Check for updates

ELSEVIER

Blood 142 (2023) 7161–7163

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

803.EMERGING TOOLS, TECHNIQUES AND ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

The Use of Next Generation Flow in Multiple Myeloma Patients: A Preliminary Real-Life Multicenter MRD Harmonization Experience

Stefania Oliva, MD PhD[1], Elona Saraci, MsC[2], Valentina Trimarco, PhD[3], Marco Chiarini, PhD[4], Nunziatina Laura Parrinello, PhD[5], Renato Zambello, MD[6], Iole Cordone, MD PhD[7], Tania Villanova, PhD[8], Serena Masi, PhD[9], Giovanni Rossi, MD PhD[10], Sara Marino, PhD[11], Anna Maria Triolo, PhD[12], Aldo Roccaro, MDPhD[13], Angelo Michele Carella, MD[14], Francesco Buccisano, MD PhD[15], Angelo Belotti, MD[16], Maria Irno Consalvo, PhD[17], Alessandra Romano, MD[18], Alessia Tonini, PhD[19], Silvio Mercadante, PhD[20], Benedetto Bruno, MD PhD[21,22], Carolina Terragna, PhD[23], Elena Zamagni, MD PhD[24]

[1] Division of Hematology, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, University of Torino, TORINO, Italy
[2] Division of Hematology, Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Torino, Italy
[3] Department of Medicine, Hematology and Clinical Immunology Branch, Padua University School of Medicine, Padua, Padua, ITA
[4] Clinical Chemistry Laboratory, Flow Cytometry Section, ASST Spedali Civili di Brescia, Brescia, ITA
[5] A.O.U. Policlinico "G. Rodolico - S.Marco". Hematology unit with BMT, Catania, catania, Italy
[6] Department of Medicine (DIMED), Hematology and Clinical Immunology section, Padua University School of Medicine, Padova, Italy
[7] IRCCS Regina Elena National Cancer Institute, Rome, ITA
[8] Division of Hematology, Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Torino, ITA
[9] IRCCS Regina Elena National Cancer Institute Clinical Pathology, Rome, rome, Italy
[10] Department of Hematology and Stem cell Unit, Fondazione IRCCS "Casa Sollievo della Sofferenza, San Giovanni Rotondo, San Giovanni Rotondo, ITA
[11] A.O.U. Policlinico "G. Rodolico - S.Marco". Hematology unit with BMT, Catania, catania, Italy
[12] A.O.U. Policlinico "G. Rodolico - S.Marco". Hematology unit with BMT, Catania, catania, Italy
[13] Clinical Trial Center, Translational Research and Phase I Unit, ASST Spedali Civili di Brescia, Brescia, Italy
[14] Hematology Unit, IRCCS Casa Sollievo Della Sofferenza, San Giovanni Rotondo, Italy
[15] Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome, Italy
[16] Department of Hematology, ASST Spedali Civili di Brescia, Brescia, Italy
[17] Università Di Tor Vergata, Roma, Roma, ITA
[18] Division of Hematology, Azienda Policlinico-S. Marco, University of Catania, Catania, Italy
[19] Department of Medicine, Hematology and Clinical Immunology Branch, Padua University School of Medicine, Padua, padova, Italy
[20] Division of Hematology, Department of Molecular Biotechnology and Health Sciences, University of Torino and Division of Hematology, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Torino, Italy, Torino, Italy
[21] Division of Hematology, Department of Molecular Biotechnologies and Health Sciences, University of Torino,Division of Hematology and Stem cell transplant unit, AOU Città della Salute e della Scienza, Torino, Italy
[22] Division of Hematology, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, University of Torino, Torino, Italy
[23] Istituto di Ematologia "Seràgnoli", IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy
[24] IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia Seràgnoli, Bologna, Italy

Introduction:

Downloaded from http://ashpublications.net/blood/article-pdf/142/Supplement 1/7161/2184838/blood-3757-main.pdf by guest on 19 May 2024

© 2023 by The American Society of Hematology

Minimal residual disease (MRD) detection represents a sensitive tool to appropriately measure response in MM. The major concern about MRD detection in real-world setting is the reproducibility of results among different laboratories possibly due to methodological discrepancies. Therefore, a harmonized approach, according to criteria of Next generation Flow (NGF)/ Next generation sequencing (NGS) established by IMWG (Kumar S et al. *Lancet Oncol* 2016), is warranted. The aim of this project was to create an "Italian MM MRD network" using standardized NGF and NGS-MRD approach; here we report preliminary results of the NGF part.

Methods:

The "NGF harmonization project" includes 7 Italian Laboratories willing to commit to EuroFlow protocols after an initial MRD survey: Brescia (L1), Catania (L2), Padova (L3), Roma 1 (L4), Roma 2 (L5), S. Giovanni Rotondo (L6) and Torino (L7). Standardization of all flow cytometers settings was performed by implementation of the EuroFlow Standard Operating Protocol (SOP) for instrument setup and compensation for BD FASCCanto II, BD FACSLyric, BC Navios and BC DxFlex flow cytometers (www.euroflow.org).

Bone marrow (BM) aspirates were collected from newly diagnosed MM patients treated with 4 cycles of Dara-VTD (Daratumumab, bortezomib, thalidomide, dexamethasone) induction followed by autologous stem cell transplantation (ASCT) in complete-response/very-good-partial-response at day 100 (+/- 15 days) after ASCT. Anonymized samples were split equally and shipped at room temperature to the participati ng laboratories and simultaneously analyzed.

Analyses were carried out following NGF methodology (Flores-Montero J et al. *Leukemia* 2017) by using a two-tube 8-color antibody panel for monoclonal plasma cells identification (Tube 1:CD27, CD138, CD38, CD56, CD45, CD19, CD117, CD81 and Tube 2: CD27, CD138, CD38, CD56, CD45, CD19, cytoplasmic κ and λ light-chain).

We aimed to acquire $\geq$ 3,000,000 events per tube for a sensitivity of at least 1×10^{-5}; a sample was considered MRD positive when $\geq$ 20 monoclonal plasma cells were detected. Intraclass Correlation Coefficient (ICC) was performed to evaluate degree of correlation and agreement between measurements; standard deviation (SD) and Coefficient of variation (CV) to measure variability of the dataset.

Results.

In stage 1 of the study, before starting MRD evaluation on freshsamples, 4 laboratories (L1, L2, L3, L7) performed a blinded analysis of the same 5 anonymous flow-cytometry files from a retrospective data repository of MM patients with/without MRD, to evaluate the inter-operator variability: 100% of the participants were concordant that samples #1, #2 and #4 were MRD positive. Sample #3 was considered MRD positive by 75% of participants whereas 75% considered sample #5 as MRD negative (ICC=0.91, 95% CI 0.69-0.98, $p<0.001$).

In stage 2, a total of 7 samples have been distributed and processed after 48 hours from specimen collection, due to different shipping time in all laboratories. The inter-laboratory correlation study showed a concordance of 100 % for the sample #1 and sample #3 considered as MRD positive, 100% of the participants considered sample #5 and sample #6 as MRD negative, sample #2 was considered MRD positive by 71% of participants whereas sample #4 was considered MRD negative by 86 % of participants. Sample #7 was considered as not evaluable from all participants due to a high percentage of dead cells. (ICC=0.61, 95% CI 0.31-0.91, $p<0.001$) (Fig. 1).

The highest difference in term of antigen expression of monoclonal plasma cells was recorded for CD45 and CD27. We obtained a median of 7×10^{-6} of Limit of detection (LOD, range 6×10^{-5} - 2×10^{-6}) and 1×10^{-5} Limit of Quantification (LOQ, range 1×10^{-4}- 5×10^{-6}) for all samples. A centralized revision (in L7 lab) of all FCS files is ongoing to confirm our preliminary results; moreover, the study will be corroborated increasing the number of fresh samples.

Conclusion: our preliminary results demonstrate the importance of a harmonized NGF-MRD assessment to improve the accuracy and comparability of MM-MRD testing among different laboratories. Major discrepancies have been found in fresh samples vs the retrospective dataset suggesting an impact of the transportation time and sample processing on the concordance of our results.

Disclosures Oliva: *Takeda:* Honoraria; *Celgene/Bristol Myers Squibb:* Honoraria; *Adaptive Biotechnologies:* Consultancy; *Amgen:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria; *Abbvie:* Honoraria. **Saraci:** *Beckman Coulter:* Honoraria. **Zambello:** *amgen:* Honoraria; *takeda:* Honoraria; *Menarini:* Honoraria; *Janssen:* Honoraria; *sanofi:* Honoraria. **Rossi:** *Janssen:* Honoraria; *Pfizer:* Honoraria; *Abbvie:* Honoraria; *Becton Dickinson:* Honoraria. **Roccaro:** *Italian Foundation for Cancer Research; Transcan2-ERANET; AstraZeneca:* Research Funding; *Amgen, Celgene, Janssen. Takeda:* Consultancy. **Buccisano:** *Jazz Pharmaceuticals:* Consultancy, Honoraria; *BMS:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria; *Astellas:* Consultancy, Honoraria; *Janssen & Cylag:* Consultancy, Honoraria; *Becton Dickinson:* Research Funding; *Novartis:* Consultancy, Honoraria. **Belotti:** *GlaxoSmithKline:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *Takeda:* Membership on an entity's Board of Directors or advisory committees; *Janssen:* Membership on an entity's Board of Directors or advisory committees; *Amgen:* Membership on an entity's Board of Directors or advisory committees. **Zamagni:** *Amgen:* Honoraria; *Janssen:* Honoraria; *Bristol-Myers-Squibb:* Honoraria; *Takeda:* Honoraria.

Downloaded from http://ashpublications.net/blood/article-pdf/142/Supplement 1/7161/2184838/blood-3757-main.pdf by guest on 19 May 2024

Figure1: Results of MRD assessment in inter-laboratory comparability study. Sample #4, #5 and #6 did not contain monoclonal plasma cells. % PC mono: % of monoclonal Plasma cells

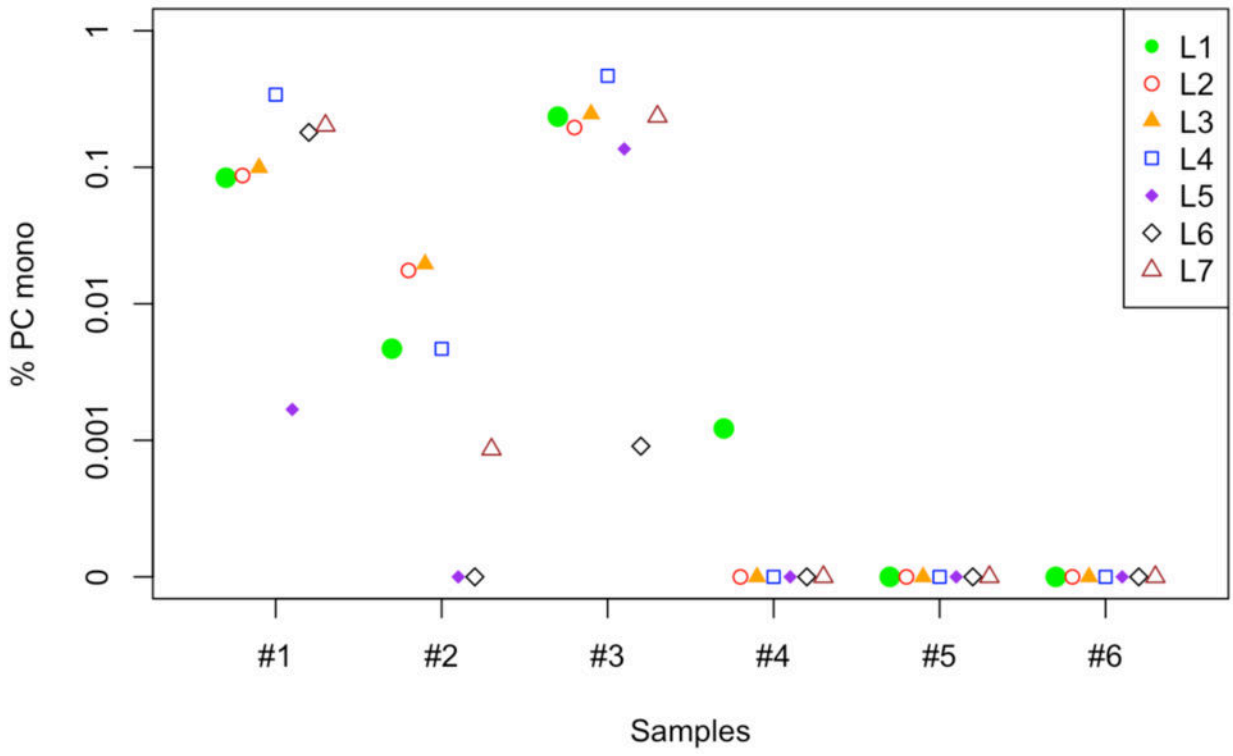

Figure 1

https://doi.org/10.1182/blood-2023-186536

Downloaded from http://ashpublications.net/blood/article-pdf/142/Supplement 1/7161/2184838/blood-3757-main.pdf by guest on 19 May 2024