study of 60 AML patients using 8C panel CANTO platform or 10c panel NAVIOS platform

CAD Flow MRD analysis panel Tube 1



Dumezy et al, EHA 2021
SFH 2021 (Poster)

New paradigm in MRD LAM: LSC approach

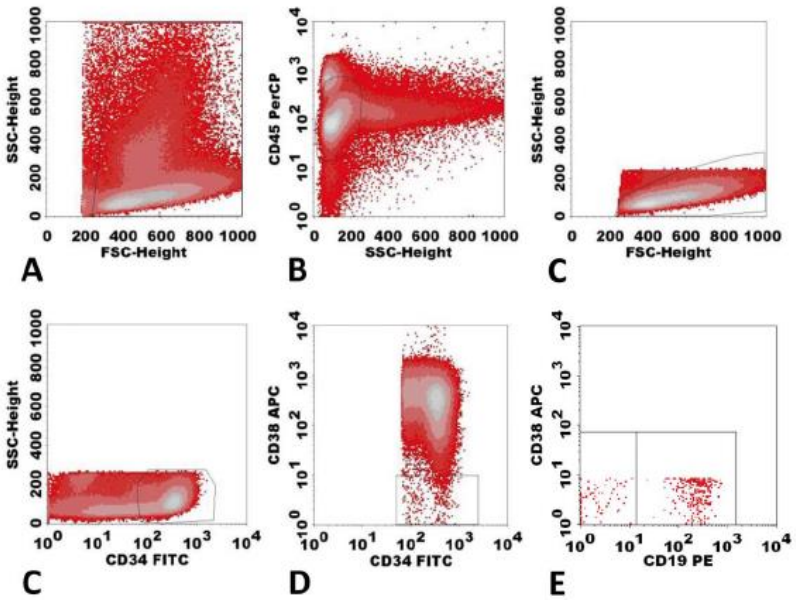
OPEN ACCESS Freely available online

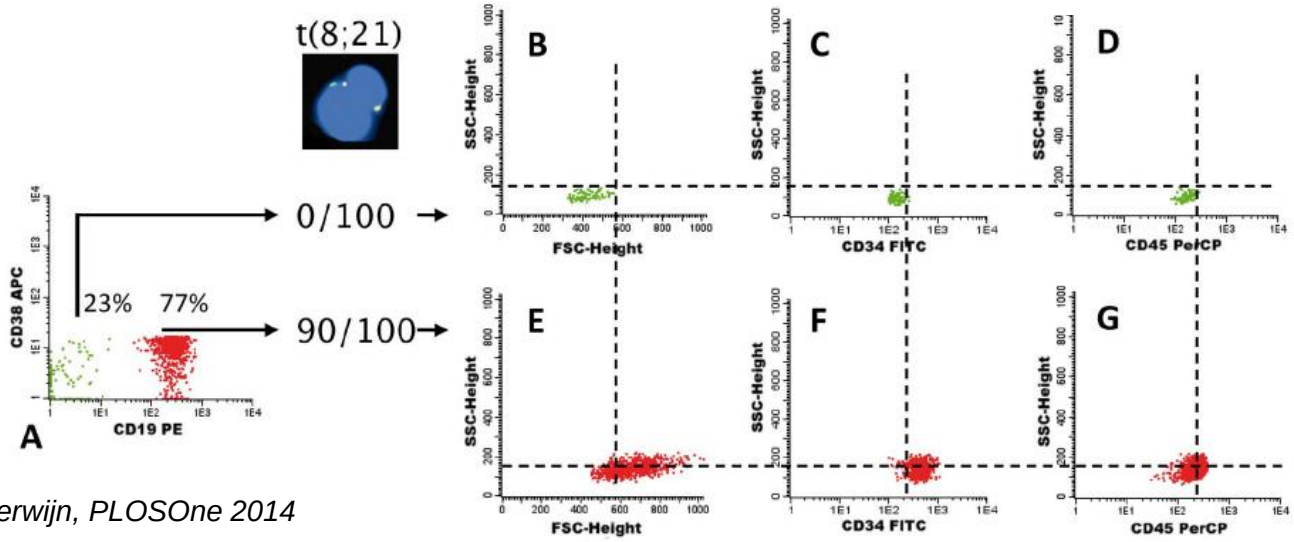
PLOS | ONE

Leukemic Stem Cell Frequency: A Strong Biomarker for Clinical Outcome in Acute Myeloid Leukemia

Monique Terwijn[1], Wendelien Zeijlemaker[1], Angèle Kelder[1], Arjo P. Rutten[1], Alexander N. Snel[1], Willemijn J. Scholten[1], Thomas Pabst[2], Gregor Verhoef[3], Bob Löwenberg[4], Sonja Zweegman[1], Gert J. Ossenkoppele[1], Gerrit J. Schuurhuis[1]*

1 Department of Hematology, VU University Medical Center, Amsterdam, The Netherlands, **2** Department of Medical Oncology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, **3** Department of Hematology, University Hospital Leuven, Leuven, Belgium, **4** Department of Hematology, Erasmus University Medical Center, Rotterdam, The Netherlands



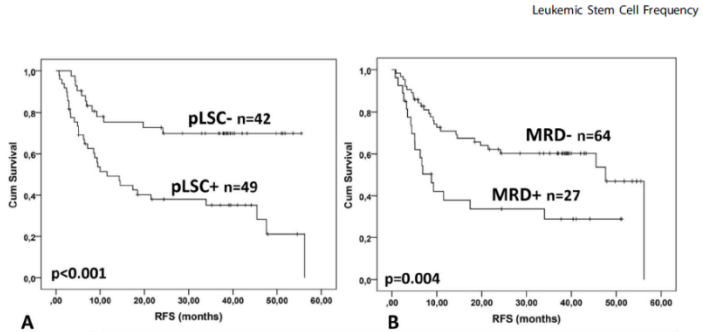


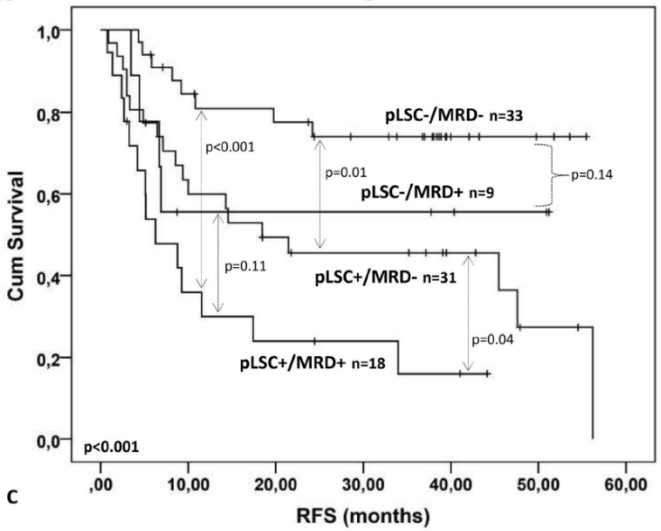
nHSC

LSC

M Terwijn, PLOSOne 2014

New concept of AML follow up: Scoring of MRDflow (LAIP/DFN/LSC)





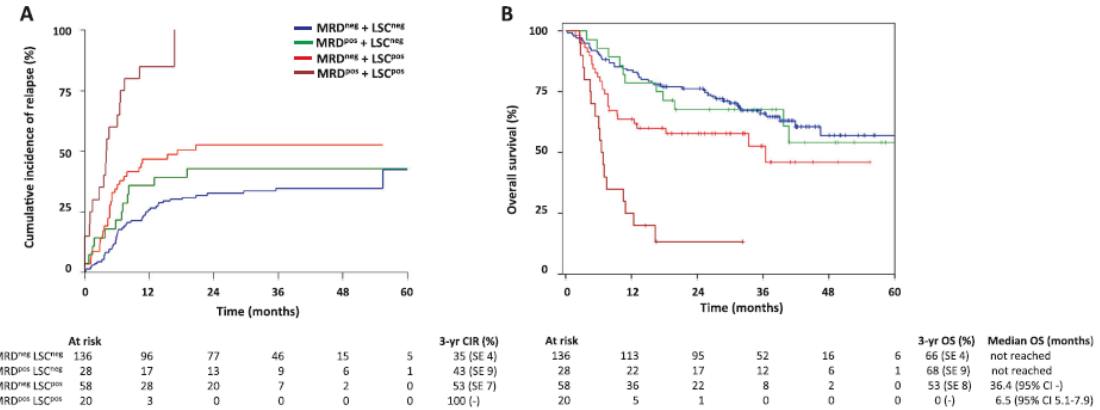
Leukemia
https://doi.org/10.1038/s41375-018-0326-3

ARTICLE

Acute myeloid leukemia

$CD34^{+}CD38^{-}$ leukemic stem cell frequency to predict outcome in acute myeloid leukemia

Wendelien Zeijlemaker[1] · Tim Grob[2] · Rosa Meijer[3] · Diana Hanekamp[1] · Angèle Kelder[1] · Jannemieke C. Carbaat-Ham[1] · Yvonne J. M. Oussoren-Brockhoff[1] · Alexander N. Snel[1] · Dennis Veldhuizen[1] · Willemijn J. Scholten[1] · Johan Maertens[4] · Dimitri A. Breems[5] · Thomas Pabst[6] · Markus G. Manz[7] · Vincent H. J. van der Velden[8] · Jennichjen Slomp[9] · Frank Preijers[10] · Jacqueline Cloos[1,11] · Arjan A. van de Loosdrecht[1] · Bob Löwenberg[2] · Peter J. M. Valk[2] · Mojca Jongen-Lavrencic[2] · Gert J. Ossenkoppele[1] · Gerrit J. Schuurhuis[1]



	At risk						3-yr CIR (%)	At risk						3-yr OS (%)	Median OS (months)
MRD^{neg} LSC^{neg}	136	96	77	46	15	5	35 (SE 4)	136	113	95	52	16	6	66 (SE 4)	not reached
MRD^{pos} LSC^{neg}	28	17	13	9	6	1	43 (SE 9)	28	22	17	12	6	1	68 (SE 9)	not reached
MRD^{neg} LSC^{pos}	58	28	20	7	2	0	53 (SE 7)	58	36	22	8	2	0	53 (SE 8)	36.4 (95% CI -)
MRD^{pos} LSC^{pos}	20	3	0	0	0	0	100 (-)	20	5	1	0	0	0	0 (-)	6.5 (95% CI 5.1-7.9)

Fig. 3 Prognostic value of MRD/LSC status as defined at follow-up. Fig. 3a shows cumulative incidence of relapse (CIR) for the four different MRD/LSC patient groups. This figures shows the important difference in both CIR (3 A) and OS (3B) for the different MRD/LSC patient groups: prognosis becomes better in the sequence MRD^{neg}/LSC^{neg} and $MRD^{pos}/LSC^{neg} > MRD^{neg}/LSC^{pos}$ » MRD^{pos}/LSC^{pos}. At the bottom CIR, 3-years OS and median OS, are summarized for the different groups

M Terwijn, PLOSOne 2014

W Zeijlemaker, Leukemia 2018

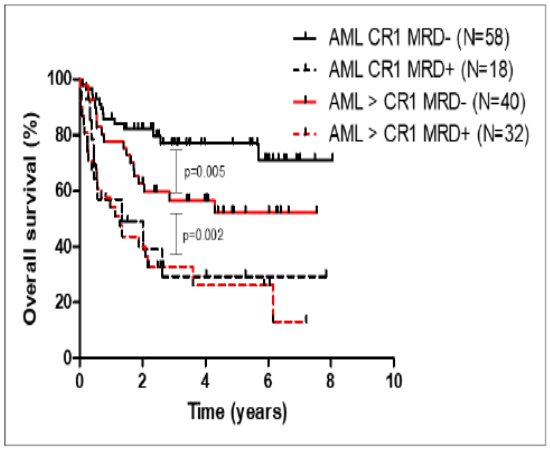
EHA EUROPEAN HEMATOLOGY ASSOCIATION

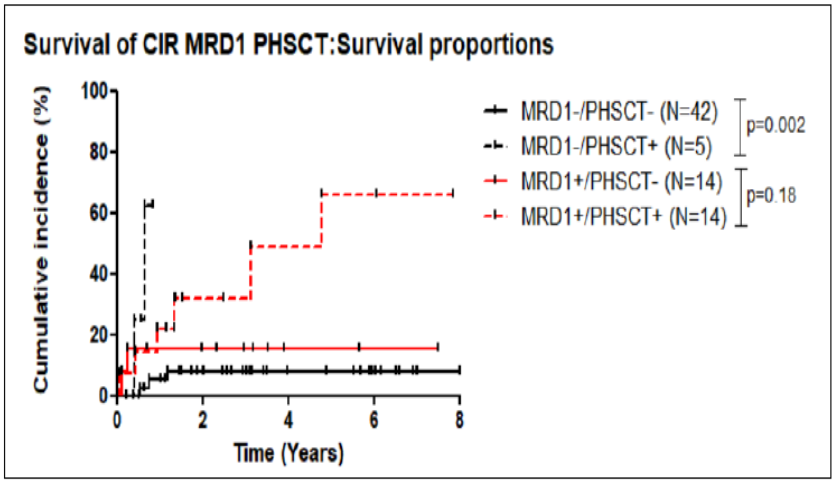
SURVIVAL AFTER SEQUENTIAL FLAMSA-BU CONDITIONING REGIMEN IS HIGHLY DEPENDENT ON PRE-HSCT MRD STATUS IN HIGH-RISK MYELOID NEOPLASM

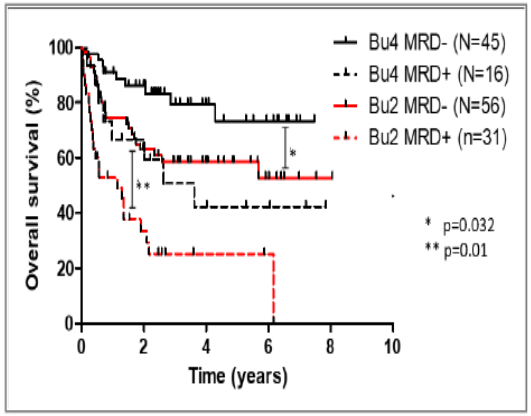
G. LE MEUR[1], A. PLESA[2], M. BALSAT[1], M. RENAULT[1], M. LARCHER[1], G. FOSSARD[1], F. BARRACO[1], S. DUCASTELLE-LEPRETRE[1], L. GILS[1], X. THOMAS[1], H. GHESQUIERES[1],H. LABUSSIERE-WALLET[1] and M. HEIBLIG[1]

1. Service d'hématologie clinique, Hospices Civils de Lyon, Pierre Bénite, France
2. Service d'hématologie biologique, Hospices Civils de Lyon, Pierre-Bénite France

Valeur prédictive de la MRD pré-allogreffe en fonction de l'intensité du conditionnement







- La MRD CMF pré-HSCT est le seul facteur prédictif de rechute post-greffe en analyse multivariée
- Problème de cinétique plus que de valeur absolue ?

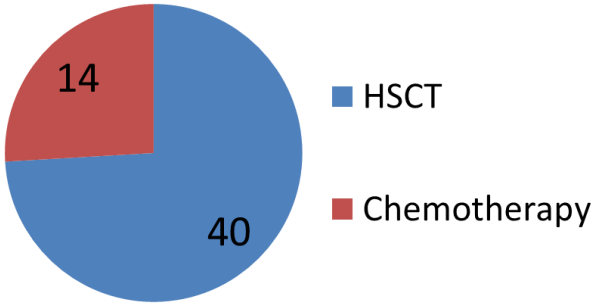
Le Meur et al. EHA 2021

LEUKEMIC STEM CELL (LSC) QUANTIFICATION BY MULTIPARAMETER FLOW CYTOMETRY (MFC): A TOOL TO EVALUATE PEDIATRIC AML PATIENTS WITH GREATER BENEFIT FROM ALLOGENEIC HSCT?

EBMT 44th Annual Meeting of the European Society for Blood and Marrow Transplantation
18-21 March, 2018 • Lisbon, Portugal

Patients:54 pediatric AML patients were treated in Lyon clinical center (IHOP)
between 2008 and 2016 according to the ELAM02 clinical trial.

- 40 children (aged 0,3-19 years) undergoing HSCT based on the following criteria: high-risk AML in CR1 (29/40) and 11/40 in CR2.



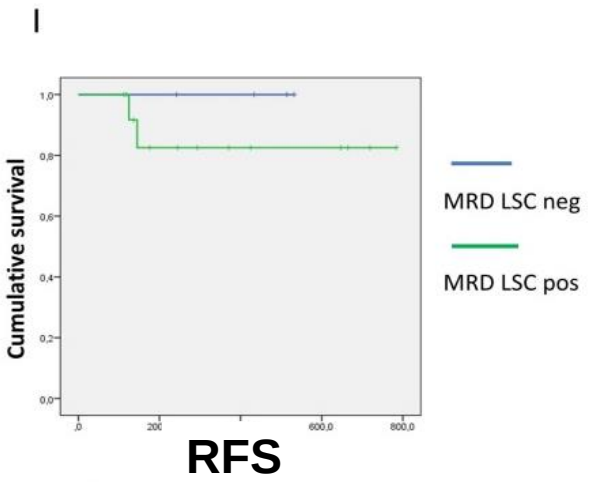
- The pre-transplant conditioning regimen was based on busulfan combined with Cyclophosphamide or fludarabine for all patients.

- GvHD prophylaxis consisted in CsA alone after in vivo T cell depletion (using anti-thymocyte globulin) for bone marrow unrelated donors and prednisolone for cord blood cell stem cell sources.

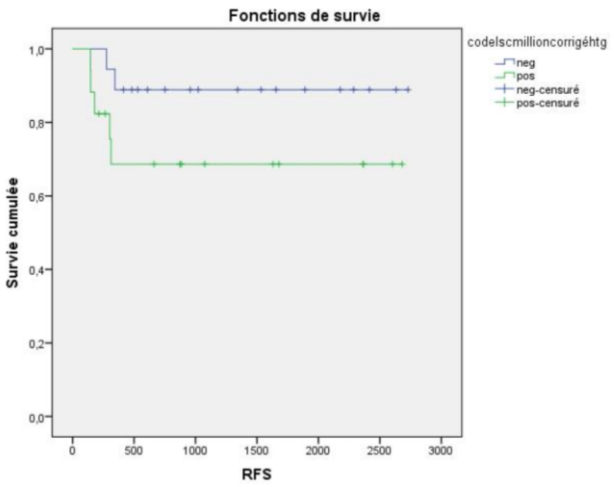
- Half of the HSCT were from HLA-MSD (matched sibling donor) and the Others from MURD (matched unrelated donor) or MMURD (miss-matched unrelated donor).

A Plesa, C Roumier, EBMT 2018

Impact of LSC frequency at MRD1 time point in pediatric AML cohort



MRD LSC
cut off 0,01%



Legend:
I- DFS according to MRD LSC level on pediatric AMLC

Comparaisons globales

	Khi-deux	ddl	Sig.
Log Rank (Mantel-Cox)	2,380	1	,123
Breslow (Generalized Wilcoxon)	2,654	1	,103

Test d'égalité des distributions de survie pour les différents niveaux de codelscmillioncorrigéhtg.

Récapitulatif de traitement des observations

codelscmillioncorrigéhtg	N total	Nombre d'événements	Censuré	
			N	Pourcentage
neg	18	2	16	88,9%
pos	17	5	12	70,6%
Global	35	7	28	80,0%

- Presence of the LSC CD34+CD38- subpopulation representing more than 0,9% of total “bulk leukemic cells” at diagnosis could help to identify patients with poor outcome.
- Despite heterogeneity and complexity of the AML LSC compartment, we should still use LSC quantification as a biomarker of response to HSCT therapy.
- In our study, greater benefit of GVL effect seems to be observed in the patients with low-level of LSC.
For the patients with high-level of LSC other therapeutic modalities should be chosen to eradicate LSC using targeting immunotherapy before allograft.
- Monitoring of the LSC fraction should be useful in most clinical trials to overcome chemoresistance of LSC.

A Plesa, C Roumier, EBMT 2018

Que-est que c'est une MRDpos?

Clonal Hematopoiesis? Clonal selection? MRD LSC?

- CD34+CD38- distinct populations:

1) nHSC
2) CH (clonal hematopoiesis)
3) LSC (clonal selection/evolution)

Crucial to integrate CD38 in MRDflowPanel:

-complementary of MRDflow +rqPCR+NGS

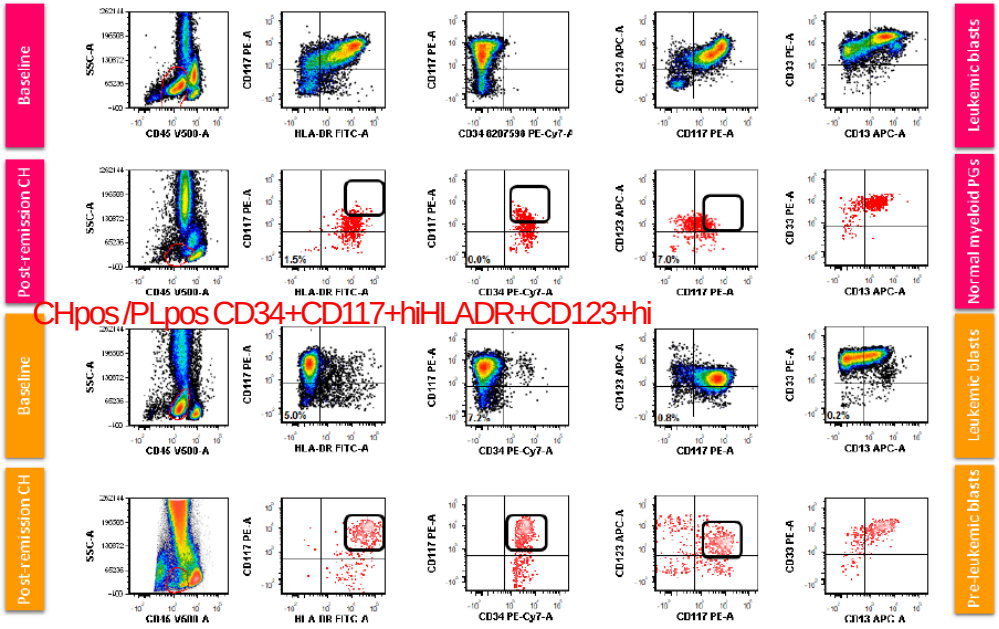
-scoring MRD based on subtypes of AML in every time points (NPM1, CBF, …)

-integrating in KB scoring, Unsupervised integrative MRD quantification…

Flow cytometric immunophenotypic alterations of persistent clonal haematopoiesis in remission bone marrows of patients with *NPM1*-mutated acute myeloid leukaemia

S Loghavi et al, BJH 2020

CHpos /Plneg CD34+CD117+loHLADR+CD123+lo



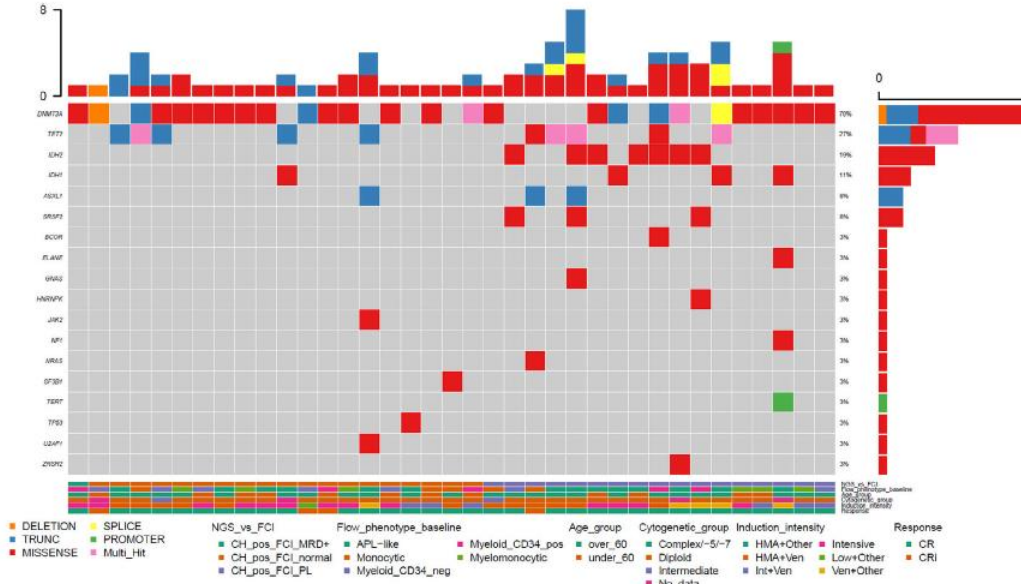
CHpos /PLpos CD34+CD117+hiHLADR+CD123+hi

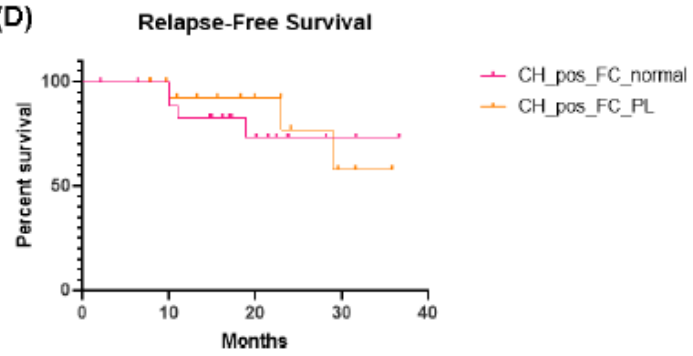
-61 AML NPM1 deNovo(50 patients MRD NPM1neg suivi en parallèle avec MRDflow -PL/ NGS-CH)

- 26% (#13) CHneg / 74% (#37) CHpos (DNMT3a 70%, TET2 27%, IDH2 19%, IDH1 11%)
- CHneg tous sont PLneg
- CHpos: 51% PLneg et 49% PLpos

PreLeukemic clone <1% CD34+ profil abb: 34+13+33+ et CD117highCD123high et CD38lowHLADRlow

S. Loghavi *et al.*



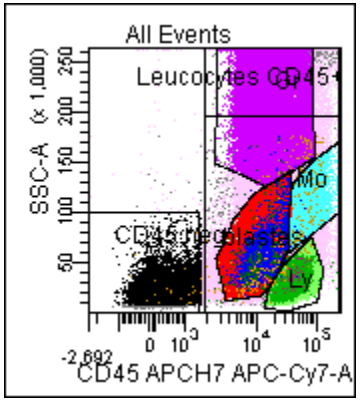


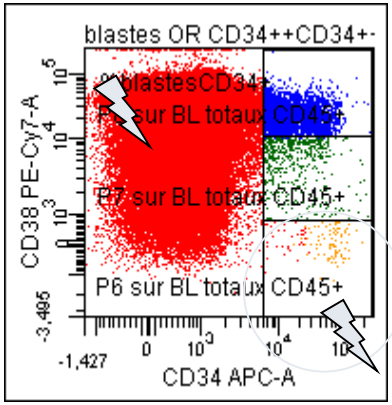
- IDH2, SRSF2 most in PL+CH+ (et dysplasie)
- PL+ pas correlé avec age, intensité induction, RFS

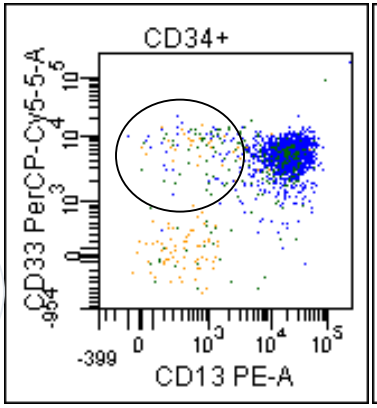
!!!!!Complementairitée dans les suivis MRD NPM1 et MRDflow

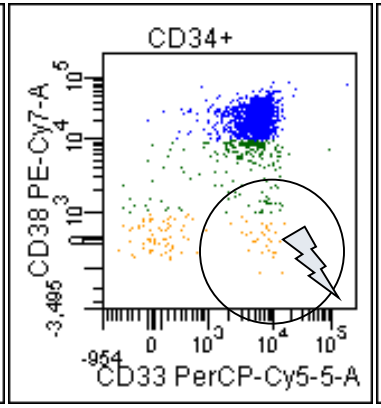
Patient AML4 15/06/2012 relapse 07/01/2013
minoritary subclone 34+38- du dg (0,4% from blastes)
at dg: WT1+, NPM1+, FLT3ITD-, EVI1-, CEBPa-, DNMT3A+, N caryotype
relapse: WT1+, NPM1+, FLT3ITD+!!! N caryotype (Relapse Clonal sélection LSC)

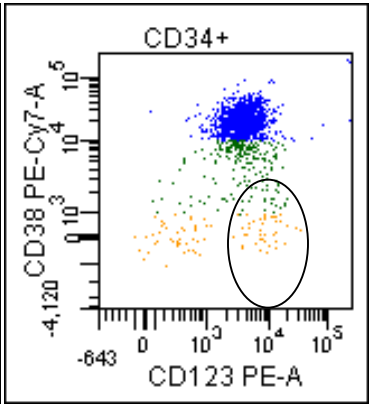
Diagnostic





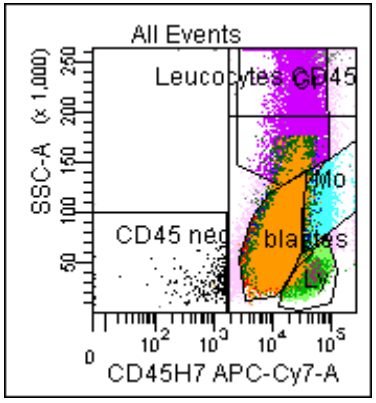


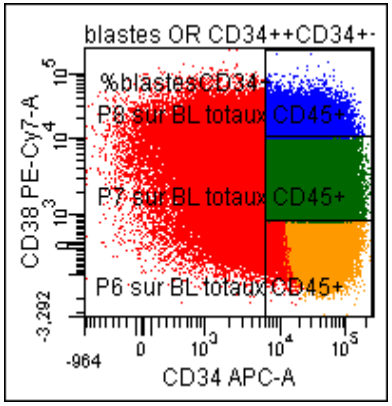


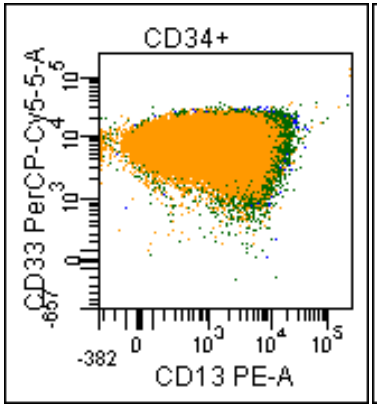


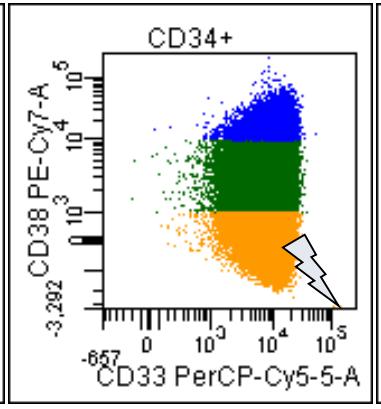
Relapse

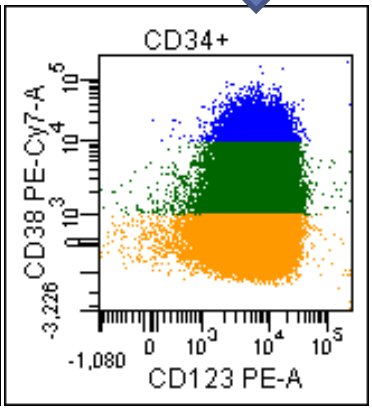
Relapse Clonal selection LSC



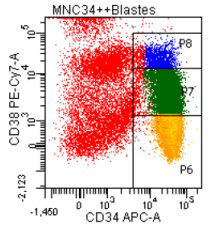




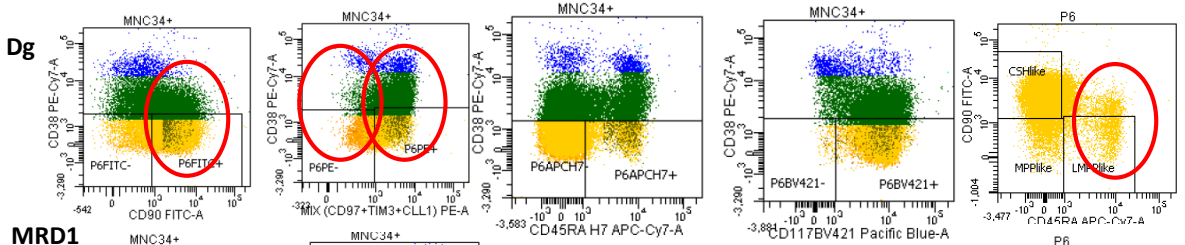


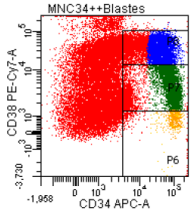


Patient#4 Responsive induction Vyxeos CPX351 CRi-MRDflowpos LAIP/DfN+LSC+ MPN/ET JAK2+ dg 2002---Hydrea---AML sec normal karyotype JAK2+EVI1+ dg 27-7-2020 (20Y later) Induction Vyxeos 2cycles---Allog HSCT FLAMSA RIC Endox BU2, CSP10/10 ---partial engraftment----Reject +4M chimerism >95% receptor-- MPN/ET with myelofibrosis JAK2+EVI1-, CR morphology

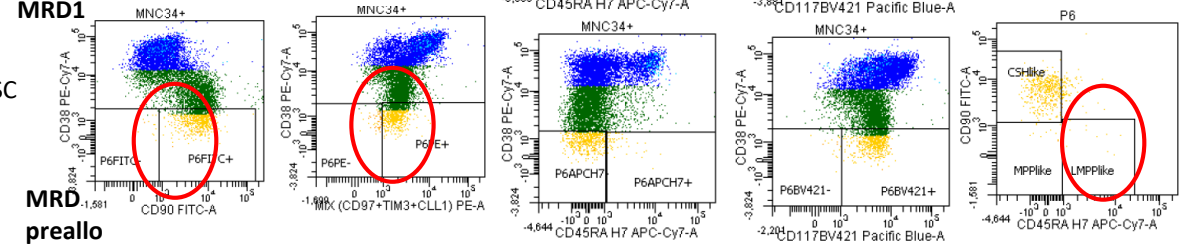


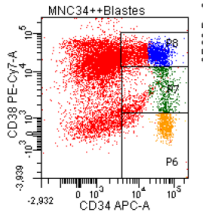
Dg
13%Bl/LSC6%
Jak2+/EVI1+



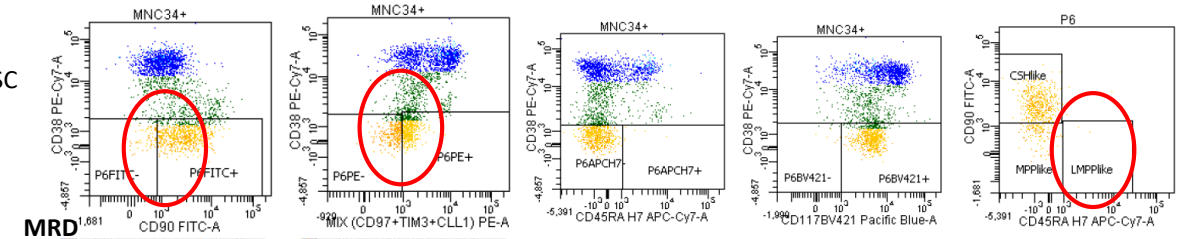


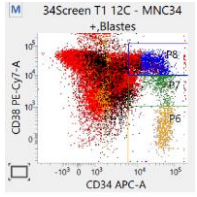
MRD1 pos
6% LAIP/0,2%LSC
EVI1+J/AK2nd



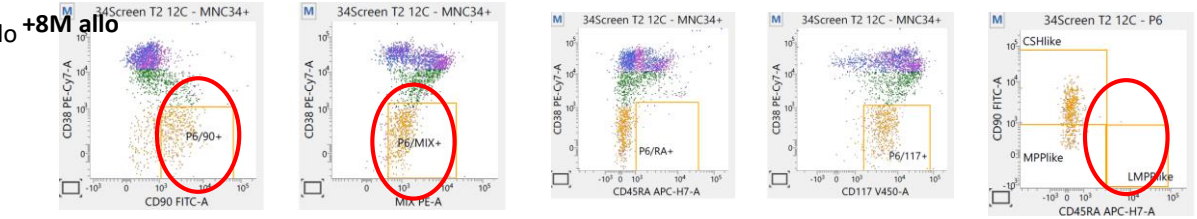


MRD preallo pos
0,8% LAIP/0,7%LSC
EVI1-JAK2+(51%)





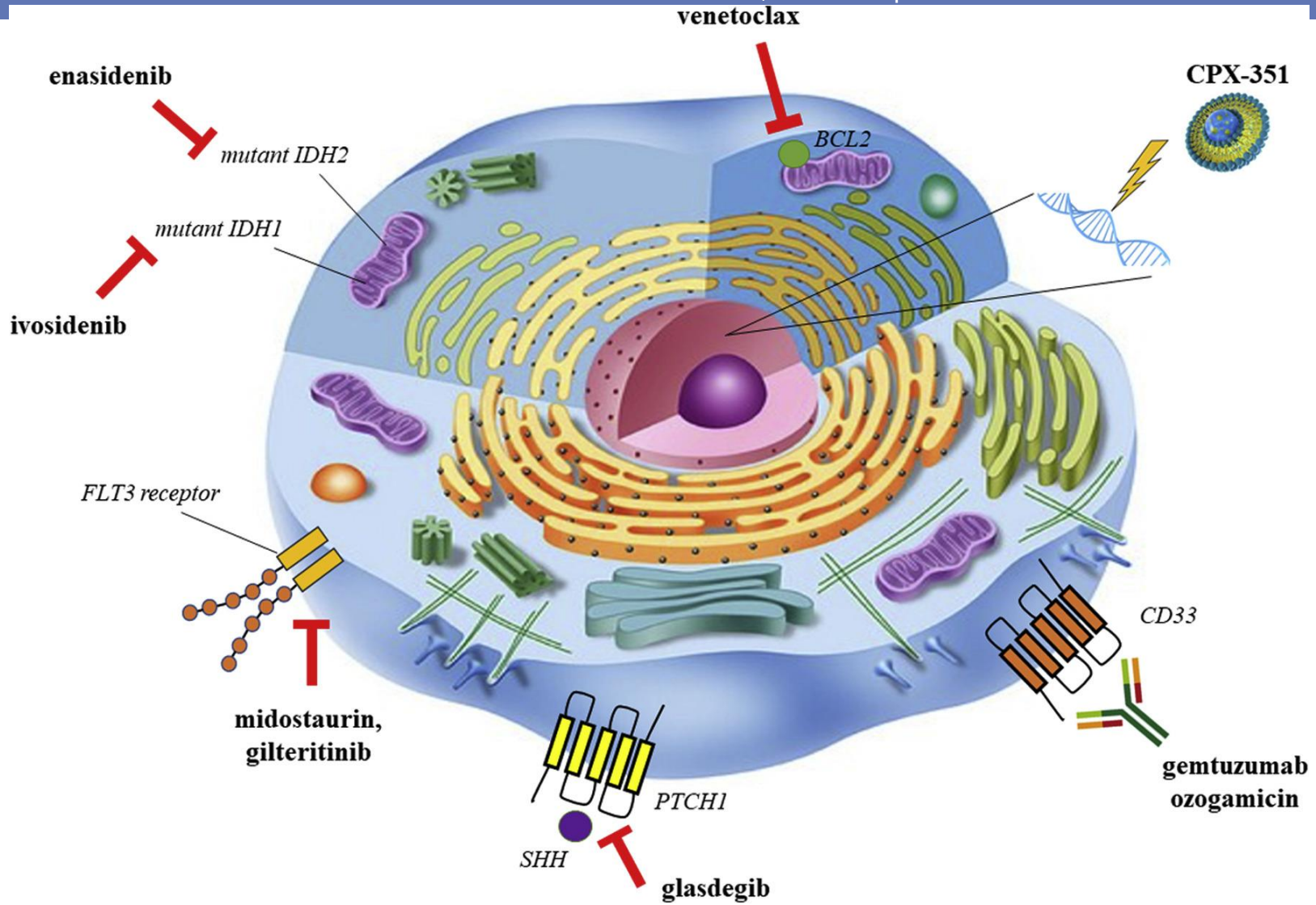
MRD pos +8M allo
0,2%SC
EVI1-JAK2+(20%)



Clonal Hematopoiesis - MRDflow LSC détectable mais stable (pas en rechute)

Définition Rechute MRD ELN 2021:

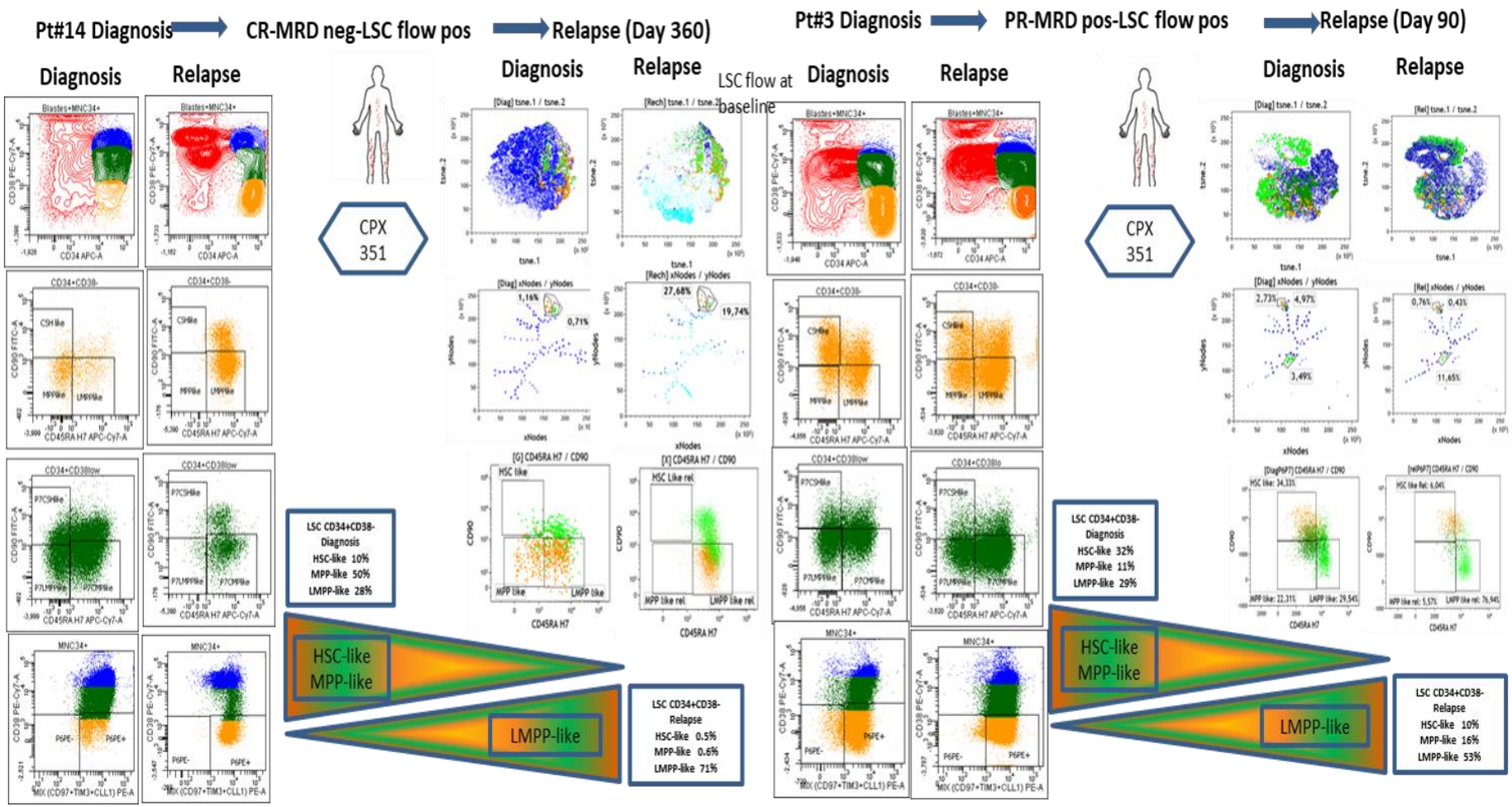
- Conversion MRD neg en MRDpos
- Augumentation d'une MRD détectable de >1log



Shyam A. Patel, Jonathan M. GerberClinical Lymphoma, Myeloma & LeukemiaMay 2020-279
https://doi.org/10.1016/j.clml.2020.01.011

Bridge for Allograft -LSC target identification- personalised immuntherapy, CART… and time point

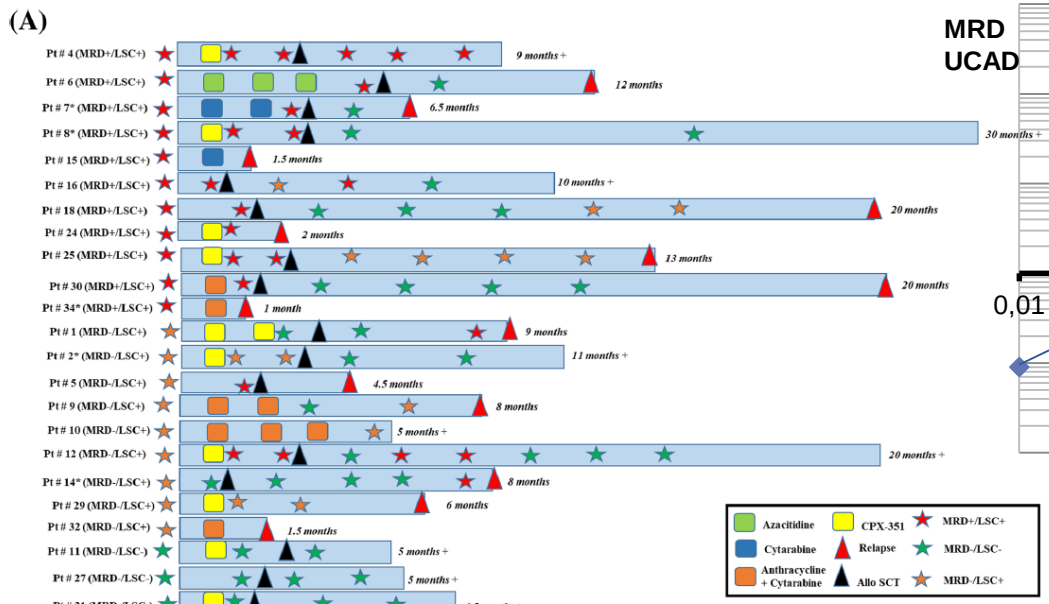
Measurable residual disease including AML leukemia stem cell flow evaluation of CPX-351 therapy by multi-parameter flow cytometry

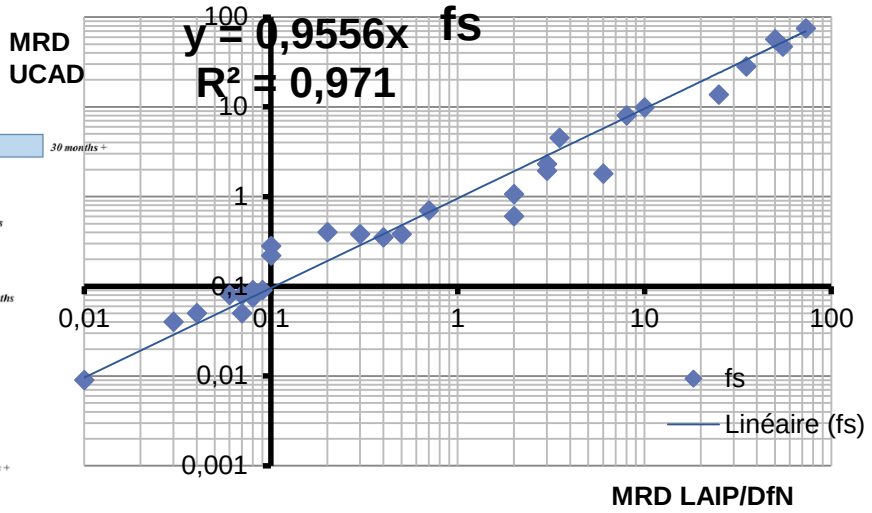


A Plesa et al, Leukemia Research, July 2021
SFH 2021 (Poster)

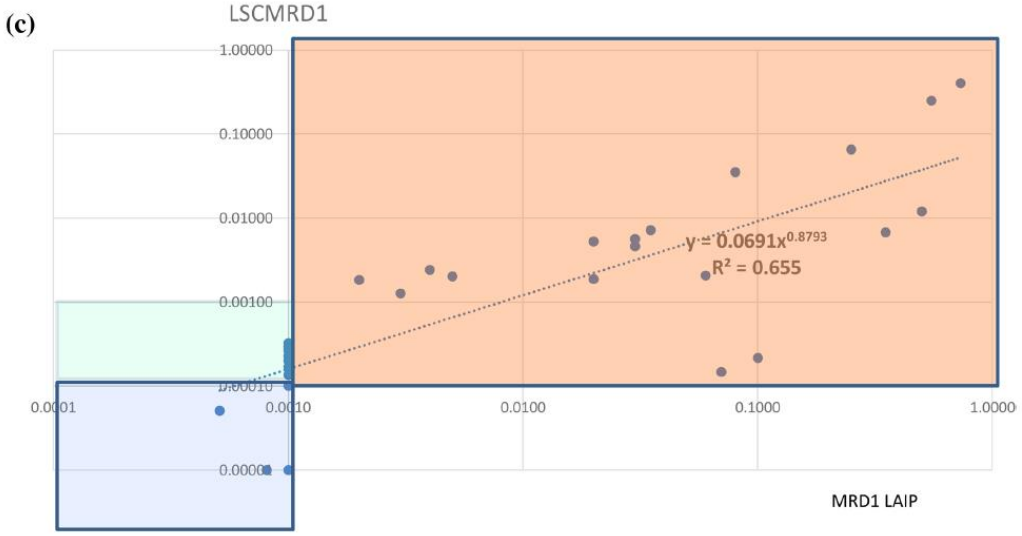
Correspondence

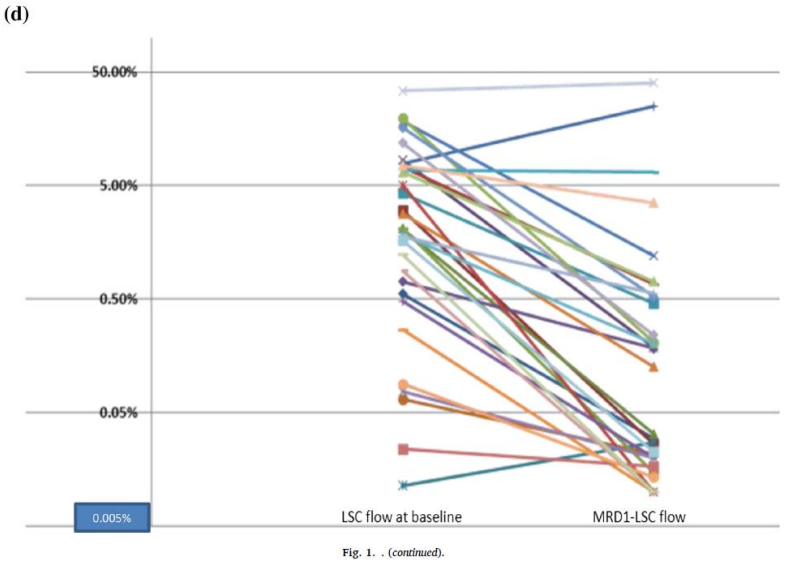
Leukemia Research 111 (2021) 106673





Corrélation MRD1 méthode MRDflow classique LAIP/DfN vs UCAD (Unsupervised Computer Assisted Design)

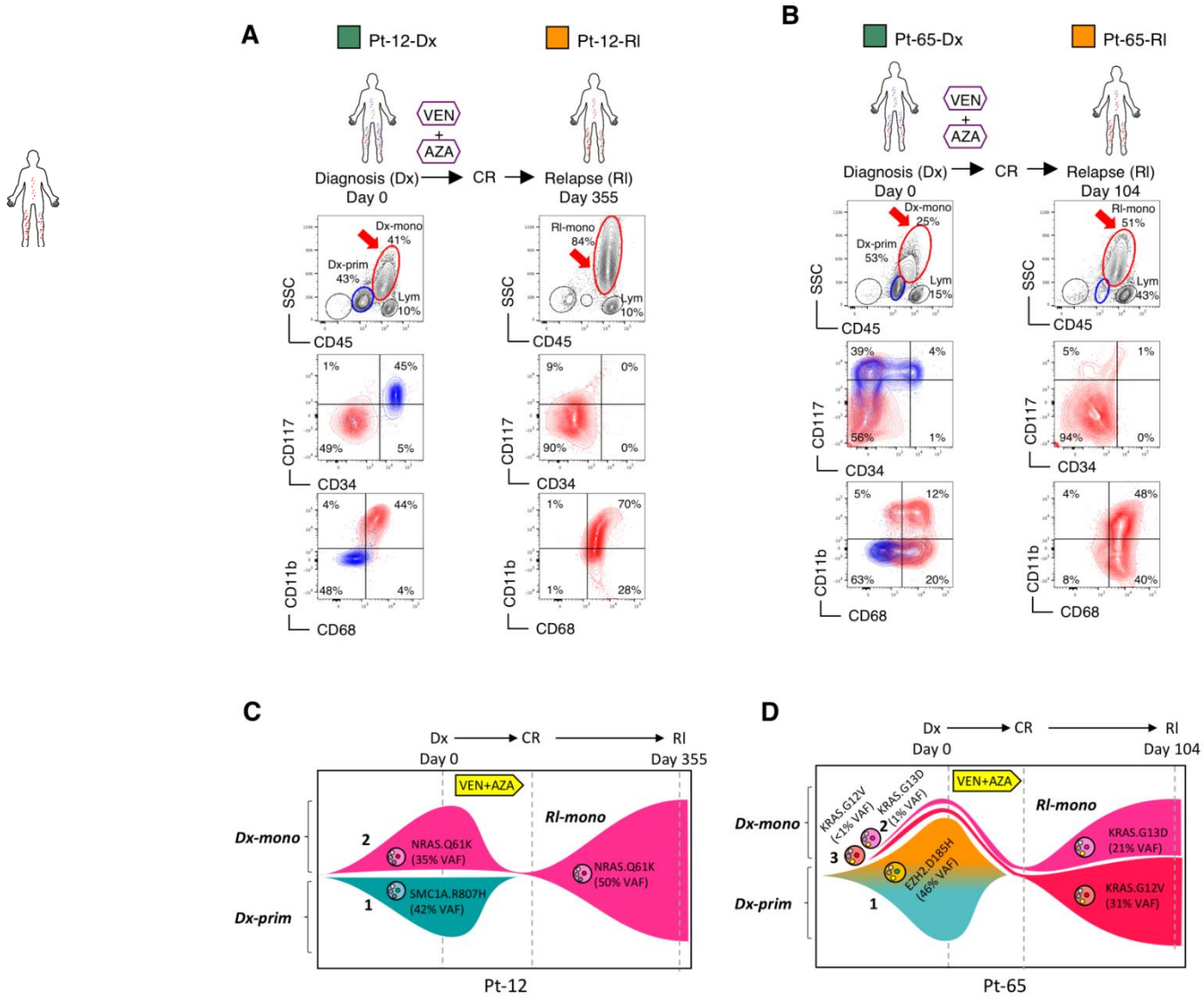




A Plesa et al, Leukemia Research, July 2021
SFH 2021 (Poster)

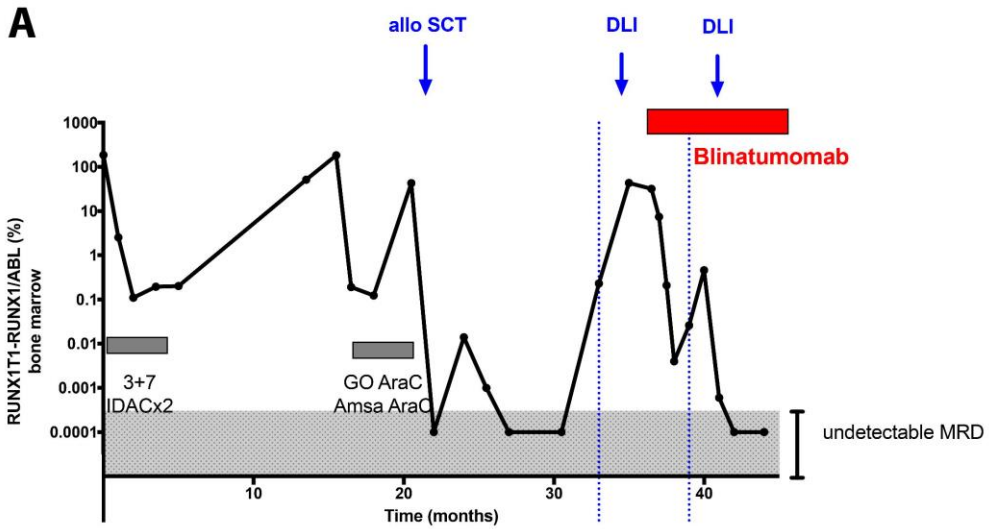
Developmental Plasticity of Acute Myeloid Leukemia Mediates Resistance to Venetoclax-Based Therapy

Figure 4



Shanshan Pei, Blood, 2019

MRDflow&LSC- Immunotherapy AML: Bridge Preallo, MRD relapse postallo

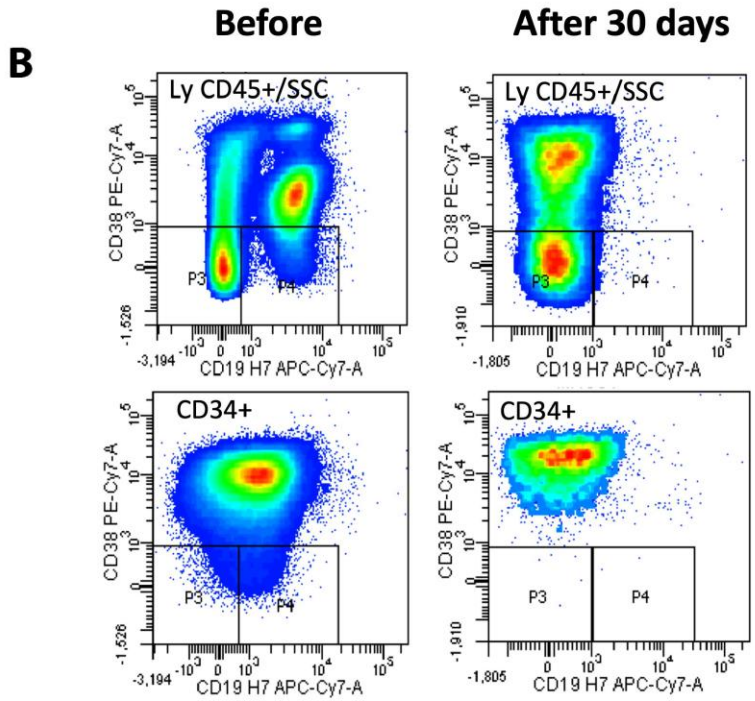


haematologica
Journal of The Ferrata Storti Foundation

Efficiency of blinatumomab in a t(8;21) acute myeloid leukemia expressing CD19

by Adriana Plesa, Hélène Labussière-Wallet, Sandrine Hayette, Gilles Salles, Xavier Thomas, and Pierre Sujobert

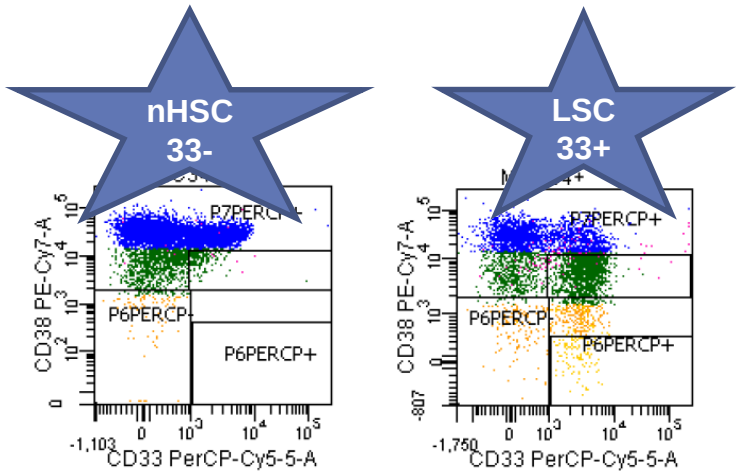
Haematologica 2019 [Epub ahead of print]



A Plesa et al, Hematologica 2019

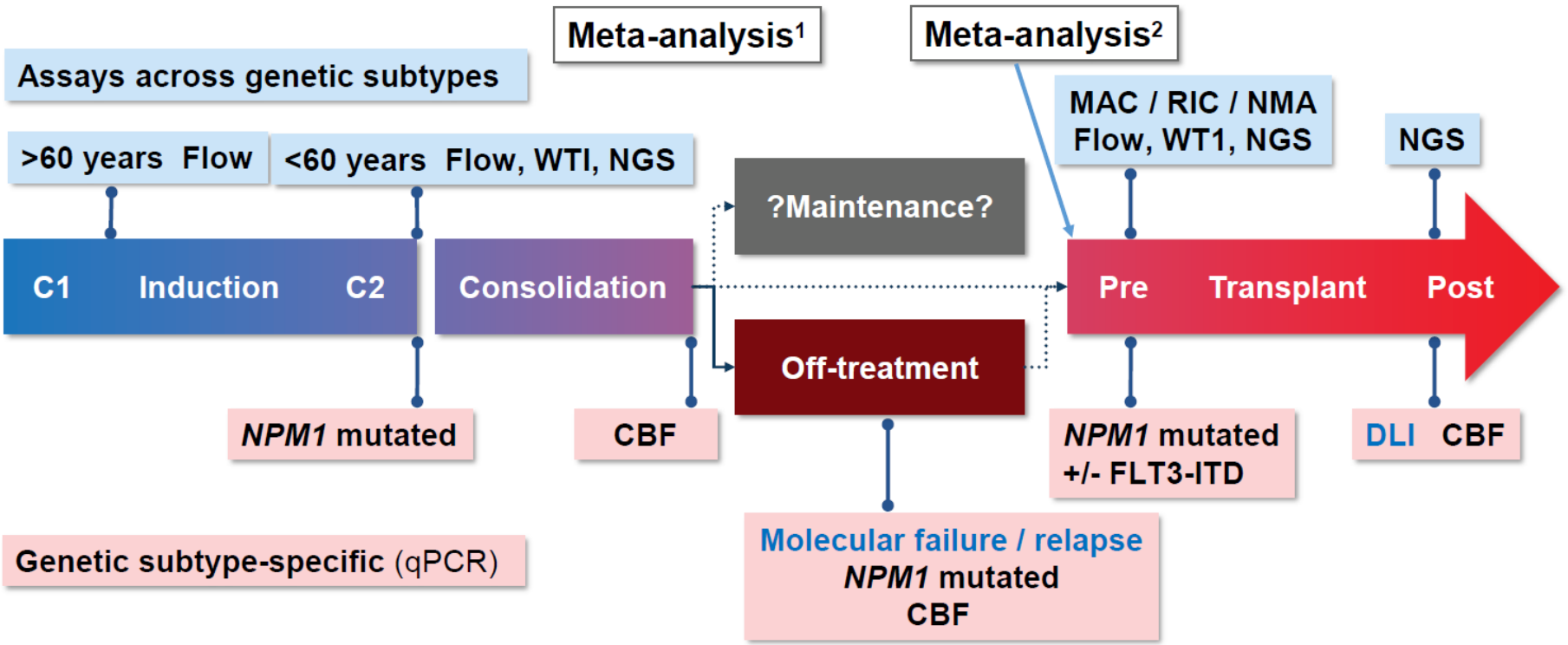
Acute myeloid leukemia stem cells and CD33-targeted immunotherapy

Roland B. Walter, Frederick R. Appelbaum, Elihu H. Estey and Irwin D. Bernstein



R Walter et al, Blood 2012

Strong correlation between MRD status and Clinical Outcomes



1. Short NJ, et al. *JAMA Oncol*. 2020 2. Buckley SA, et al. *Haematologica*. 2017

ELN 2021: MRD pos preallogreffe

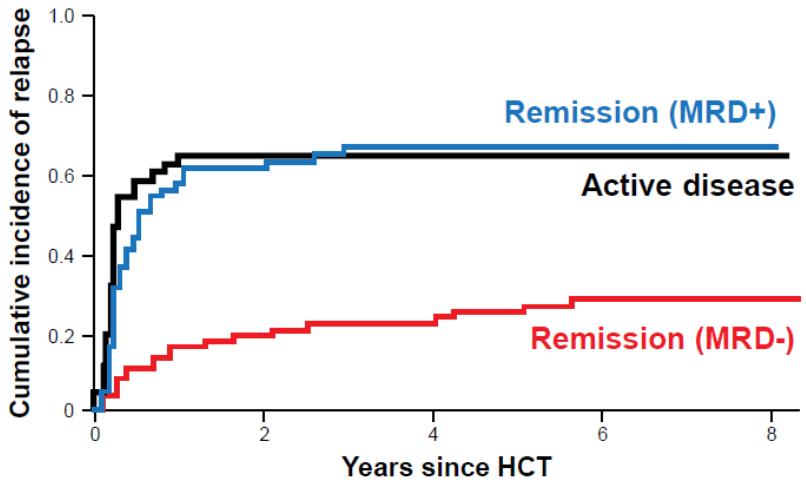
- Ne dois pas influencer la décision de l'allogreffe
- Conditionnement myeloablatif à considérer

S Freeman

Transplant decisions

Should pre-SCT MRD+ result alter decisions to transplant?

Relapse by MRD status pre MAC SCT[1]



Summary of published data

MRD testing across genetic subtypes

Relapse incidences for transplant cohorts

Other retrospective studies by flow or NGS

2-year CIR ~30% to 60%

Large EBMT study (retrospective)[2]

CTN 0901 (randomised [NGS MRD])[3]

2-year CIR ~25% MRD- vs ~40% MRD+

1. Adapted from Araki D, et al. *J Clin Oncol*. 2016..

2. Gilleece MH, et al. *Am J Hematol*. 2018.

3. Hourigan CS, et al. *J Clin Oncol*. 2020

ELN 2021: MRD pos preallogreffe

- Ne dois pas influencer la décision de l'allogreffe
- Conditionnement myeloablatif à considérer

S Freeman

Conclusion: MRDflow LAM & Allogreffe

Quand? Comment? Interprétation avec les autres marqueurs de suivi? (Biomol, NGS, chimerism…)

- Timing: preallogreffe (dans <1Mois preallo) et postallo +1M/3+M/+6M/+9M/+12M…2 ans)
- Prélèvement: Moelle-EDTA 0.5-1ml pour MRDflow (sang en cours d'évaluation) selon panel ELN2021

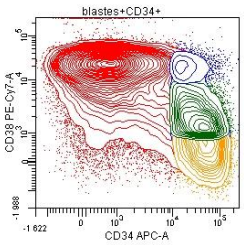
-MRDflow- clinical cut-off 0,1% LAIP (low level MRD cut-off 0,01% LSC)

-MRDflow : analyse classique (strategie nonsupervisé en cours d'evaluation)

- Intégration avec d'autres marqueurs de suivi :
- Si pas Marq Molec: MRDflow LAIP/DFN+LSC
- Si Marqueur moléculaire NPM1, AML1/ETO, WT1 + NGS : MRDflow LAIP/DFN+LSC
- Chimerism (sang et/ou moelle, cellules totales, populations triés CD34, CD3)

Guidelines 2021 ELN/SFGM/EBMT, adultes et enfants

Sept 2021: 30 Flow Labs: 18 BD (Canto / Lyric) - 12 BC (Navios)
Intergroupe MRDflow BIG Trial: ALFA & FILO



Flow Cytometric Labs
ALFA Clinical Trial (18 Labs)

Lyon: Adriana Plesa, Delphine Manzoni
Lille: Christophe Roumier, Florent Dumezy
Paris St Louis: Stephanie Mathis, Anna Raimbault
Paris St Cloud: Valerie Bardet
Paris Creteil: Orianne Wagner Ballon
Paris Versailles: Victoria Raggueneau
Paris IGR: Veronique Saada
Paris Pitie Salpetriere+Trousseau
: Magali Le Garf Tavernier, Helene Lapillone
Paris Bobigny: Remi Letestu
Paris St Antoine: Frederic Feger
Lille St Vincent: Agnes Charpentier
Amiens: Veronique Harrivel
Rouen: Elsa Bera
Caen: Veronique Salaun, Edouard Cornet
Dijon: Julien Guy
Marseille CHU+Nice : Isabelle Arnoux
Limoges: Jean Feuillard, Estelle Guerin
Valenciennes: Claire Hemar

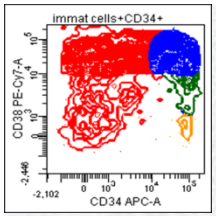
REMERCIEMENTS

Clinical coordinators: **Hervé Dombret, Cristian Recher**
Biological coordinator: **Claude Preudhomme**
ALFA coordinator: **Karine Celli-Lebras, Renaud Bufet**

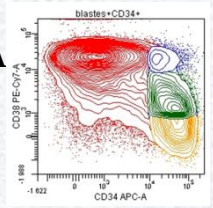
Yves Bertrand, IHOP, Lyon
Xavier Thomas, CHLS, Lyon

Flow Cytometric Labs
Part of FILO Clinical Trial (12 Labs)

Toulouse: Francois Vergez
Marseille IPC: Anne Catherine Lhoumeau
Angers: Franck Geneviève
Paris Cochin: Nicolas Chapuis
St Etienne: Lydia Campos, Jeremie Stagnara
Grenoble: Marie Christine Jacob, Tatiana Raskovalova
Clermont Ferrand: Richard Veyrat Masson
Rennes: Mikael Roussel
Moulhouse: Agathe Debliquis
Montpelier: Caroline Bret
Strasbourg: Caroline Mayeur-Rousse
Besançon: Anne Roggy, Thomas Fournet, Francine Garnache



Flow AML MRD Intergroup ALFA



AML MRD LSC

French Flow Intergroup

MERCI à TOUS!!!