Letter to Editor

An mSMART-based 5-probe high-risk FISH panel should suffice for an early risk stratification in a newly diagnosed multiple myeloma in a resource-limited setup

We read the recently published article by Jimmy *et al.*[1] in Cancer Research, Statistics and Treatment journal titled "Clinical utility and significance of seven-probe FISH in risk stratification of multiple myeloma (MM) in resource-limited countries". We take this opportunity to highlight a few points regarding the need for this 7-probe interphase fluorescent *in situ* hybridization (iFISH) panel for optimal risk stratification and also to debate the choice of probes included in this panel. The latest stratification for myeloma and risk-adapted therapy (mSMART) guidelines mention five high-risk (HR) cytogenetic markers, del17p-TP53, t(4;14), t(14;16), t(14;20), and 1q gain/amplification or 1p deletion, and three standard-risk (SR) cytogenetic markers, trisomies (suggesting hyperdiploidy), t(11;14), and t(6;14).[2] The seven-probe FISH panel proposed by the authors in the risk stratification of MM includes a mix of four HR markers (TP53 deletion, 1p1q amplification, t(4;14), and t(14;16)), two SR markers (hyperdiploidy and t(11;14)), and an additional generic IGH gene rearrangement probe.

We have some comments for the authors to consider:

(i) In the presence of specific IGH translocation probes such as t(4;14), t(14;16), and t(11;14) in the panel, adding a generic IGH rearrangement probe, in the same panel, has limited value. (ii) The authors compared their panel with a few 5-probe panels, which do not include all the HR markers, especially the probe for detecting 1q abnormalities. Additionally, their panel is short of t(14;20), an HR marker. We suggest comparing their panel to the HR panel based on mSMART, which includes deletion 1p/gain 1q and t(14;20) probes.

(iii) The authors have included SR markers, such as t(11;14) and hyperdiploidy, in their proposed 7-probe iFISH panel. Hyperdiploidy has been shown to improve prognosis in a few HR patients.[2,3] In resource-limited setups, the absence of HR markers using HR iFISH probes should be enough to determine the appropriate therapeutic strategy for SR patients. The established five HR markers used as a panel based on mSMART are optimal to detect HR MM.[2,4]

(iv) Using a generic IGH gene rearrangement probe instead of specific t(4;14), t(14;16), and t(14;20) probes for the initial screening of IGH translocations can further reduce the initial probe panel size to 3. Specific IGH translocation partners can be checked sequentially only if the initial screen detects any IGH gene rearrangement. The initial 3-probe panel involving IGH gene rearrangement can also screen for the two SR abnormalities: t(11;14) and t(6;14). IGH translocations are seen in about 40% of cases of newly diagnosed multiple myeloma (NDMM).[2,5] Thus, in almost half of the cases of NDMM, even a 3-probe screening panel comprising IGH rearrangement, del 17p-TP53 gene, and del 1p/gain 1q can exclude the HR subgroup.

(v) The CD138 positive selection method for sorting plasma cells may not always yield adequate cells for a 7-probe FISH panel.[6] A lower percentage of bone marrow plasma cells should be considered for a sequential iFISH panel to ensure optimal resource use. Thus, a 3-probe screening panel or a 5-probe HR diagnostic panel should suffice in a resource-limited setup.

(vi) The presumption that iFISH detects new cytogenetic abnormalities compared to karyotyping is misguided. The iFISH test can only be used to look for known targets. At the same time, though tedious, karyotyping presents a microscopic snapshot of the entire genome and is, hence, more likely to show newer and evolving cytogenetic abnormalities.[7]

Acknowledgements

We acknowledge all our team members from the Department of Pathology and Microbiology at Apollo Hospital, Navi Mumbai (AHNM), and Helix Genetic and Pathology Laboratory, Powai, for performing this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Access this article online

Website: https://journals.lww.com/crst

DOI: 10.4103/crst.crst_167_24

Quick Response Code

How to cite this article: Jain P, Jain P, Bathija H. An mSMART-based 5-probe high-risk FISH panel should suffice for an early risk stratification in a newly diagnosed multiple myeloma in a resource-limited setup. Cancer Res Stat Treat 2024;XX:XX-XX.

Submitted: 14-Jul-2024 **Revised:** 04-Aug-2024
Accepted: 19-Aug-2024 **Published:** ***

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