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Clinicians' Perspectives and Methodological Application of Fluorescence *in situ* Hybridization (FISH) to Define Cytogenetic Risk in Multiple Myeloma: An Italian, Real-World, Survey-Based Report From the European Myeloma Network (EMN) Italy

Lorenzo Cani,[1] Maria Teresa Petrucci,[2] Katia Mancuso,[3,4] Renato Zambello,[5] Laura Paris,[6] Sara Aquino,[7] Flavia Lotti,[8] Francesco Vassallo,[9] Norbert Pescosta,[10] Micol Quaresima,[11] Patrizia Tosi,[12] Iolanda Donatella Vincelli,[13] Sonia Ronconi,[14] Nicola Giuliani,[15] Francesco Pisani,[16] Mario Luppi,[17] Rita Rizzi,[18,19] Rita Mazza,[20] Delia Rota-Scalabrini,[21] Claudia Cellini,[22] Silvia Mangiacavalli,[23] Giuseppe Pietrantuono,[24] Maria Luisa Pioltelli,[25] Antonietta Pia Falcone,[26] Elisabetta Antonioli,[27] Angelo Belotti,[28] Sonia Morè,[29] Benedetto Bruno,[1] Mario Boccadoro,[30] Mattia D'Agostino[1]

[1]Department of Molecular Biotechnology and Health Sciences, Division of Hematology, AOU Città della Salute e della Scienza di Torino, University of Torino, Torino, Italy
[2]Haematology, Department of Translational and Precision Medicine, Azienda Ospedaliera Policlinico Umberto I, Sapienza University of Rome, Rome, Italy
[3]Istituto di Ematologia "Seràgnoli", IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy
[4]Dipartimento di Scienze Mediche e Chirurgiche, Università di Bologna, Bologna, Italy
[5]Department of Medicine (DIMED), Hematology, Padua University, Padua, Italy
[6]Department of Oncology and Hematology, Azienda Socio-Sanitaria Territoriale Papa Giovanni XXIII, Bergamo, Italy
[7]Ematologia e Terapie cellulari, IRCCS Ospedale Policlinico San Martino, Genova, Italy
[8]Sezione di Ematologia e Immunologia Clinica, Ospedale Santa Maria della Misericordia, località Sant'Andrea delle Fratte, Perugia, Italy
[9]S.C. Ematologia, Azienda Ospedaliera Santa Croce e Carle, Cuneo, Italy
[10]Reparto Ematologia e TMNO, Ospedale Provinciale Bolzano, Bolzano, Italy
[11]Azienda USL - IRCCS di Reggio Emilia, Reggio Emilia, Italy
[12]Hematology Unit, Infermi Hospital, Rimini, Italy
[13]Department of Hemato-Oncology and Radiotherapy, Hematology Unit, Grande Ospedale Metropolitano "Bianchi-Melacrino-Morelli", Reggio Calabria, Italy
[14]IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, Italy
[15]Department of Medicine and Surgery, University of Parma and Hematology, University Hospital of Parma, Parma, Italy
[16]Unità di Ematologia e Trapianti, IRCCS Istituto Nazionale dei Tumori Regina Elena, Roma, Italy
[17]Dipartimento di Scienze Mediche e Chirurgiche Materno Infantili e dell'Adulto, UNIMORE, UOC Ematologia, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[18]Department of Precision and Regenerative Medicine and Ionian Area, "Aldo Moro" University School of Medicine, Bari, Italy
[19]Hematology and Stem Cell Transplantation Unit, AOU Consorziale Policlinico, Bari, Italy
[20]Department of Oncology and Hematology, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy
[21]Medical Oncology Department, Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Italy
[22]AUSL Romagna, Ospedale Santa Maria delle Croci, Ravenna, Italy
[23]Division of Hematology, IRCCS Fondazione Policlinico San Matteo, Pavia, Italy
[24]Hematology and Stem Cell Transplantation Unit, IRCCS Centro di Riferimento Oncologico della Basilicata, Rionero in Vulture, Italy
[25]SC Ematologia, GOM Niguarda, Milano, Italy
[26]Hematology, IRCCS "Casa Sollievo della Sofferenza" Hospital, San Giovanni Rotondo, Italy
[27]Hematology Unit, AOU Careggi, Florence, Italy
[28]Department of Hematology, ASST Spedali Civili di Brescia, Brescia, Italy
[29]AOU delle Marche, Università Politecnica delle Marche, Ancona, Italy
[30]European Myeloma Network (EMN), Turin, Italy

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Address for correspondence: Mattia D'Agostino, MD, Department of Molecular Biotechnology and Health Sciences, Division of Hematology, AOU Città della Salute e della Scienza di Torino, University of Torino, Corso Bramante 88/90, Torino, 10126, Italy.
E-mail contact: mattia.dagostino@unito.it

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Abstract

We conducted a survey among 70 Italian centers treating multiple myeloma to record laboratory and clinicians' perspectives about the application of fluorescence *in situ* hybridization (FISH), with a focus on 1q alterations. In Italy, FISH was widely accessible and emerged as a crucial prognostic technique. Most centers performed FISH at diagnosis in all patients. Our data confirmed the need for more standardized protocols and clearer guidelines on the management of cytogenetic abnormalities in multiple myeloma within the Italian setting.

Background: Fluorescence *in situ* hybridization (FISH) is the standard technique for the prognostic detection of cytogenetic abnormalities (CA) in multiple myeloma (MM). In Italy, the application of practical guidelines for FISH testing in clinical studies and the degree of standardization of laboratory techniques are largely unknown. **Methods:** We conducted a survey from April to July 2023 among 70 MM-treating centers associated with the European Myeloma Network Italy and geographically well distributed across Italy. We aimed to record laboratory and clinicians' perspectives about FISH application in Italy, with a focus on 1q alterations. **Results:** FISH was widely accessible across the country, with 71% of centers performing it locally, while the remaining centers (predominantly those with <30 newly diagnosed MM cases/year) sent samples to external laboratories. Variability in laboratory techniques, such as $CD138^+$ cell purification and CA detection thresholds, was observed among centers. The centers analyzed del(17p) (100%), t(4;14) (100%), t(14;16) (98%), 1q+ (96%, with 70% distinguishing between gain and amplification), t(11;14) (90%), del(1p32) (88%), del(13q) (68%), and hyperdiploidy (52%). FISH emerged as a crucial prognostic technique, since 94% of centers used the Revised International Staging System (R-ISS) at diagnosis, and 69% implemented the recent R2-ISS. Most centers performed FISH at diagnosis in all patients, while others did not routinely perform FISH in some categories of patients (e.g., aged >80 years). At relapse, 53% of centers routinely repeated FISH testing, 9% did not, while others repeated it selectively. **Conclusions:** This overview of FISH use in Italy provides a basis for future standardization efforts.

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Introduction

Multiple myeloma (MM) is a clinically and biologically heterogeneous neoplasm with a complex plasma-cell genomic evolution.[1] MM commonly evolves from the premalignant stages monoclonal gammopathy of unknown significance (MGUS) and smoldering multiple myeloma (SMM). Several genetic events contribute to the transformation of normal plasma cells to myeloma cells.[2,3] The most frequent cytogenetic abnormalities (CA) with prognostic value in MM include copy-number alterations such as gain/amp(1q21), del(1p), del(17p), del(13), and translocations involving the immunoglobulin heavy chain (IgH) locus on chromosome 14q32, such as t(11;14), t(4;14), t(14;16), and t(14;20). The detection of CA has become integrated into routine clinical practice in the diagnostic-therapeutic pathway for MM patients.[4] However, cytogenetic analysis can be challenging. Conventional metaphase karyotyping is not recommended due to the low proliferation rate of plasma cells and complex structural alterations. Therefore, interphase fluorescence *in situ* hybridization (FISH) has become the standard of care for CA detection in MM, offering greater sensitivity, efficiency, and precision. The European Myeloma Network (EMN) guidelines report on FISH application and related technical approaches was published more than ten years ago. Since then, there have been new FISH developments in MM prognostication and therapy.[5] In terms of prognosis, the recent Second Revision of the International Staging System (R2-ISS) incorporated in the R-ISS the detection of the chromosome 1q21 gain/amplification (1q+), which was shown to indicate a poor prognosis. The R2-ISS resulted in a better stratification of intermediate-risk newly diagnosed (ND)MM patients, as compared with the R-ISS.[6] Despite not being a standard approach, baseline CA assessment has the potential to guide treatment strategy. For instance, many centers use tandem autologous stem-cell transplantation (ASCT) in patients with genetically defined high-risk disease, while a venetoclax-based therapy can be considered for the treatment of relapsed/refractory (RR)MM patients with t(11;14).[7] In addition, performing FISH at the time of disease relapse can be useful in terms of prognosis and efficacy of drug combination from the second line of treatment, as showed in the subgroup analysis of the ICARIA trial, in which isatuximab-pomalidomide-dexamethasone significantly improved outcomes even in patients with gain/amp(1q21).[8]

Beyond guidelines and recommendations, real-world clinical practice often presents a different scenario. Some onco-hematology centers may lack access to FISH testing, requiring them to send samples to external laboratories. The degree of uniformity in laboratory methods used to purify $CD138^+$ cells and of the cut-offs applied to identify CA in clinical practice is largely unknown. Moreover, although the performance of FISH at diagnosis and relapse is outlined in guidelines, and there is consensus on the panel of CA to routinely assess, these recommendations are not always adhered to in clinical practice.

With this survey, we aimed to provide current data on the prevalence and laboratory characteristics of the use, in Italy, of FISH testing to define cytogenetic risk in MM. Our secondary aim was to analyze current practices regarding the definition, availability, and interpretation of 1q abnormalities, which have only recently been incorporated into MM staging systems.

Methods

We developed an online questionnaire that included 49 questions (Supplemental Appendix, Supplemental Tables 1-4). The questionnaire was reviewed by the Italian branch of the EMN and then sent to 118 Italian centers treating MM patients, 70 of which responded. The centers were well distributed geographically throughout Italy. Data were collected using REDCap.[9,10] A descriptive analysis was performed based on the responses from all centers. Subgroup analyses were performed according to the number of NDMM patients in 2022 and geographic macro-areas. All survey questions were written in Italian; an English translation of the questions is provided in the Supplemental Appendix. In each center, a physician and a biologist possessing expertise in FISH participated in the survey. Access to the online survey was provided to hematology clinicians across Italy between April and July 2023. The 2 last questions, ("Would you be interested in receiving further information about 1q+ in a clinical context?" and "Would you be interested in a discussion with an experienced laboratory expert in FISH for MM to optimize cytogenetic investigations and 1q+ identification?") were outside the scope of the present analysis and are not discussed in this contribution.

Results

A total of 70 Italian centers treating MM completed the survey: 26 (37%) in northern Italy, 29 (42%) in central Italy, and 15 (21%) in southern Italy (Supplemental Table 5). Twenty-three (34%) centers were considered low-volume centers (≤30 NDMM patients treated per year), 23 (34%) medium-volume centers (31-50), and 22 (32%) high-volume centers (>50). Two centers did not provide the number of new MM diagnoses and were excluded from the analysis by center volume. The analysis of the responses according to center volume is detailed here, while the analysis according to geographic macro-area is included in the Supplemental Appendix (Supplemental Tables 1-2).

The first set of questions focused on the availability and methodology of the FISH technique across the 70 MM-treating centers. Seventy-one percent (50/70) of centers performed FISH locally, 27% (19/70) sent samples to external laboratories, and 1% (1/70) did not perform FISH at all. Low-volume centers had the greatest need to send their samples to third-party centers (48%, 11/23), while 91% (20/22) of high-volume centers performed FISH locally (Figure 1). Eighty-nine percent (62/70) of centers performed FISH analysis on purified $CD138^+$ cells, and in 74% (46/62) of these centers, sample purity was assessed after $CD138^+$ enrichment. In 21% of centers (13/62), sample purity was not assessed after $CD138^+$ enrichment. Medium-volume centers were the least likely to verify the purity of the purified $CD138^+$ cells (33%, 7/21).

We also asked the 50 centers that performed FISH locally which specific CA they routinely analyzed and which cut-offs they applied for the median percentage of positive nuclei (Table 1 and Figure 2). While del(17p), t(4;14), t(14;16), 1q+, t(11;14), and del(1p32) were analyzed by almost all centers performing FISH, del(13q) and hyperdiploidy were the least analyzed CA. Fifty-eight percent of medium-volume centers and 45% of high-volume centers did not test for hyperdiploidy, while 70% of medium-volume centers and 36% of high-volume centers did not test for del(13q).

As shown in Table 1, the applied cut-offs were highly variable, particularly for hyperdiploidy, t(4;14), 1q+, and t(11;14). Moreover, the cut-off for the definition of del(17p) positivity is still a matter of debate: among all centers, 18% (9/50) applied a cut-off of ≥20%, which was included in the new definition of high risk recently proposed by the International Myeloma Society (IMS),[11] while no centers applied a higher prognostic cut-off of ≥55% as proposed by Thakurta et al.[12]

Most centers (83%, 58/70) routinely analyzed 1q+ without a specific request from the treating physician, while 14% (10/70) performed it only upon physician's request. Two centers did not respond. In the laboratories that performed 1q+ analysis only upon request, reasons for not performing it routinely included costs (1%, 1/10), lack of wide availability of the test (1%, 1/10), and perception that it is not a standard practice (2%, 2/10), while 2% (2/10) of centers cited unspecified reasons for not performing the test routinely and 4 centers did not respond. Eighty-four percent (59/70) of physicians working in the MM-treating centers stated that the laboratory data received were sufficiently clear and comprehensive for detecting 1q+. Sixty-nine percent (48/70) of centers included the 1q copy number found in monoclonal plasma cells in their FISH report. However, 30% of low-volume (7/23), 29% of medium-volume (5/23), and 18% of high-volume centers did not report this information. Most centers (70%, 49/70) received a FISH report that distinguished between gain and amplification of 1q, while 20% (14/70) did not have access to this information and 10% (7/70) did not answer. Among those centers that did not distinguish between gain(1q21) and amp(1q21), 86% (12/14) believed that this distinction could be important for clinical practice. Most centers (79%, 55/70) reported using the same cut-offs for both gain(1q21) and amp(1q21), using the percentage of positive nuclei with 3 or >3 1q copies, respectively.

The second part of the survey focused on the prognostic aspects of the FISH technique. The participating centers were asked whether the FISH evaluation needed to be specifically requested at diagnosis or if it was a standard test performed for every patient. Seventy percent (49/70) confirmed that they routinely performed it, while 16% (11/70) requested it only for selected categories of patients, with similar percentages among centers with different volumes. One percent (1/70) of centers did not perform FISH at diagnosis, and 13% (9/70) did not answer. Among the 11 centers that requested FISH only for selected categories of patients, 91% (10/11) required it for transplant-eligible patients, 55% (6/11) required it for transplant-ineligible patients aged ≤80 years, 45% (4/11) did not require it for transplant-ineligible patients aged ≤80 years, and none of these centers required it for transplant-ineligible patients aged >80 years.

Almost all centers (94%, 66/70) used the R-ISS for the prognostic evaluation at diagnosis, and 69% (48/70) also used the updated R2-ISS. Twenty-nine percent (20/70) did not perform R2-ISS, with 30% of both low- and medium-volume centers (7/23, 7/23) and 27% of high-volume centers (6/22) not using this score.

At first relapse, 53% (37/70) of centers performed again FISH analysis and re-evaluated the prognostic risk, 36% (25/70) conducted this analysis only for selected patients, 9% (6/70) did not

Figure 1 Does the laboratory associated with your center perform FISH analysis in patients with multiple myeloma? Abbreviations: FISH = fluorescence *in situ* hybridization; NDMM = newly diagnosed multiple myeloma.

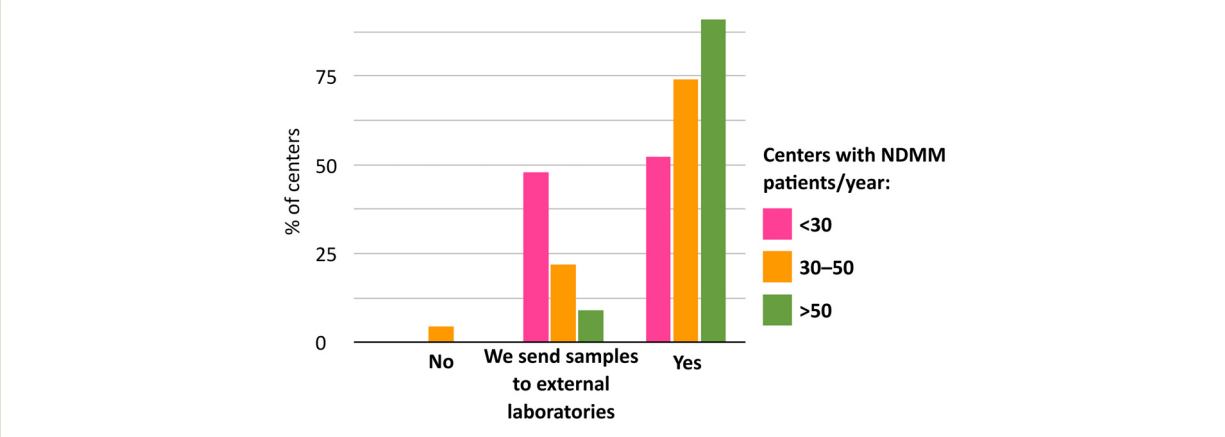


Table 1 More Frequently Analyzed Cytogenetic Abnormalities and Related Cut-Offs in Centers Performing FISH Locally

CA	% Of Centers Analyzing Such CA ($n = 50$)[a]	Laboratory Cut-Offs, Median % of Positive Nuclei (Range)			
		All Centers	Low-Volume Centers (<30)[b]	Medium-Volume Centers (30-50)[b]	High-Volume Centers (>50)[b]
del(17p)	100	10 (5-50)[d]	10 (6-20)	10 (5-50)	10 (5-30)
t(4;14)	100	5 (0.01-50)	6.5 (0.03-10)	5 (0.1-50)	10 (0.01-30)
t(14;16)	98	10 (1-50)	10 (2-10)	5 (1-50)	10 (1-30)
1q+[c]	96	10 (3-50)	10 (3-20)	10 (5-50)	10 (5-30)
t(11;14)	90	10 (1-50)	10 (2-10)	7.5 (2-50)	10 (1-30)
del(1p32)	88	10 (5-50)	10 (6-20)	10 (5-50)	10 (5-30)
del(13q)	68	10 (4-50)	10 (6-10)	10 (5-50)	10 (4-30)
Hyperdiploidy	52	10 (1-50)	10 (4-20)	7.5 (5-50)	5 (1-10)

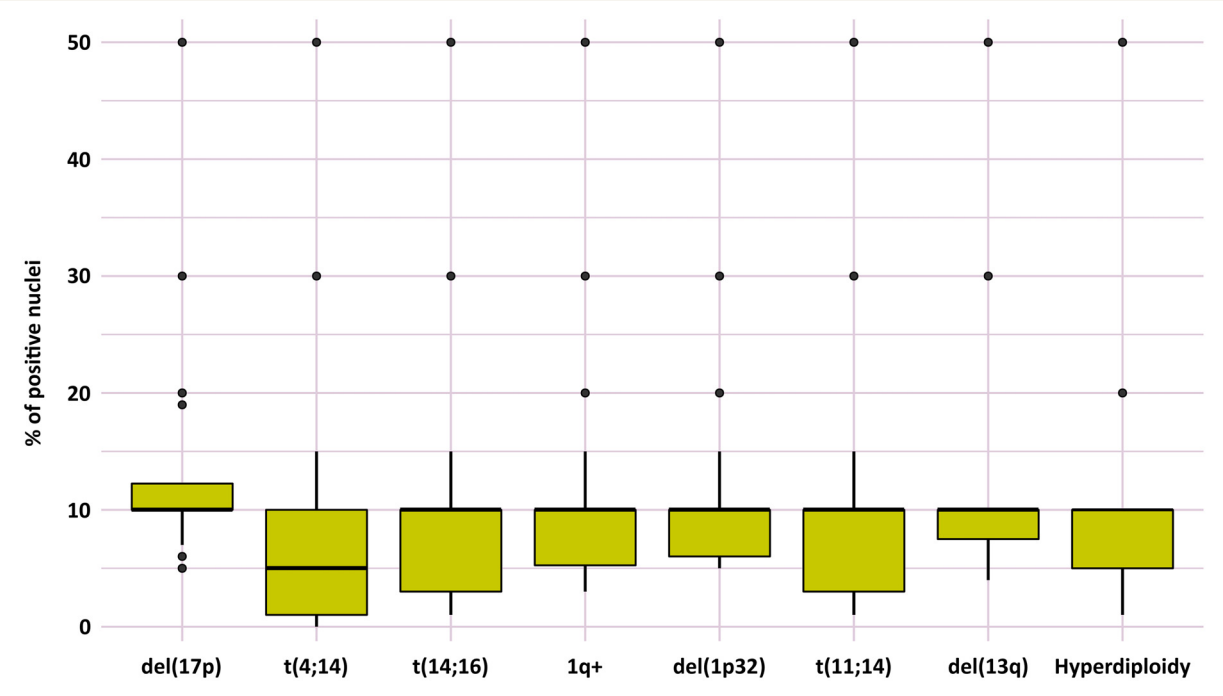
[a] Only centers performing FISH locally were asked this question.
[b] Number of NDMM patients/year.
[c] 1q21 gain or amplification.
[d] The percentage of positive nuclei was prognostically important for most of the centers ($n = 62$ [88%]).
Abbreviations: CA = cytogenetic abnormality; del = deletion; FISH = fluorescence *in situ* hybridization; IQR = interquartile range; n = number; NA = not available; NDMM = newly diagnosed multiple myeloma; t = translocation.

perform it at relapse, and 3% (2/70) did not answer. High-volume centers (64%, 14/22) re-evaluated FISH at relapse more frequently than medium-volume (52%, 12/23) and low-volume (48%, 11/23) centers. The 25 centers that required FISH only for specific patient categories at relapse were further surveyed regarding the age groups for which FISH was required: 40% (10/25) required FISH for patients aged <60 years, 52% (13/25) for those <70 years, 28% (7/25) for those <75 years, while no centers required it for patients aged ≥75 years at relapse.

The last part of the survey selectively focused on clinicians' considerations regarding 1q alterations. Among all centers, 93% (65/70) considered 1q+ *a* high-risk CA at baseline. Regarding its prognostic value at diagnosis, 39% (27/70) and 50% (35/70) of centers respectively attributed high and quite high importance to it, while 4% (3/70) did not consider it an important factor in baseline prognostic evaluation. When considering the co-occurrence of 1q+ with other abnormalities, such as del(17p), t(4;14) and t(14;16), 83% (58/70) of centers believed that prognostic differences existed between patients with isolated 1q+ and those with additional CA, while 6% (4/70) believed that there were no significant differences. Additionally, 69% (48/70) of centers believed that prognostic differences existed between patients with gain(1q21) and those with amp(1q21), with similar percentages across centers with different patient volumes.

Most centers reported rates of 30%-50% of NDMM patients positive for 1q+. In 63% (44/70) of centers, the presence of 1q+

Figure 2 Box and whisker analysis of the percentage of positive nuclei for the main cytogenetic abnormalities across the 50 Italian centers performing FISH locally. Abbreviations: FISH = fluorescence *in situ* hybridization; del = deletion; t = translocation; 1q+ = 1q21 gain or amplification.



at diagnosis did not influence the choice of first-line therapy, while in 27% (19/70) it did. In similar percentages of low-volume (30%, 7/23), medium-volume (22%, 5/23), and high-volume (32%, 7/22) centers first-line therapy was only slightly influenced by the presence of 1q+. At relapse, 39% (27/70) of centers reported that around 50% of their patients were positive for 1q+, while 29% (20/70) estimated rates around 30%. As compared with positivity for 1q+ at diagnosis, more centers (58%, 41/70) believed that the presence of 1q+ did not influence therapy choices at relapse, while only 29% (20/70) believed that it did. Finally, the participating centers were asked whether personalized treatment could be made available for patients with 1q+ based on data from published randomized controlled trials. The responses were mixed: 49% (34/70) of centers believed that personalized treatment was not feasible, 30% (21/70) that it was feasible, and 19% (13/70) were unsure. Interestingly, a higher percentage of low-volume centers believed that personalized therapy was a possible option (43%, 10/23), as compared with medium-volume (26%, 6/23) and high-volume (23%, 5/22) centers. Conversely, a higher percentage of high-volume centers believed that personalized therapy for this subset of patients was not possible (72%, 16/22), as compared with medium-volume (43%, 10/23) and low-volume (35%, 8/23) centers. Among the approved therapeutic classes, anti-CD38 monoclonal antibodies (mAbs) were considered the most effective agents for the treatment of this subset of patients (54%, 38/70), as compared with immunomodulatory drugs and proteasome inhibitors, and 59% (41/70) of centers were familiar with the available data on the use of regimens containing anti-CD38 mAbs for the treatment of patients positive for 1q+.

Discussion

In this survey, we obtained valuable insights into current clinical and laboratory practices for FISH testing in Italy, observing both adherence to and divergence from established guidelines. Our data revealed notable variability in the availability of testing, methodologies used, and interpretation of CA. This heterogeneity can impact both the accuracy of risk stratification and the consistency of treatment approaches.

Although most Italian centers performed FISH analysis, nearly half of low-volume centers had to send samples to third-party laboratories, which may have delayed prognostic evaluation and patient care. This is especially significant given that personalized treatment options are likely to become available in the future, highlighting the need for increased access to local FISH testing in smaller centers.

Additionally, 20% of centers did not verify the purity of $CD138^+$ cells after the purification process, thus negatively impacting the accuracy of FISH results and potentially leading to unreliable data and false-negative results in case of low purity. These findings suggest the need for more consistent quality control measures across different centers to ensure accurate and timely cytogenetic testing.

The findings regarding FISH availability and usage across Italian centers provide a valuable benchmark for assessing the future applicability of next-generation sequencing (NGS). The role of NGS

in defining MM patient risk is increasingly emphasized, particularly with regard to the detection of mutations such as TP53 and biallelic deletions of 1p32. These genomic alterations cannot be reliably identified by traditional FISH analysis; however, they are poised to play a pivotal role in the new definition of high-risk MM currently proposed by the IMS. Given the complexity and costs associated with NGS, it is likely that a greater proportion of centers will initially need to send samples to external laboratories for testing, similar to the current practices that we observed in small-volume centers regarding FISH testing.

A further key challenge highlighted by this survey is the significant variability in the cut-offs used to define CA among different centers. The range of thresholds applied to determine the positivity for a specific CA in real-world practice is wide, which reflects a broader issue that is present also among different clinical trials that report FISH alterations using different cut-offs. To better address this issue, clear international guidelines regarding the appropriate cut-offs for FISH analysis should be established. For example, in the new definition of high risk proposed by the IMS, a cut-off of ≥20% was suggested for del(17p).[11] This underscores the importance of standardizing positivity thresholds across centers to align with these updated cut-offs, ensuring consistency and facilitating reliable comparisons across different practices. Moreover, in the FISH reports, the actual percentage of positive nuclei for each alteration should be documented, allowing for a retrospective review of FISH results as new data emerge in the future.

Based on this survey, the high percentage of centers performing FISH at diagnosis aligns with international recommendations, while the relatively lower rates of FISH reassessment at relapse—particularly in low- and medium-volume centers—may indicate suboptimal application of prognostic reassessment in later stages of the disease. This discrepancy may be attributed to logistical limitations, different institutional priorities, or lack of consensus on the clinical benefit from repeating FISH analysis at relapse. Interestingly, while most centers required baseline FISH testing for transplant-eligible patients and transplant-ineligible patients aged <80 years, there was a clear tendency to avoid FISH evaluation in older, transplant-ineligible patients, likely due to the limited therapeutic options and reduced clinical impact of prognostic stratification in this population. The difference in the rates of FISH reassessment at relapse between high- and low-volume centers (64% vs. 48%) may suggest that centers with higher patient volumes had greater access to resources or adhered more strictly to updated guidelines. Additionally, the lower rates of FISH testing for older patients at relapse further confirmed the tendency to limit invasive or complex diagnostic procedures in older populations, in which the potential therapeutic impact may be diminished.

The widespread use of the R-ISS for prognostic assessment at diagnosis reflects its established role in clinical practice. The R2-ISS has also been implemented, though to a lesser extent, with approximately two-thirds of centers adopting it.

Despite widespread recognition of 1q+ as a high-risk feature, there is significant variation in how this abnormality is tested and reported, particularly in terms of differentiating between gain and amplification. The survey also highlighted that, while most centers considered 1q+ an important prognostic marker, the influence of this abnormality on treatment choices was inconsistent. At diagnosis, many centers reported that the presence of 1q+ may guide therapy choices, but at relapse, the majority of centers did not incorporate it into treatment options, reflecting a lack of clear therapeutic guidance for patients positive for 1q+ or a limited access to specific therapies in real-world settings.

Lastly, the mixed responses on the feasibility of personalized therapy for patients positive for 1q+ reflect an ongoing debate within the clinical community. While some centers, particularly the low-volume ones, were optimistic about the potential of personalized treatment based on cytogenetic profiles, others, especially the high-volume ones, remained skeptical, likely due to the limited evidence available from randomized controlled trials.

Overall, our findings confirm the need for more standardized protocols and clearer guidelines on the management of cytogenetic abnormalities in MM within the Italian setting, particularly with regard to methodologies, use of FISH at relapse, and clinical implications of 1q+ alterations. Further research and collaboration are essential to harmonize practices and ensure that all patients benefit from the latest advancements in MM prognosis and treatment. Applying a similar survey approach globally, hopefully with the support of international societies involved in the study of MM, can help identify country-specific heterogeneities and differences in access to techniques.

Clinical Practice Points

- Although most Italian centers performed fluorescence *in situ* hybridization (FISH), there is a need for increased access to local FISH testing in smaller centers, since personalized treatment options are likely to become available in the future.
- Our data confirmed the need for standardized guidelines on the management of cytogenetic abnormalities in multiple myeloma (MM) within the Italian setting, particularly with regard to methodologies, use of FISH at relapse, and clinical implications of 1q+ alterations.
- Our findings suggest the need for more consistent quality control measures, given that 20% of centers did not verify the purity of $CD138^+$ cells after the purification process.
- In the future, given the complexity and costs of next-generation sequencing, a greater proportion of centers will initially send samples to third parties for testing mutations such as TP53 and biallelic deletions of 1p32, which are likely to play a role in the new definition of high-risk MM.
- We observed a significant variability in the cut-offs used to define cytogenetic abnormalities (CA) among different centers. Clear international guidelines should be established, not only defining a consistent threshold, but also suggesting that each center reports the percentage of positive nuclei for a given alteration.
- There was a clear tendency to avoid FISH evaluation in older, transplant-ineligible patients, likely due to the limited therapeutic options and reduced clinical impact of prognostic stratification in this population.
- The difference in the rates of FISH reassessment at relapse between high- and low-volume centers (64% vs. 48%) may suggest that centers with higher patient volumes had greater access to resources or adhered more strictly to updated guidelines.

- The widespread use of the Revised International Staging System (R-ISS) for prognostic assessment at diagnosis reflects its established role in clinical practice. The R2-ISS has also been implemented, though to a lesser extent.
- Despite widespread recognition of 1q+ as a high-risk feature, there was significant variation in how it was tested and reported, particularly in terms of differentiating between gain and amplification. At relapse, the majority of centers did not incorporate 1q+ testing, reflecting a lack of clear therapeutic guidance and/or a limited access to specific therapies.
- Many high-volume centers remained skeptical about the potential of personalized treatment based on cytogenetic profiles, likely due to the limited evidence available from randomized trials.

Data Sharing

After the publication of this article, data collected for this analysis and related documents will be made available to others upon reasonably justified request, which needs to be written and addressed to the attention of the corresponding author. The responsible party of this analysis, EMN Trial Office S.r.l. Impresa Sociale, via the corresponding author, is responsible to evaluate and eventually accept or refuse every request to disclose data and their related documents, in compliance with the ethical approval conditions, in compliance with applicable laws and regulations, and in conformance with the agreements in place with the involved subjects, the participating institutions, and all the other parties directly or indirectly involved in the participation, conduct, development, management and evaluation of this analysis.

Disclosure

MTP has received honoraria from and served on the advisory boards for Johnson & Johnson, Bristol Myers Squibb, Amgen, Sanofi, GlaxoSmithKline, Takeda, Oncopeptides, Pfizer, Menarini, and AbbVie. KM has received honoraria from Sanofi, Amgen, Janssen, GlaxoSmithKline, Celgene, and Oncopeptides. RZ has served on the advisory boards for Amgen, GlaxoSmithKline, Sanofi, Janssen, Oncopeptides, and Menarini. LP has received honoraria from Takeda, Amgen, Bristol Myers Squibb, Sanofi, and Janssen; has served on the advisory boards for Bristol Myers Squibb, Amgen, Sanofi, and Janssen; has received consultancy fees from Janssen. SA has served on the advisory boards for Menarini Stemline Italia S.r.l. MQ has served on the advisory boards for Novartis. NG has received research funding from Pfizer; has served on the advisory boards for Takeda, Pfizer, Stemline (Menarini); has received speaker fees from Amgen and Sanofi. ML has served on the advisory boards for and has received honoraria for participation in meetings from AbbVie, Jazz Pharma, Novartis, Grifols, Sanofi, Incyte, Istituto Gentili, Roche, and AstraZeneca. RM has served on advisory boards and has provided training and scientific consultancy for Sanofi, Johnson & Johnson, Menarini Stemline, and Takeda. CC has served on the advisory boards for Janssen and Amgen; has provided consultancy for Menarini, Sanofi, and Takeda. SM has received honoraria from Sanofi, Janssen, Bristol Myers Squibb, Pfizer, Menarini Stemline, GlaxoSmithKline, and Takeda; has served on the advisory boards for Janssen, GlaxoSmithKline, Pfizer, and Menarini Stemline. EA has received honoraria from Sanofi; has served on the advisory boards for GlaxoSmithKline, Pfizer, and Menarini Stemline. AB has served on the advisory boards for Amgen, Janssen, GlaxoSmithKline, and Menarini Stemline. SM has received honoraria from GlaxoSmithKline, Janssen, Menarini, and Pfizer. MB has received honoraria from Sanofi, Celgene, Amgen, Janssen, Novartis, Bristol Myers Squibb, and AbbVie; has served on the advisory boards for Janssen and GlaxoSmithKline; has received research funding from Sanofi, Celgene, Amgen, Janssen, Novartis, Bristol Myers Squibb, and Mundipharma. MD has received honoraria from GlaxoSmithKline, Sanofi, and Janssen; has served on the advisory boards for GlaxoSmithKline, Sanofi, Bristol Myers Squibb, and Adaptive Biotechnologies; has received research support from Janssen. The other authors declare no competing financial interests.

CRediT authorship contribution statement

Lorenzo Cani: Writing – review & editing, Writing – original draft, Visualization, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Maria Teresa Petrucci:** Writing – review & editing, Resources, Investigation. **Katia Mancuso:** Writing – review & editing, Resources, Investigation. **Renato Zambello:** Writing – review & editing, Resources, Investigation. **Laura Paris:** Writing – review & editing, Resources, Investigation. **Sara Aquino:** Writing – review & editing, Resources, Investigation. **Flavia Lotti:** Writing – review & editing, Resources, Investigation. **Francesco Vassallo:** Writing – review & editing, Resources, Investigation. **Norbert Pescosta:** Writing – review & editing, Resources, Investigation. **Micol Quaresima:** Writing – review & editing, Resources, Investigation. **Patrizia Tosi:** Writing – review & editing, Resources, Investigation. **Iolanda Donatella Vincelli:** Writing – review & editing, Resources, Investigation. **Sonia Ronconi:** Writing – review & editing, Resources, Investigation. **Nicola Giuliani:** Writing – review & editing, Resources, Investigation. **Francesco Pisani:** Writing – review & editing, Resources, Investigation. **Mario Luppi:** Writing – review & editing, Resources, Investigation. **Rita Rizzi:** Writing – review & editing, Resources, Investigation. **Rita Mazza:** Writing – review & editing, Resources, Investigation. **Delia Rota-Scalabrini:** Writing – review & editing, Resources, Investigation. **Claudia Cellini:** Writing – review & editing, Resources, Investigation. **Silvia Mangiacavalli:** Writing – review & editing, Resources, Investigation. **Giuseppe Pietrantuono:** Writing – review & editing, Resources, Investigation. **Maria Luisa Pioltelli:** Writing – review & editing, Resources, Investigation. **Antonietta Pia Falcone:** Writing – review & editing, Resources, Investigation. **Elisabetta Antonioli:** Writing – review & editing, Resources, Investigation. **Angelo Belotti:** Writing – review & editing, Resources, Investigation. **Sonia Morè:** Writing – review & editing, Resources, Investigation. **Benedetto Bruno:** Writing – review & editing, Resources, Investigation. **Mario Boccadoro:** Writing – review & editing, Supervision, Resources, Methodology, Conceptualization. **Mattia D'Agostino:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

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Supplementary materials

Supplementary Tables S1-S5.

Table S1 Geographic survey analysis - laboratory setting

Question	Italy	Northern Italy	Central Italy	Southern Italy
	N=70	n=26	n=29	n=15
Does the laboratory associated with your center perform FISH analysis for patients with MM?				
- No	1	1	-	-
- No, we send sample to third parties		4	7	8
- Yes		21	22	7
Is FISH performed on purified CD138$^+$ cells?				
- No	6	1	3	2
- Yes	62	24	26	12
- *Missing*	2	1	-	1
For FISH performed on purified CD138$^+$ cells, is the purity of the sample assessed after the separation of CD138$^+$ cells?	n=62	n=24	n=26	n=12
- No	13	4	7	2
- Yes	46	19	18	9
- *Missing*	3	1	1	1
Routinely tested CA: del(17p)	n=50	n=21	n=22	n=7
- Yes	50	21	22	7
Routinely tested CA: t(4;14)	n=50	n=21	n=22	n=7
- Yes	50	21	22	7
Routinely tested CA: t(14;16)	n=50	n=21	n=22	n=7
- No	1	-	1	-
- Yes	49	21	21	7
Routinely tested CA: del(1p32)	n=50	n=21	n=22	n=7
- No	3	-	1	1
- Yes	44	19	19	6
- *Missing*	3	2	2	
Routinely tested CA: t(11;14)	n=50	n=21	n=22	n=7
- No	4	-	4	-
- Yes	45	19	17	7
- *Missing*	1	2	1	-
Routinely tested CA: del(13q)	n=50	n=21	n=22	n=7
- No	15	4	11	-
- Yes	34	16	11	7
- *Missing*	1	1	-	-
Routinely tested CA: hyperdiploidy	n=50	n=21	n=22	n=7
- No	23	6	14	3
- Yes	26	14	8	4
- *Missing*	1	1	-	-
Routinely tested CA: 1q+	n=50	n=21	n=22	n=7
- No	2	-	1	1
- Yes	48	21	21	6
FISH cut-off	n=50	n=21	n=22	n=7
- No cut-off	4	2	2	-
- Yes	40	17	18	5
- *Missing*	6	2	2	2

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Table S1 *(continued)*

Question	Italy	Northern Italy	Central Italy	Southern Italy
	N=70	n=26	n=29	n=15
Routinely used cut-offs: del(17p)	n=50	n=21	n=22	n=7
- Median (IQR)	10 (10–12.25)	10 (10–20)	10 (10–10)	10 (7–20)
- *Missing*	10	4	4	2
Routinely used cut-offs: t(4;14)	n=50	n=21	n=22	n=7
- Median (IQR)	5 (1–10)	10 (3–10)	1.5 (0.1–4.5)	10 (5–10)
- *Missing*	10	4	4	2
Routinely used cut-offs: del(1p32)	n=50	n=21	n=22	n=7
- Median (IQR)ss	10 (6–10)	10 (9.75–16.25)	10 (6–10)	8 (5.75–20)
- *Missing*	16		8	3
Routinely used cut-offs: t(11;14)	n=50	n=21	n=22	n=7
- Median (IQR)	10 (3–10)	10 (5–10)	3 (2–10)	10 (7–10)
- *Missing*	17	4	11	2
Routinely used cut-offs: del(13q)	n=50	n=21	n=22	n=7
- Median (IQR)	10 (7.5–10)	10 (9.75–10)	10 (7–10)	10 (6–10)
- *Missing*	26	9	15	2
Routinely used cut-offs: hyperdiploidy	n=50	n=21	n=22	n=7
- Median (IQR)	10 (5–10)	10 (5–10)	5 (4.25–5.75)	50 (50–50)
- *Missing*	35	13	16	6
Routinely used cut-offs: 1q+	n=50	n=21	n=22	n=7
- Median (IQR)	10 (5.25–10)	10 (10–15)	10 (5–10)	8 (5.75–20)
- *Missing*	12	4	5	3
Cut-off for 1q21 gain and amplification 1q21 gain	n=6	n=4	n=2	n=0
10% of positive nuclei with 3 1q21 copies 1q21 amplification	6	4	2	-
<10% of positive nuclei with >3 1q21 copies	1	-	1	-
≥20% of positive nuclei with >3 1q21 copies	5	4	1	-
Do you think that the percentage of nuclei positive for the del(17p) alteration has prognostic implications?				
- No	5	2	3	-
- Yes	62	23	25	14
- *Missing*	3	1	1	1
Does your reference laboratory provide 1q+ data as part of cytogenetic evaluation, either routinely or upon request?				
- Routinely	58	22	26	10
- Upon request	10	4	3	3
- *Missing*	2	-	-	2
If your laboratory does not provide data on 1q+ presence, what is the reason?	n=10	n=4	n=3	n=3
- Costs	1	-	1	1
- Test unavailable	1	-		1
- Not a standard test	2	-		-
- Other	2	1	1	-
- *Missing*	4	3	1	-
Do you find your laboratory data clear and comprehensive for detecting the presence of the 1q+ alteration?				
- No	8	4	3	1
- Yes	59	22	25	12
- *Missing*	3	-	1	2
Does your laboratory provide the number of 1q21 copies present in the nuclei of monoclonal plasma cells?				
- No	16	3	7	6
- Yes	48	22	21	5
- *Missing*	6	1	1	4

(*continued on next page*)

Table S1 (*continued*)

Question	Italy	Northern Italy	Central Italy	Southern Italy
	N=70	n=26	n=29	n=15
Do the data provided by the laboratory allow you to distinguish between 1q21 gain and amplification?				
- No	14	4	7	3
- Not sure	6	-	2	4
- Yes	49	22	20	7
- *Missing*	1	-	-	1
If you do not distinguish between 1q21 gain and amplification, do you believe this could be an important factor for your clinical practice?	n=14	n=4	n=7	n=3
- No	2	-	2	-
- Yes	12	4	5	3
What cut-off is used to consider patients positive for 1q+?				
- <10%	14	3	6	5
- 10%	30	15	11	4
- 20%	11	6	4	1
- 30%	1	-	1	-
- 50%	2	-	1	1
- 60%	1	-	1	-
- *Missing*	11	2	5	4
Are different cut-offs used for 1q21 gain and amplification?				
- No	55	20	23	12
- Yes	6	4	2	-
- *Missing*	9	2	4	3

Abbreviations. FISH, fluorescence *in situ* hybridization; MM, multiple myeloma; CA, cytogenetic abnormalities; del, deletion; IQR, interquartile range; t, translocation; 1q+, 1q21 gain or amplification.

Table S2 Geographic survey analysis - clinical and prognostic setting

Question	Italy	Northern Italy	Central Italy	Southern Italy
	N=70	n=26	n=29	n=15
If not routinely provided, is cytogenetic risk assessment required at diagnosis?				
- No	1	1	-	-
- Yes	49	19	18	12
- Only for selected categories	11	4	4	3
- *Missing*	9	2	7	-
Detail the categories of patients for whom cytogenetic risk assessment is required at diagnosis.				
- Transplant-eligible patients	n=11	n=4	n=3	n=3
- No	1	1	-	-
- Yes	10	3	4	3
Transplant-ineligible patients ≤80 years				
- No	5	1	1	3
- Yes	6	3	3	-
Transplant-ineligible patients >80 years				
- No	11	4	4	3
Do you use the R-ISS for prognostic evaluation of patients at diagnosis?				
- No	2	1	1	-
- Yes	66	24	27	15
- *Missing*	2	1	1	-
Do you consider 1q+ a high cytogenetic-risk factor?				
- No	3	-	3	-
- Yes	65	25	25	15

(*continued on next page*)

Table S2 *(continued)*

Question	Italy	Northern Italy	Central Italy	Southern Italy
	N=70	n=26	n=29	n=15
- *Missing*	2	1	1	-
Do you use the R2-ISS for prognostic evaluation of patients at diagnosis?				
- No	20	6	8	6
- Yes	48	19	20	9
- *Missing*	2	1	1	-
Based on your experience, what is the percentage of patients presenting with 1q+ at diagnosis?				
- ≤5%	7	3	3	1
- ≤15%	17	7	3	7
- ≤30%	26	14	8	4
- ≤50%	14	1	12	1
- ≤80%	1	-	1	-
- *Missing*	5	1	2	2
Based on the available data, do you think there are prognostic differences between patients with 1q+ alone and those with a co-presence of 1q+ and other cytogenetic abnormalities (e.g., del(17p), t(4;14), t(14;16))?				
- No	4	1	2	1
- Yes	58	22	23	13
- *Missing*	8	3	4	1
Based on the available data, do you think there are prognostic differences between patients with gain(1q21) and those with amp(1q21)?				
- No	14	6	5	3
- Yes	48	18	21	9
- *Missing*	8	2	3	3
What prognostic importance do you attach to the presence of 1q+ at diagnosis?				
- Significant	27	8	14	5
- Moderate	35	15	11	9
- Minimal	3	1	2	-
- Not sure	1	1	-	-
- *Missing*	4	1	2	1
Is the presence of 1q+ at diagnosis a factor that guides therapy choice in the first line?				
- No	44	16	18	10
- Not sure	2	-	-	2
- Yes	19	7	9	3
- *Missing*	5	3	2	-
Do you perform cytogenetic risk assessment at first relapse?				
- No	6	3	2	1
- Yes	37	13	17	7
- Only for selected categories of patients	25	9	9	7
- *Missing*	2	1	1	-
Detail the categories of patients for whom cytogenetic risk assessment is required at first relapse.	n=25	n=9	n=9	n=7
- Patients <60 years				
- No	15	7	6	2
- Yes	10	2	3	5
- Patients <70 years				
- No	12	4	4	4
- Yes	13	5	5	3
- Patients <75 years				
- No	18	5	6	7
- Yes	7	4	3	-
- Patients ≥75 years				
- No	25	9	9	7

(*continued on next page*)

Table S2 (*continued*)

Question	Italy	Northern Italy	Central Italy	Southern Italy
	N=70	n=26	n=29	n=15
Based on your experience, what is the percentage of patients who present with +1q at first relapse?				
- ≤5%	2	1	1	-
- ≤15%	10	2	3	5
- ≤30%	20	10	5	5
- ≤50%	27	11	14	2
- ≤80 %	4	-	3	1
- *Missing*	7	2	3	2
Does the presence of 1q+ at relapse guide your treatment choice?				
- No	41	13	20	8
- Not sure	7	2	1	4
- Yes	20	10	7	3
- *Missing*	2	1	1	-
Based on data from currently published RCTs, is it possible to make targeted treatment decisions for patients with 1q+?				
- No	34	11	21	2
- Not sure	13	6	1	6
- Yes	21	8	6	7
- *Missing*	2	1	1	-
Are there any approved therapeutic classes that you believe are more effective for treating patients with 1q+?				
- Anti-CD38 mAbs	38	12	15	11
- IMiDs	4	2	1	1
- PIs	17	8	9	-
- *Missing*	11	4	4	3
Are you aware of any limited data available on the 1q+ population in the context of therapies with the two approved anti-CD38 mAbs?				
- No	26	9	10	7
- Yes	41	16	18	7
- *Missing*	3	1	1	1
Would you be interested in learning more about 1q+ from a clinical perspective?				
- No	1	-	1	-
- Yes	67	25	27	15
- *Missing*	2	1	1	-
Would you be interested in a discussion with an experienced laboratory expert in FISH for MM to optimize cytogenetic investigations and 1q+ identification?				
- No	8	3	5	-
- Yes	60	22	23	15
- *Missing*	2	1	1	-
How many patients were diagnosed with MM at your center in 2022?				
- <10 MM patients	1	1	-	-
- 10–30 MM patients	22	7	7	8
- 31–50 MM patients	23	10	9	4
- >50 MM patients	22	7	12	3
- *Missing*	2	1	1	-

Abbreviations. R-ISS, Revised International Staging System; 1q21+, 1q21 gain or amplification; R2-ISS, Second Revision of the International Staging System; del, deletion; t, translocation; amp, amplification; RCTs, randomized controlled trials; mAbs, monoclonal antibodies; IMiDs, immunomodulatory drugs; PIs, proteasome inhibitors; FISH, fluorescence *in situ* hybridization; MM, multiple myeloma.

Table S3 Volume size survey analysis - laboratory settings

Question	Italy	Low-volume centers (<30)[a]	Medium-volume centers (30–50)[a]	High-volume centers (>50)[a]
	N=68	n=23	n=23	n=22
Does the laboratory associated with your center perform FISH analysis for patients with MM?				
- No	1	-	1	-
- No, we send sample to third parties	18	11	5	2
- Yes	49	12	17	20
- Is FISH performed on purified CD138^{+} cells?				
- No	6	3	1	2
- Yes	60	19	21	20
- *Missing*	2	1	1	-
- For FISH performed on purified CD138^{+} cells, is the purity of the sample assessed after the separation of CD138+ cells?	n=60	n=19	n=21	n=20
- No	13	3	7	3
- Yes	46	16	13	15
- *Missing*	3	-	1	2
- Routinely tested CA: del(17p)	n=49	n=12	n=17	n=20
- Yes	49	12	17	20
- Routinely tested CA: t(4;14)	n=49	n=12	n=17	n=20
- Yes	49	12	17	20
- Routinely tested CA: t(14;16)	n=49	n=12	n=17	n=20
- No	1	-	-	1
- Yes	48	12	17	19
- Routinely tested CA: del(1p32)	n=49	n=12	n=17	n=20
- No	3	-	2	1
- Yes	43	11	15	17
- *Missing*	3	1	-	2
- Routinely tested CA: t(11;14)	n=49	n=12	n=17	n=20
- No	4	12	3	1
- Yes	44	-	14	18
- *Missing*	1		-	1
- Routinely tested CA: del(13q)	n=49	n=12	n=17	n=20
- No	14	2	7	5
- Yes	34	10	10	14
- *Missing*	1	-	-	1
- Routinely tested CA: hyperdiploidy	n=49	n=12	n=17	n=20
- No	22	3	10	9
- Yes	26	9	7	10
- *Missing*	1	-	-	1
- Routinely tested CA: 1q+	n=49	n=12	n=17	n=20
- No	2	-	1	1
- Yes	47	12	16	19
- FISH cut-off	n=49	n=12	n=17	n=20
- No cut-off	4	-	1	3
- Yes	40	17	13	15
- *Missing*	5	-	3	2
- Routinely used cut-offs: del(17p)	n=49	n=12	n=17	n=20

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Table S3 (*continued*)

Question	Italy	Low-volume centers (<30)[a]	Medium-volume centers (30–50)[a]	High-volume centers (>50)[a]
	N=68	n=23	n=23	n=22
- Median (IQR)	10 (10–12.25)	10 (9.5–12.5)	10 (9–10)	10 (10–4.5)
- *Missing*	9	-	4	5
- Routinely used cut-offs: t(4;14)	n=49	n=12	n=17	n=20
- Median (IQR)	5 (1–10)	6.5 (0.1–10)	5 (2–5)	10 (1–15)
- *Missing*	9	-	4	5
- Routinely used cut-offs: del(1p32)	n=49	n=12	n=17	n=20
- Median (IQR)	10 (6–10)	10 (7–16.25)	10 (7–10)	10 (5–10)
- *Missing*	15	2	6	7
- Routinely used cut-offs: t(11;14)	n=49	n=12	n=17	n=20
- Median (IQR)	10 (3–10)	10 (5–10)	7.5 (5–10)	10 (2.5–15)
- *Missing*	16	1	7	8
- Routinely used cut-offs: del(13q)	n=49	n=12	n=17	n=20
- Median (IQR)	10 (7.5–10)	10 (8–10)	10 (7–10)	10 (8.75–10)
- *Missing*	25	3	10	12
- Routinely used cut-offs: hyperdiploidy	n=49	n=12	n=17	n=20
- Median (IQR)	10 (5–10)	10 (7–17.5)	7.5 (5–20)	5 (2–10)
- *Missing*	34	6	13	15
- Routinely used cut-offs: 1q+	n=49	n=12	n=17	n=20
- Median (IQR)	10 (5.25–10)	10 (9–10)	10 (5–10)	10 (6.25–10)
- *Missing*	11	-	5	6
- Cut-off for 1q21 gain and amplification	n=6	n=1	n=3	n=2
- 1q21 gain 10% of positive nuclei with 3 1q21 copies	6	1	3	2
- 1q21 amplification <10% of positive nuclei with >3 1q21 copies	1	-	1	-
- ≥20% of positive nuclei with >3 1q21 copies	5	1	2	2
- Do you think that the percentage of nuclei positive for the del(17p) alteration has prognostic implications?				
- No	5	-	3	2
- Yes	60	21	19	20
- *Missing*	3	2	1	
- Does your reference laboratory provide 1q+ data as part of cytogenetic evaluation, either routinely or upon request?				
- Routinely	56	16	19	19
- Upon request	10	4	4	2
- *Missing*	2	1	-	1
- If your laboratory does not provide data on 1q+ presence, what is the reason?	n=10	n=4	n=4	
- Costs	1	-	1	-
- Test unavailable	1	1	-	-
- Not a standard test	2	2	-	-
- Other	2	-	1	1
- *Missing*	4	1	2	1
- Do you find your laboratory data clear and comprehensive for detecting the presence of the 1q+ alteration?				
- No	16	7	5	4
- Yes	46	13	17	16
- *Missing*	6	3	1	2

(*continued on next page*)

Table S3 (*continued*)

Question	Italy	Low-volume centers (<30)[a]	Medium-volume centers (30–50)[a]	High-volume centers (>50)[a]
	N=68	n=23	n=23	n=22
- Does your laboratory provide the number of 1q21 copies present in the nuclei of monoclonal plasma cells?				
- No	16	3	7	6
- Yes	48	22	21	5
- *Missing*	6	1	1	4
- Does the data provided by the laboratory allow you to distinguish between 1q21 gain and amplification?				
- No	14	5	5	4
- Not sure	6	2	2	2
- Yes	47	15	16	16
- *Missing*	1	-	-	1
- If you do not distinguish between 1q21 gain and amplification, do you believe this could be an important factor for your clinical practice?	n=14	n=5	n=5	
- No	2	-	2	-
- Yes	12	5	3	4
- What cut-off is used to consider patients positive for 1q+?				
- <10%	14	5	5	4
- 10%	30	9	11	10
- 20%	9	3	3	3
- 30%	1	1	-	-
- 50%	2	-	1	1
- 60%	1	1	-	-
- *Missing*	11	4	3	4
- Are different cut-offs used for 1q21 gain and amplification?				
- No	53	19	17	17
- Yes	6	1	3	2
- *Missing*	9	3	3	3

[a]Number of NDMM patients/year.
Abbreviations. FISH, fluorescence *in situ* hybridization; MM, multiple myeloma; CA, cytogenetic abnormalities; del, deletion; IQR, interquartile range; t, translocation; 1q21+, 1q21 gain or amplification; NDMM, newly diagnosed multiple myeloma.

Table S4 Volume size survey analysis - clinical and prognostic setting

Question	Italy	Low-volume centers (<30)[a]	Medium-volume centers (30–50)[a]	High-volume centers (>50)[a]
	N=68	n=23	n=23	n=22
- If not routinely provided, is cytogenetic risk assessment required at diagnosis?				
- No	1	1	-	-
- Yes	49	18	16	15
- Only for selected categories	11	3	4	4
- *Missing*	7	1	3	3
Detail the categories of patients for whom cytogenetic risk assessment is required at diagnosis.	n=11			
- Transplant-eligible patients			n=3	n=3
- No	1	-	1	-
- Yes	10	3	3	4
- Transplant-ineligible patients ≤80 years				
- No	5	2	1	2
- Yes	6	1	3	2
- Transplant-ineligible patients >80 years				
- No	11	3	4	4
- Do you use the R-ISS for prognostic evaluation of patients at diagnosis?				
- No	2	1	-	1
- Yes	66	23	22	21
- Do you consider 1q+ a high cytogenetic-risk factor?				
- No	3	1	2	-
- Yes	65	22	21	22
- Do you use the R2-ISS for prognostic evaluation of patients at diagnosis?				
- No	20	7	7	6
- Yes	48	16	16	16
- Based on your experience, what is the percentage of patients presenting with 1q+ at diagnosis?				
- ≤5 %	7	3	2	2
- ≤15 %	17	8	3	6
- ≤30 %	26	7	13	6
- ≤50 %	14	4	4	6
- ≤80 %	1	-	-	1
- *Missing*	3	1	1	1
- Based on the available data, do you think there are prognostic differences between patients with 1q+ alone and those with a co-presence of 1q+ and other cytogenetic abnormalities (e.g., del(17p), t(4;14), t(14;16))?				
- No	4	-	1	3
- Yes	58	20	21	17
- *Missing*	6	3	1	2
- Based on the available data, do you think there are prognostic differences between patients with gain(1q21) and those with amp(1q21)?				
- No	14	4	6	4
- Yes	48	16	15	17
- *Missing*	6	3	2	1
- What prognostic importance do you attach to the presence of 1q+ at diagnosis?				
- Significant	27	7	11	9
- Moderate	35	14	9	12
- Minimal	3	1	2	-

(*continued on next page*)

Table S4 (*continued*)

Question	Italy	Low-volume centers (<30)[a]	Medium-volume centers (30–50)[a]	High-volume centers (>50)[a]
	N=68	n=23	n=23	n=22
- Not sure	1	-	-	1
- *Missing*	2	1	1	-
- Is the presence of 1q+ at diagnosis a factor that guides therapy choice in the first line?				
- No	41	13	14	14
- Not sure	7	2	3	2
- Yes	20	8	6	6
- Do you perform cytogenetic risk assessment at first relapse?				
- No	6	3	1	2
- Yes	37	11	12	14
- Only for selected categories of patients	25	9	10	6
Detail the categories of patients for whom cytogenetic risk assessment is required at first relapse.	n=25	n=9	n=10	n=6
- Patients <60 years				
- No	15	5	8	2
- Yes	10	4	2	4
- Patients <70 years				
- No	12	3	5	4
- Yes	13	6	5	2
- Patients <75 years				
- No	18	7	6	5
- Yes	7	2	4	1
- Patients ≥75 years				
- No	25	9	10	6
- Based on your experience, what is the percentage of patients who present with +1q at first relapse?				
- ≤5%	2	1	1	-
- ≤15%	10	4	3	3
- ≤30%	20	8	7	5
- ≤50%	27	7	10	10
- ≤80 %	4	2	1	1
- *Missing*	5	1	1	3
- Does the presence of 1q+ at relapse guide your treatment choice ?				
- No	41	13	20	8
- Not sure	7	2	1	4
- Yes	20	10	7	3
- *Missing*	2	1	1	-
- Based on data from currently published RCTs, is it possible to make targeted treatment decisions for patients with 1q+?				
- No	34	8	10	16
- Not sure	13	5	7	1
- Yes	21	10	6	5
- Are there any approved therapeutic classes that you believe are more effective for treating patients with 1q+?				
- Anti-CD38 mAbs	38	16	11	11
- IMiDs	4	-	3	1
- PIs	17	4	6	7
- *Missing*	9	3	3	3

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Table S4 (*continued*)

Question	Italy	Low-volume centers (<30)[a]	Medium-volume centers (30–50)[a]	High-volume centers (>50)[a]
	N=68	n=23	n=23	n=22
- Are you aware of any limited data available on the 1q+ population in the context of therapies with the two approved anti-CD38 mAbs?				
- No	26	11	9	6
- Yes	41	11	14	16
- *Missing*	1	1	-	-
- Would you be interested in learning more about 1q+ from a clinical perspective?				
- No	1	-	-	1
- Yes	67	23	23	21
- Would you be interested in a discussion with an experienced laboratory expert in FISH for MM to optimize cytogenetic investigations and 1q+ identification?				
- No	8	2	4	2
- Yes	60	21	19	20

[a] Number of NDMM patients/year.

Abbreviations. R-ISS, Revised International Staging System; 1q+, 1q21 gain or amplification; R2-ISS, Second Revision of the International Staging System; del, deletion; t, translocation; amp, amplification; RCTs, randomized controlled trials; mAbs, monoclonal antibodies; IMiDs, immunomodulatory drugs; PIs, proteasome inhibitors; FISH, fluorescence *in situ* hybridization; NDMM, newly diagnosed multiple myeloma.

Table S5 Regions across Italy represented by centers participating in the surveys

Northern Italy n=26	Central Italy n=29	Southern Italy n=15
Lombardia	Abruzzo	Basilicata
Piemonte	Emilia Romagna	Calabria
Valle d'Aosta	Lazio	Campania
Veneto	Liguria	Molise
	Marche	Puglia
	Sardegna	Sicilia
	Toscana	
	Umbria	