

PLASMA-CELL DISORDERS

Multidimensional identification, clonality & defensible myeloma MRD

CFCM / CLINICAL POSTER SERIES / SPECIALIST CLINICAL FLOW CYTOMETRY

Expert diagnostic and follow-up framework. Published eight-colour figures are distinct from the proposed higher-colour design brief.

1 Clinical question & context	2 Phenotype & clonality	3 12-marker design brief
Identify, then characterise Find plasma cells without assuming that every clone is CD38-bright, CD138-bright, CD19-negative or CD56-positive. Flow does not define myeloma alone A clonal plasma-cell population must be interpreted with morphology, clinical and laboratory evidence; the disease category is integrated. Before calling MRD negative Assess marrow quality, treatment history, informative events and achieved assay sensitivity. A haemodiluted aspirate can yield a misleading negative [1,3].	Use several independent views Assess CD38 / CD138 with CD45, CD19, CD56, CD27, CD81 and CD117. Expression varies within and between clones. Confirm within the right subset Evaluate cytoplasmic kappa / lambda within informative plasma-cell subpopulations, with suitable normal / B-cell controls [1]. Treatment-aware identification Anti-CD38 therapy can alter detectability. Verify the chosen clone and alternative markers for the treatment context; do not declare every alternative universally reliable [1].	Identity / compartment CD38 CD138 CD45 CD19 Aberrancy / normal comparison CD56 CD27 CD81 CD117 Additional differentiation CD20 CD28 cyKappa cyLambda Design versus validation A single 12-colour surface / intracellular tube requires local verification. Riebl et al. published a ten-colour surface approach but excluded daratumumab-treated patients [2]. Do not extend that validation to them.

4 Published dot plots & visual interpretation	5 Acquisition & interpretation
Figure 1: retain marrow context while identifying plasma cells Figure 1 reproduced from Cordone et al. [1], © 2023 authors, CC BY 4.0. Original eight-colour plots, gates and colours unchanged. Original published eight-colour example. Plasma cells are orange; marrow precursor compartments help assess sample quality. A CD45-positive-only denominator can exclude abnormal plasma cells [1].	Separate discovery from quantification Use multiple identity markers and back-gating before defining the abnormal compartment. Do not discard dim CD38 / CD138 cells by default. Check specimen adequacy Review marrow-specific populations and the clinical sampling history. Absence of a compartment alone is not a universal haemodilution cutoff [1,3]. A distinct clone is not one aberrant marker Normal plasma cells are heterogeneous. Combine phenotype and light-chain evidence rather than treating CD19 loss or CD56 gain as sufficient. Report the denominator Distinguish clonal cells among plasma cells from clonal cells among informative nucleated events. These are different measurements. Follow all supported subclones Do not limit follow-up to the most obvious baseline phenotype or a single antigen intensity.

6 Practical pitfalls	7 Clinical report	8 MRD: the quantification boundary	9 Concise evidence
Technical loss Delayed processing, reduced viability and antigen instability may diminish recovery or marker intensity [3]. Therapeutic interference Record anti-CD38 exposure and validate detection in that setting; the ten-colour reference is not that validation [2]. Other clonal compartments A restricted B-cell population requires its own interpretation; do not relabel it as plasma cells solely because light chains are restricted.	Positive / negative with limits State adequacy, plasma-cell identity, abnormal phenotype, target count, informative denominator and achieved limits [1,4]. Bound the interpretation A negative aspirate at a stated sensitivity is not proof of absence throughout a patchy marrow or extramedullary sites. No fabricated result Source-figure populations illustrate reasoning. They are not new CFCM diagnostic findings.	Detected is not always quantifiable A credible cluster at or below the validated quantification threshold is detected but not quantifiable, if detection criteria are met. No universal event cutoff Establish LoB, LoD and LoQ for the local assay. Published 20 / 50-event examples are method-specific, not transferable validation [1,4]. Sensitivity is conditional More acquired events do not repair haemodilution, poor recovery, background or incorrect cell identity.	[1] Cordone I et al. Cancers 2023;15:2060. doi:10.3390/cancers15072060. [2] Riebl V et al. Front Oncol 2021;11:708231. doi:10.3389/fonc.2021.708231. [3] Stetler-Stevenson M et al. Cytometry B 2016;90:26–30. doi:10.1002/cyto.b.21249. [4] Arrozo M et al. Cytometry B 2016;90:31–39. doi:10.1002/cyto.b.21228. Technical support: Shapiro HM. Practical Flow Cytometry. 4th ed. Wiley-Liss;2003. doi:10.1002/0471722731. No book figures reproduced.

A defensible negative result needs adequate marrow, reliable cell identification and a validated, achieved sensitivity.