

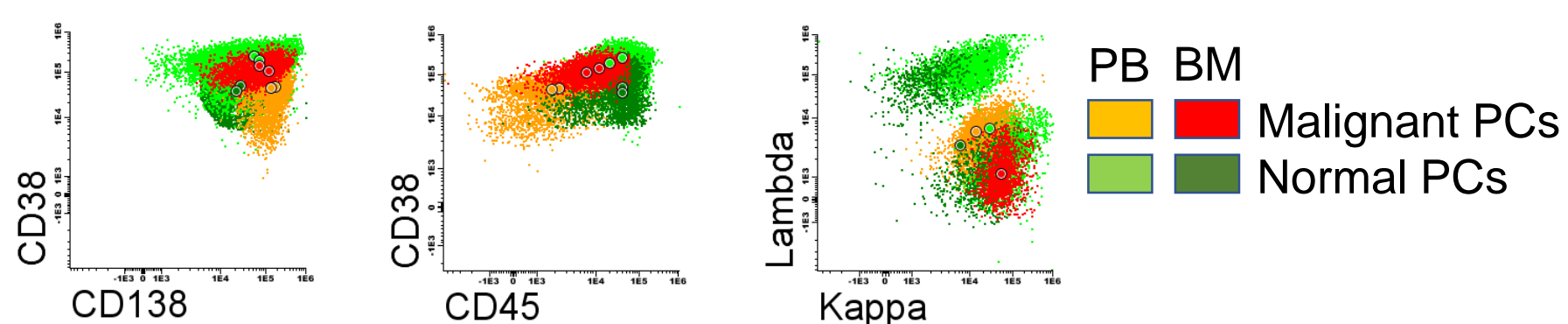
Study Group – Multiple Myeloma

ENHANCED DETECTION OF MINIMAL RESIDUAL DISEASE IN MULTIPLE MYELOMA THROUGH CD138 ENRICHMENT.

Speaker: Prof. Dr. Hermann Einsele, Department of Medicine II, University Hospital Würzburg

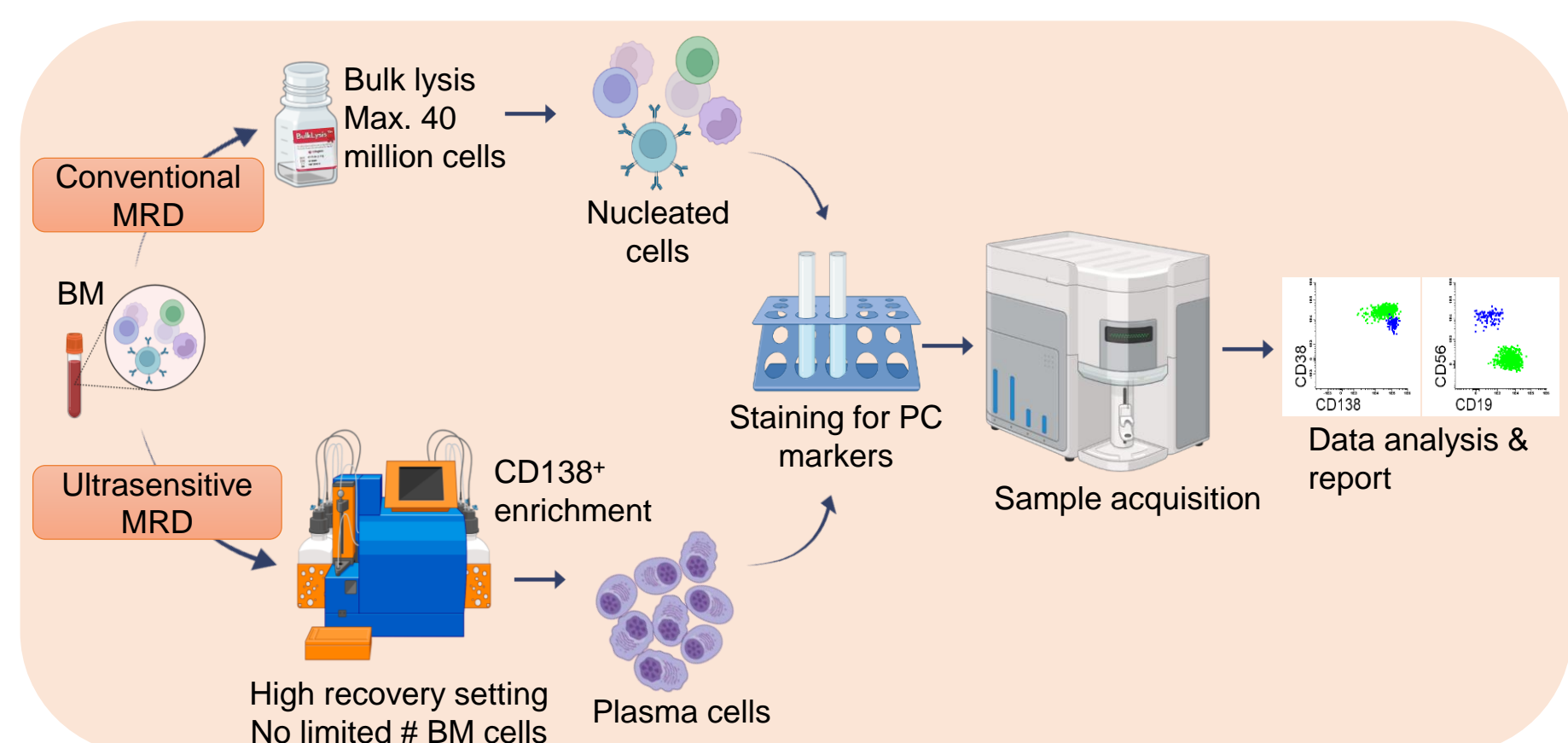
Background

Euroflow next-generation flow (NGF) cytometry sensitively assesses minimal residual disease (MRD) in multiple myeloma (MM), serving as a global standard for disease monitoring and treatment decision making. Despite Euroflow MRD diagnostic's widespread adoption in trials with advanced in anti-cancer approaches like BiTEs, CAR-T cells, and ADCs, challenges persist in aligning blood-based methods with bone marrow plasma cells (PC) analysis, necessitating heightened sensitivity to detect residual malignant cells post-therapy. The BloodFlow method, a recent innovation, achieves remarkable sensitivity up to 10^{-8} by enriching CD138⁺ PCs from 50 mL peripheral blood, presenting a unique opportunity to enhance MRD evaluation. Therefore, this study compares conventional Euroflow BM-MRD with an ultrasensitive approach using CD138 enrichment of bone marrow cells before analysis.



Methods

BM-MRD was performed according to the guidelines of the Euroflow group. For ultrasensitive assessment, CD138⁺ plasma cells were isolated using MACSprep™ CD138 MicroBeads and AutoMACS® Pro system. Data analysis was performed with Infinicyt software. Automatic gate and identification tool was used for conventional MRD, while data was manually analyzed for ultrasensitive MRD assessment.



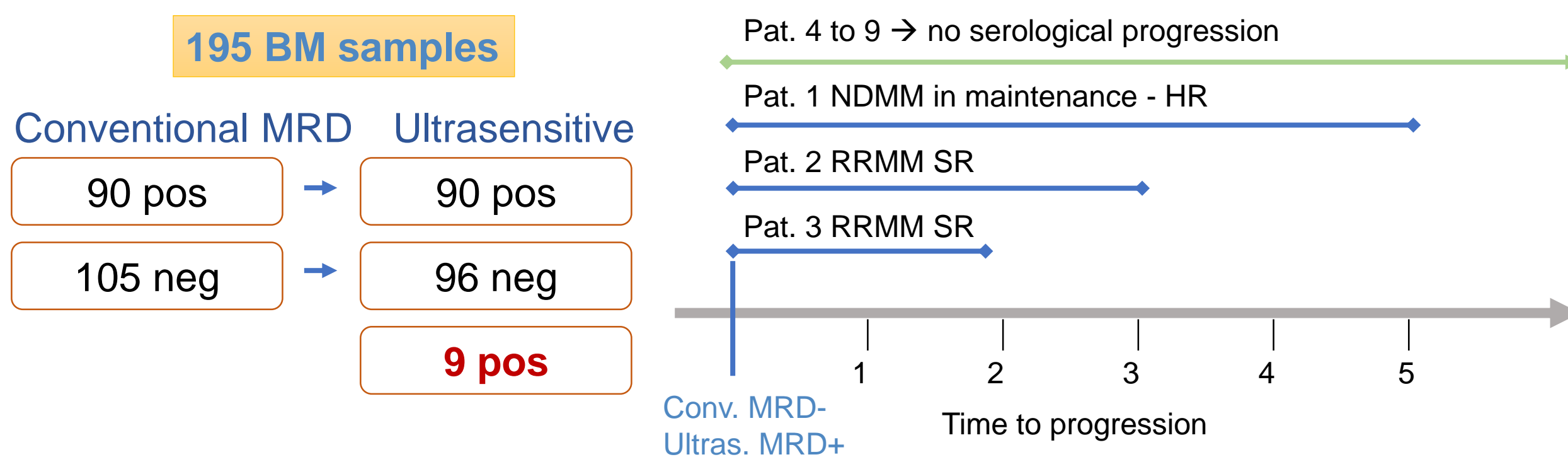
Goals

To compare the performance of conventional Euroflow MRD protocol vs ultrasensitive MRD after enrichment of CD138⁺ plasma cells, for the evaluation of minimal residual disease in patients with multiple myeloma.

Results

We compared conventional and ultrasensitive MRD in bone marrow samples randomly collected of 195 MM patients. All positive MRDs identified using conventional NGF remained positive with the ultrasensitive MRD approach. Notably, among 93 patients with negative conventional NGF-MRD, 9 cases turned positive after ultrasensitive MRD. These included 6 newly diagnosed (ND) MM and 3 relapse refractory (RR) MM, with the ultrasensitive method detecting aPCs ranging from 0,00015 to 0,0018% in all nucleated cells in the bone marrow. From the ND cohort, patients were treated with standard regimens during induction, followed by autologous stem cell transplantation, and were in CR at the time of ultrasensitive MRD. Further investigations, including imaging studies, corroborated the absence of active disease, in aligning with the results from conventional MRD assessments.

Our study advocates for the adoption of CD138 enrichment in MRD assessment, as it provides heightened sensitivity at detection levels of 10^{-7} cells, allowing for the detection of residual malignant cells that may be missed by conventional methods. This approach holds promise in improving disease monitoring and treatment decision-making for MM patients, particularly in identifying those at risk of relapse or progression.



Publications

- Poster #3342 at the 65th meeting of the American Society of Hematology (ASH) 2023: Euroflow-based ultrasensitive detection of malignant plasma cells in the bone marrow.
- Manuscript in preparation.

Long-term perspective

The comparison of diverse technologies for diagnosis and monitoring in a larger MM patient cohort, will provide data that will help to predict patient therapy efficacy and patient outcome. The Ultrasensitive MRD method will be especially relevant for patients with high risk and ultra-high risk disease, who continue to relapse despite classic MRD negativity.

Authors: Paula Tabares¹, Nina Fischer², Cäcilia Köstler^{3,4}, Christoph Klein^{3,4}, Rainer Claus², Sebastian Theurich⁵, Florian Bassermann⁶, Andreas Beilhack¹, Hermann Einsele¹.

(1) University Hospital Würzburg, (2) University Hospital Augsburg, (3) University of Regensburg, (4) Fraunhofer Institute Regensburg, (5) Ludwig Maximilians Universität München, (6) Technische Universität München.

