Gating strategies for MRD detection in AML

Francesco Buccisano (Rome, IT)

1

Conflict of Interest Disclosure

In accordance with criterion 24 of document UEMS 2012/30 "Accreditation of Live Educational Events by the EACCME®" we herewith declare to have submitted a Conflict of Interest Disclosure Form to ESCCA.

This COI Disclosure Form can be viewed at the ESCCA 2019 Conference website www.escca.eu/norway2019 - Programme section / Accreditation page

2

Designing LAIP based MRD studies

FITC	PE	PerCP-Cy5.5	PE-Cy7	APC	APC-H7	Horizon V450	Horizon V500
CD64	CD11b	CD14	CD4	CD34	HLADR	CD33	CD45
CD22	CD10	CD7	CD19	CD34	HLADR	CD33	CD45
CD15	CD117	HLADR	CD13	CD34	CD20	CD33	CD45
CD38	CD56	CD16	CD19	CD34	CD4	CD33	CD45
CD61	CD2	CD14	CD3	CD34	HLADR	CD33	CD45

Identification of LAIP → Definition of patient-specific "immunologic fingerprint" → Immunologic fingerprint used during follow-up

Venditti et al Blood 2000, Venditti et al Leukemia 2003, Buccisano et al Leukemia 2006. Maurillo et al JCO 2008, Buccisano et al Blood 2010, Buccisano et al Blood 2012

3

Backbone markers in screening panel for AML

FITC	PE	PerCP-Cy5.5	PE-Cy7	APC	APC-H7	Horizon V450	Horizon V500
CD64	CD11b	CD14	CD4	CD34	HLADR	CD33	CD45
CD22	CD10	CD7	CD19	CD34	HLADR	CD33	CD45
CD15	CD117	HLADR	CD13	CD34	CD20	CD33	CD45
CD38	CD56	CD16	CD19	CD34	CD4	CD33	CD45
CD61	CD2	CD14	CD3	CD34	HLADR	CD33	CD45

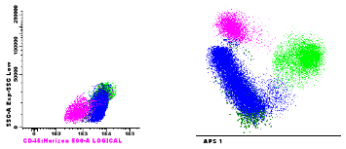
4

- The parameters and files must be similar regarding acquisition settings
  - the software will try to adjust the scales and will show a warning.
- A series of common parameters that allow to unequivocally identifying the population of interest.
- The common markers used in the panel must be marked with the same fluorochrome.
- The rest of the antibodies to be used in our study will be included in fluorescences not occupied by common parameters

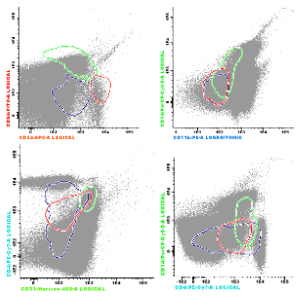
5

Automatic Population Separator (APS)

- Automatic separation of the events, analysing all the different choices of parameter combinations, based on Principal Component Analysis
- The parameters represented in these APS graphs are not a real measured parameter.

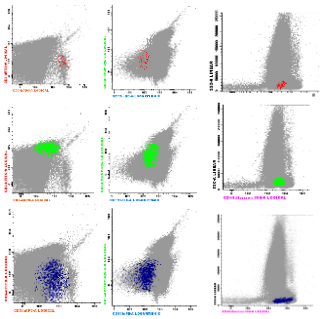


6



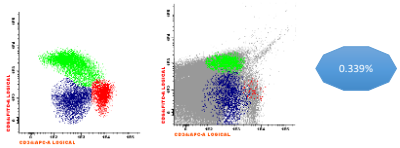
Reference image on post-consolidation BM

7



8

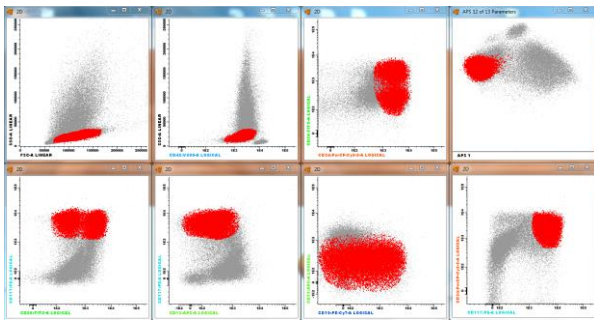
MRD determination after consolidation cycle



DIAGNOSIS

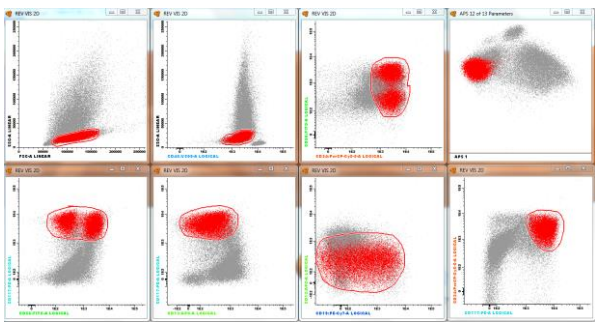
POST-CONSOLIDATION

9

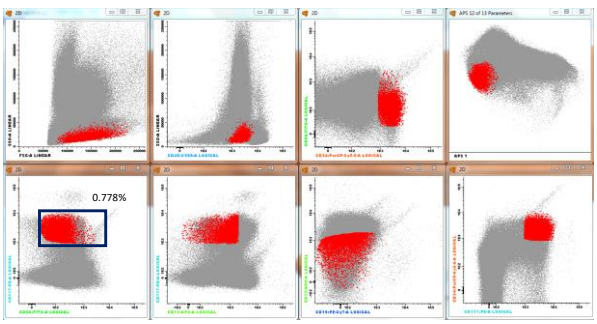


Male, 28 yrs, diagnosis of AML with RUNX/RUNX1T1 translocation, LAIP at diagnosis

10

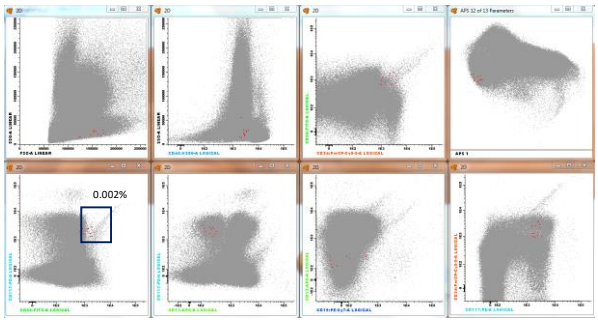


11



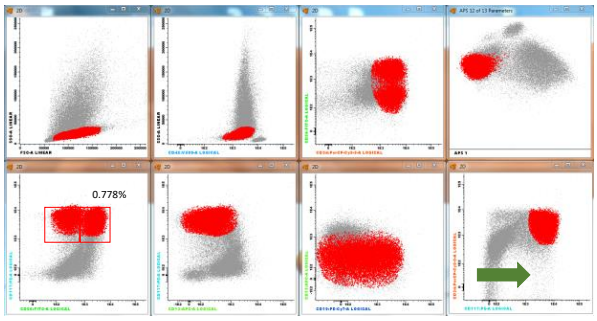
POST CONSOLIDATION MRD EVALUATION

12



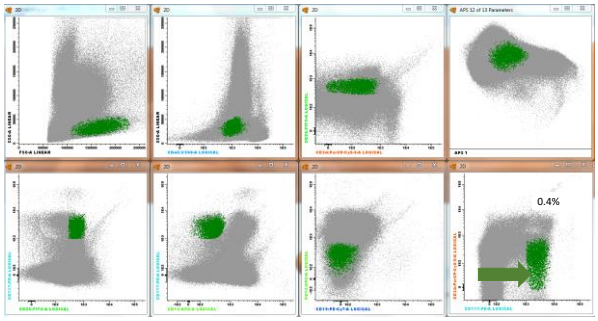
POST CONSOLIDATION MRD EVALUATION

13



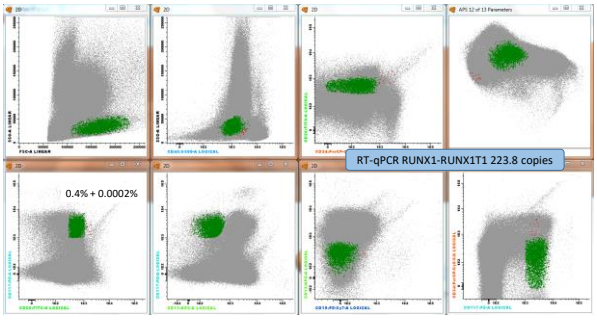
Male, 28 yrs, diagnosis of AML with RUNX/RUNX1T1 translocation, LAIP at diagnosis

14



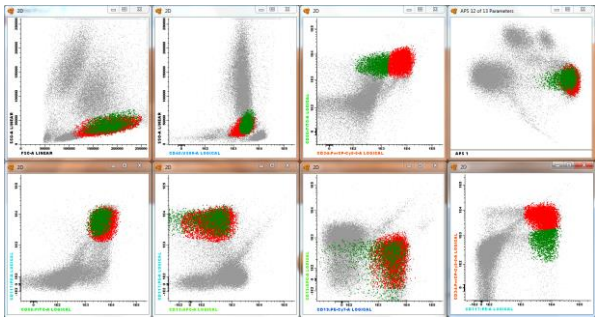
POST CONSOLIDATION MRD EVALUATION

15



POST CONSOLIDATION MRD EVALUATION

16



RELAPSE

17

TAKE HOME MESSAGES 1

- **LAIPs are DfN abnormalities in the vast majority of cases**, and the difference between these two approaches is likely to disappear if an adapted, sufficiently large panel of antibodies (preferably ≥ 8 colors) is utilized.
- **We recommend that the advantages of both approaches be combined** to best define MFC MRD burden, allowing detection of new aberrancies emerging at follow-up, and monitoring patients when there is an absence of diagnostic information.

- **New definition of "LAIP-based DfN approach"**

Schuurhuis GJ, Blood 2018

18

TAKE HOME MESSAGES 2

- At every time-point try all the possible combination of markers in the dot plots to allow a better discrimination of the heterogeneity of the leukemic clone
- Look carefully at empty spaces and unusual populations with distinctive features as compared to normal maturation curve
  - New abnormal population may occur during treatment course.
- Be not mislead by loss of single markers but keep a general vision on clone heterogeneity and complexity
  - If the residual LAIP is still relevant to define the population as abnormal go ahead…

19