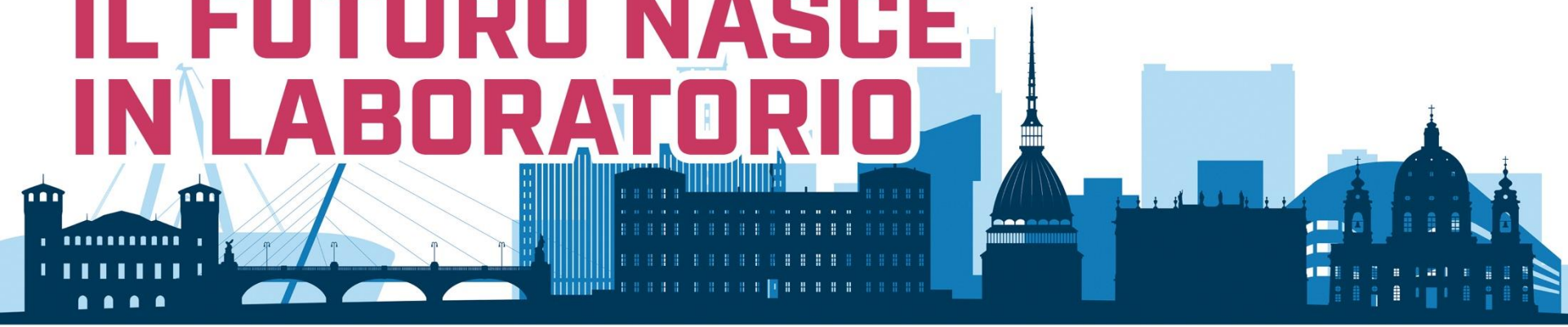
REGIONALE SIES – Delegazione Piemonte

YOUNG SCIENCE FORUM: IL FUTURO NASCE IN LABORATORIO



Standardizzazione della MRD nel Mieloma Multiplo

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TORINO, ACCADEMIA DI MEDICINA | 4-5 GIUGNO 2026

Disclosures of Elona Saraci

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

Presentation overview

MRD & Flow Cytometry

Measurable Residual Disease (MRD) and principles of Flow Cytometry

NGF & Standardization

Next-Generation Flow (NGF): establishing (SOPs), optimizing antibody panels, and implementing automated analysis.

Italian MM-MRD Network

The Italian Network results: inter-operator and inter-laboratory validation studies.

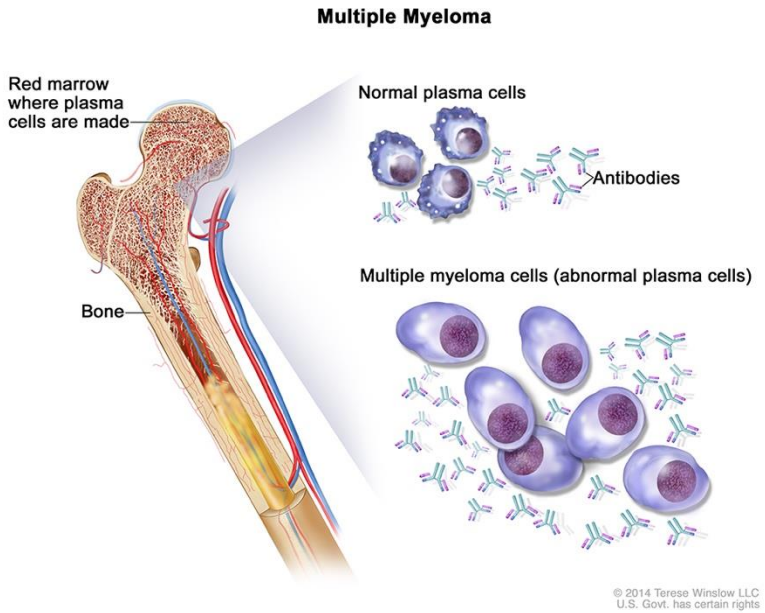
Conclusions

Final takeaways and future perspectives.

Multiple Myeloma

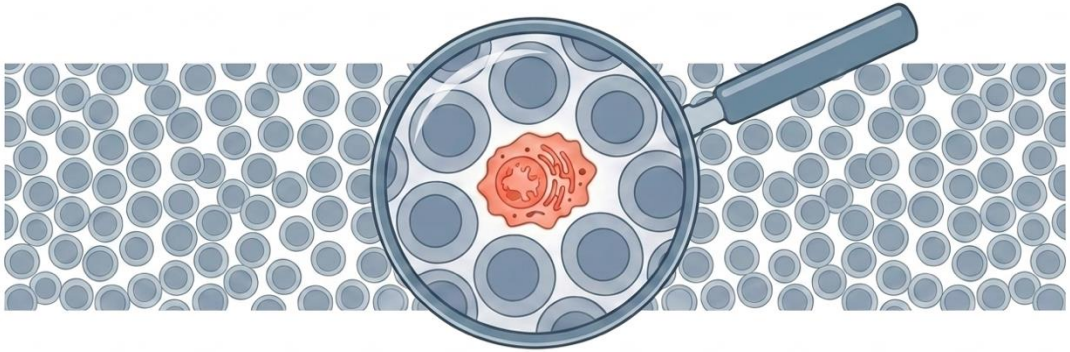
MM is a neoplastic PC disorder characterized by:

- clonal proliferation of malignant PCs in BM
- monoclonal protein in blood and/or urine
- organ disfunction



https://www.cdc.gov/cancer/myeloma/index.htm

Defining Minimal Measurable Disease (MRD)



Definition

The persistence of neoplastic plasma cells (PCs) at extremely low frequencies within the bone marrow following treatment.

The Challenge

These residual cells are undetectable by standard morphology and conventional diagnostic techniques.

The Requirement

Accurate identification requires highly sensitive molecular or flow cytometric assays.

Flow cytometry

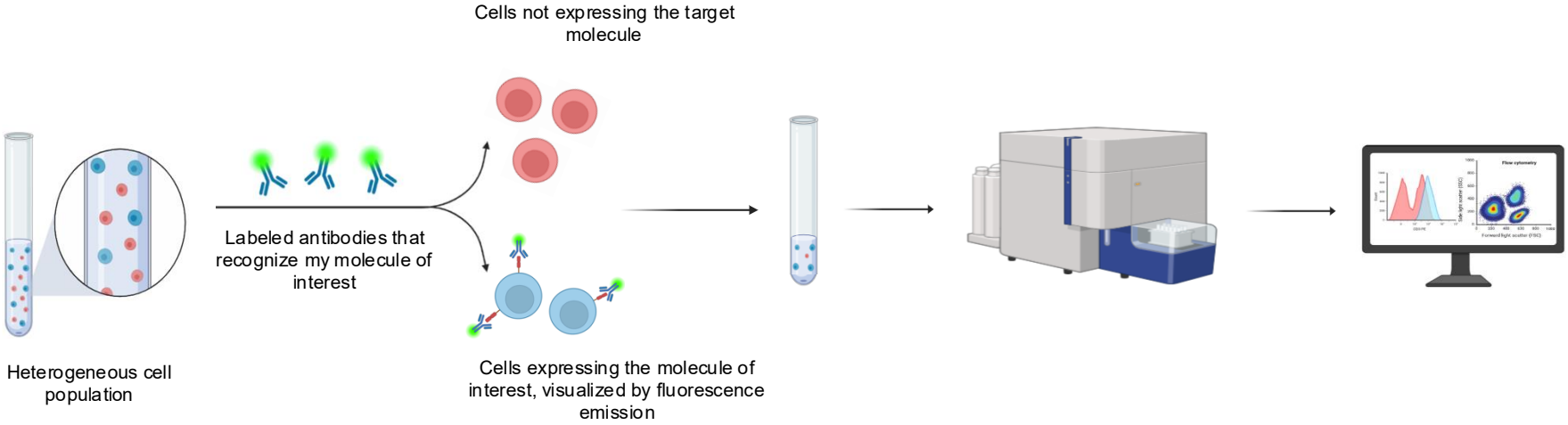
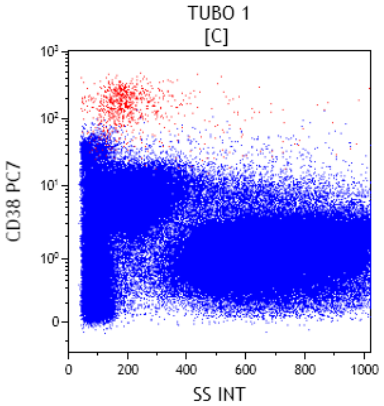


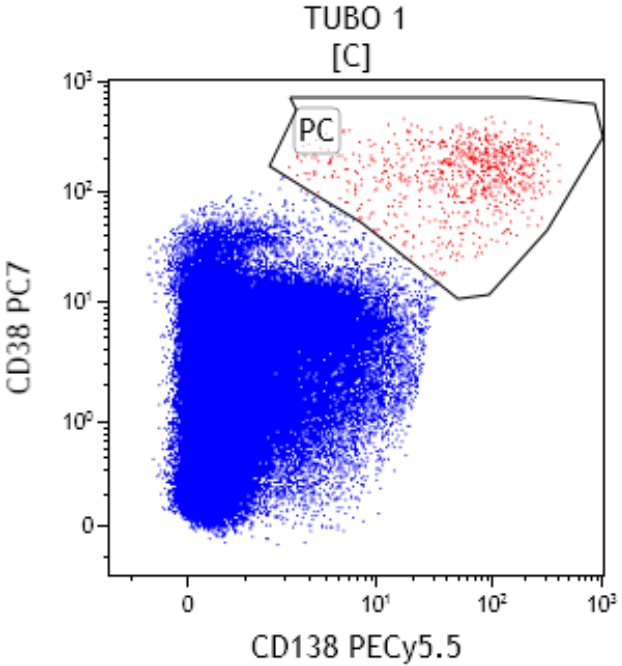
Image created with Biorender.com

Plasma cell antigens

CD38

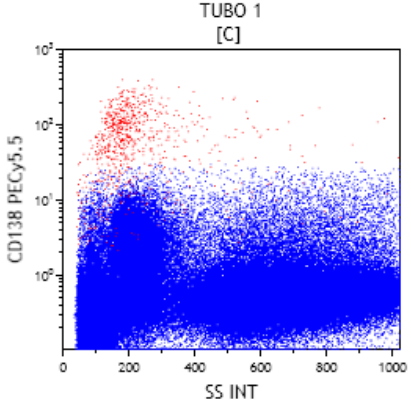
Expressed at HIGH INTENSITY on plasma cells.





CD138

Antigen expressed ONLY by plasma cells.



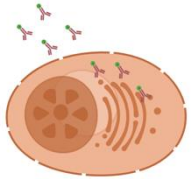
Plasma cell antigens

KEY MARKERS	Normal Plasma Cells	Abnormal Plasma Cells
CD45	+	−
CD19	+	−
CD56	−	+ (~80%)
ADDITIONAL MARKERS		
CD27	+	-/low
CD81	+	−
CD117	−	+ (~30%)

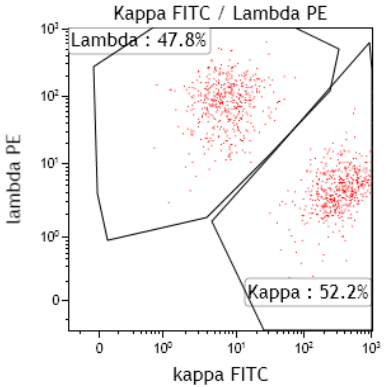
The most informative antigens which allow to distinguish between normal and pathological plasma cells in almost all patients.

Flores-Montero et al. Cytometry Part B (Clinical Cytometry) 90B:61–72 (2016)

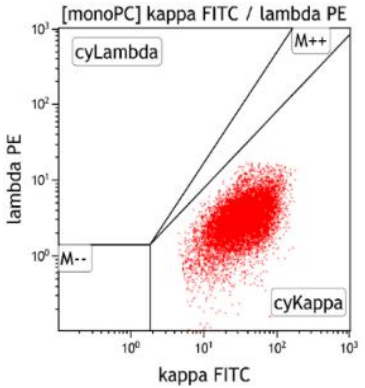
Plasma cell antigens



Normal plasma cells



Abnormal plasma cells

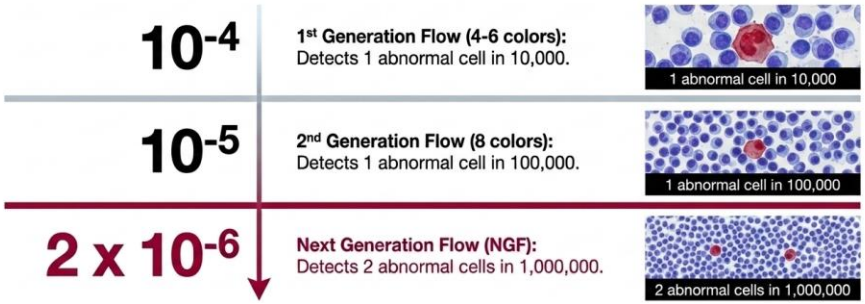


Flow Cytometry assessment of MRD

2008
1st Gen Flow

2012
2nd Gen Flow (8 colors)

2017
Next Generation Flow



We have improved detection limits by 100-fold in a decade.

Oliva S. et al. Front Oncol. 2020 Jan 31;10:1

Next Generation Flow

Pre-Analytical

- Sample Collection
- Controlled Transport

Analytical

- Optimized antibody panel
- Data Acquisition
- Instrument Setting

Post-Analytical

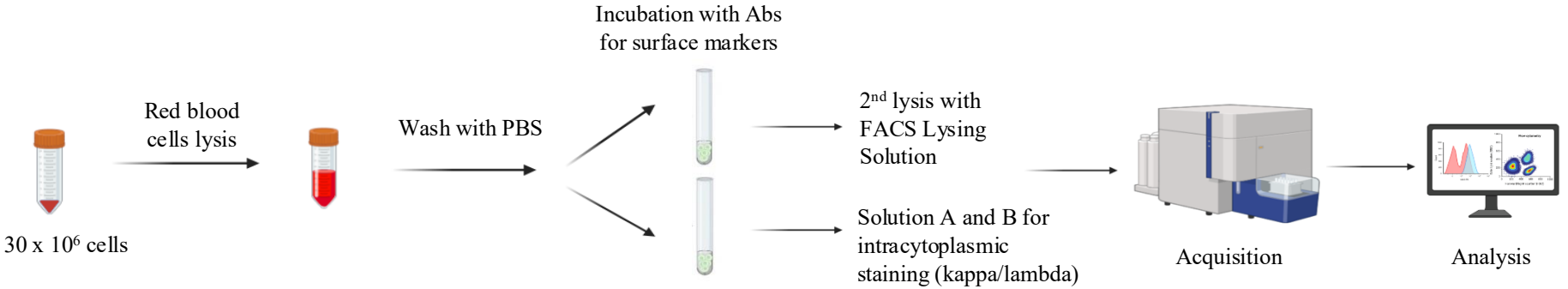
- Data Analysis
- Report

EuroFlow

www.euroflow.org

Sample processing and staining (8-color 2-tube panel)

Tube	BV421	BV510	FITC	PE	PerCP- Cy5.5	PE-Cy7	APC	APC-C750
Tube 1	CD138	CD27	CD38 - ME	CD56	CD45	CD19	CD117	CD81
Tube 2	CD138	CD27	CD38 - ME	CD56	CD45	CD19	CylgK	CylgL



At least 5 million of events acquired for each tube.

Sensitivity: 2 x 10^{-6}

EuroFlow

www.euroflow.org

Advantage of NGF over conventional flow cytometry

Standard Protocols

EuroFlow standardized procedures ensure reproducibility across different centers.

Automated Data

Software-assisted analysis reduces subjective bias in gating complex populations.

Maximum Cells

High-sensitivity detection through the analysis of up to 10 million cells.

The Future: Therapy Guidance

Response-Adapted Therapy

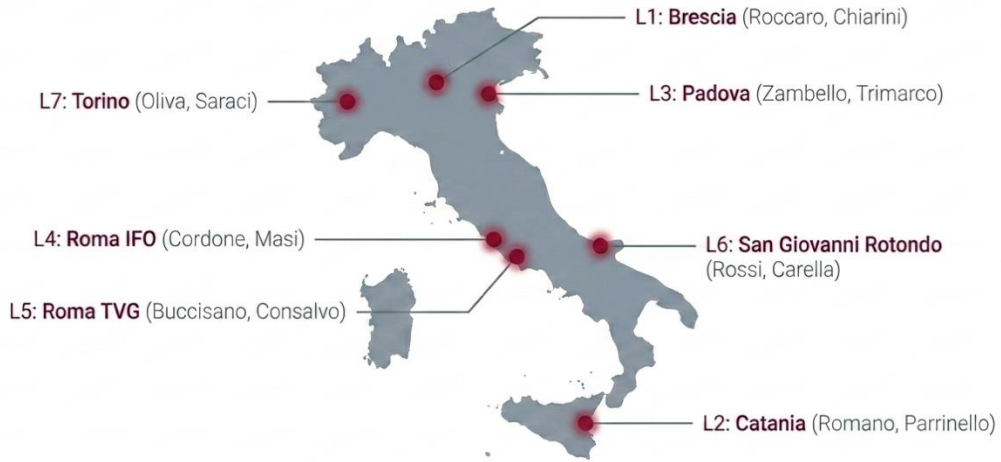
MRD is transitioning from a prognostic marker to a clinical driver. In the future, MRD status will guide:

- Treatment intensification.
- De-escalation strategies.
- Sustained MRD negativity as a criteria for therapy cessation.

Why a certified MRD network is essential: MM-MRD-Network

- High variability between laboratories → Risk of false negatives/positives
- MRD assessment requires standardization, inter-laboratory validation and quality control → Quality, reliability, interoperability
- Ensuring equal access to MRD assessment nationwide → MRD testing accessible via accredited reference labs when in-house capability is unavailable

"Italian MM-MRD network" project

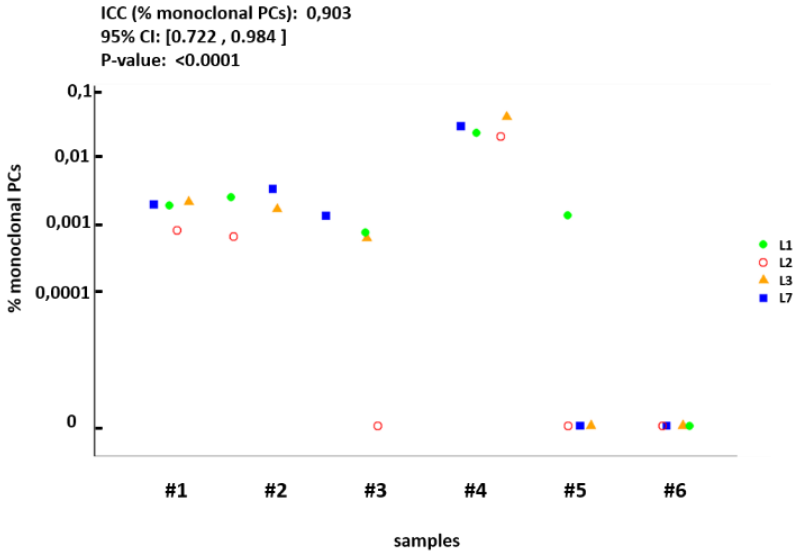


MRD harmonization across Italian centers

NGF was used in this project to assess MRD

Oliva S. Cancer Med, 2026 Mar;15(3):e71678.

Phase 1: Inter-operator Concordance



Study Design

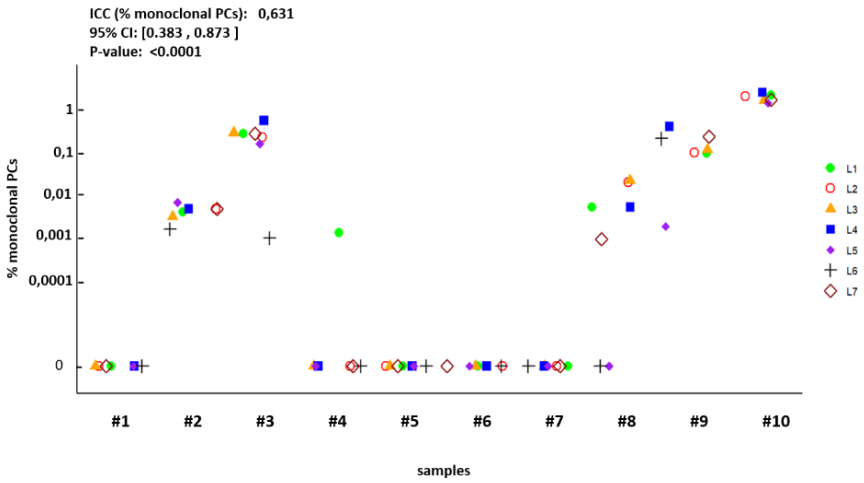
Inter-operator study involving 4 participating laboratories to evaluate reproducibility and consistency of MRD analysis across different operators and sites.

Results

- 100% concordance in 4 samples; 75% concordance in 2 samples.
- Intraclass Correlation Coefficient (ICC): **0.903** (95% CI: 0.722, 0.984)

Oliva S. Cancer Med, 2026 Mar;15(3):e71678.

Phase 2: Inter-laboratory Concordance



Study Design

Expanded inter-laboratory study incorporating all 7 MMRD-Net reference centers to test real-world application across disparate geographic locations.

Results

- 100% concordance in 8 samples; minor variations in complex samples (86% in #4, 71% in #8).
- Intraclass Correlation Coefficient (ICC): **0.631** (95% CI: 0.383, 0.873).

Oliva S. Cancer Med, 2026 Mar;15(3):e71678.

Lessons from “Italian MM-MRD network” project

Expertise Matters

Accurate assessment requires deep training, even with standardized assays.

Inter-Lab Dialogue

Regular discussions on technical challenges drive quality improvement.

Uniform Reporting

Centralized guidelines support consistent interpretation for clinicians.

Conclusions and Future perspectives

1. Accurate Assessment

Standardization and certified laboratories are essential for reliable MRD assessment.

2. Italian Network

Promoting the national MM-MRD network ensures every patient has access to gold-standard testing.

3. Harmonized Guidelines for MRD Assessment

Shared guidelines support standardized methodology, data analysis, interpretation, and reporting across centers.

4. Quality & Training

Ensure adherence to international MRD standards through quality assurance and professional training.

Acknowledgments

Divisione Universitaria di Ematologia
Prof. B. Bruno

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