MultipleMyelomaHub

General MM, Patients eligible for transplant, Patients non-eligible for transplant, Elderly patients, Relapsed/refractory patients

Microfluidic device improves detection of genetic abnormalities and treatment outcome in MM

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Treatment of multiple myeloma (MM) is guided by information on a patient's cytogenetic status in terms of the presence of certain abnormalities in their plasma cells (PCs). These are tested for using bone marrow (BM) biopsies, which in certain cases can lead to false negatives. As MM progresses it has been shown that the level of CD45 negative ($CD45^-$) PCs increases. Therefore, it was hypothesized that enrichment of BM samples for $CD45^-$ cells, via CD45 positive ($CD45^+$) cell depletion using tetrameric antibody complexes (TACs), would increase the level of relevant malignant cells, enabling more accurate detection of genetic abnormalities.

In a study published in Molecular Oncology by Li Gao and Yunjing Zeng from the University of Southern California, Los Angeles, CA, and the Xinqiao Hospital, Army Military Medical University, Chongqing, China, and colleagues, a microfluidic (MF) device was used to enrich samples with malignant PCs to analyze for cytogenetic status. BM samples were taken at diagnosis from 48 newly diagnosed (ND) MM patients (pts) and each sample was subjected to either classic flow cytometry and FISH analysis, or microfluidic enrichment of $CD45^-$ PCs and size selection. Microfluidic enrichment identified abnormalities in two patients that were undetected by classic methods, and the authors detailed the resultant treatment decisions for two patients.

Key Data:

- CD38+/CD138+ cells detected in:
  - un-manipulated bone marrow (BM) = 10.3% ± 8.5%
  - using microfluidic method enrichment (MF-$CD45^-$TAC) = 37.7% ± 20.4% (P<0.001)
- Therefore, the percentage of PCs was increased by depletion of $CD45^+$ cells
- Risk stratification of MM patients before *vs* after MF-$CD45^-$TACs enrichment:
  - Rearrangements involving the 14q32 region = 11 patients (22.9%) *vs* 27 pts (56.3%)
  - Del(13q14) = 6 pts (12.5%) *vs* 37.5% (P<0.001)
  - Del(17p) = 3 pts (6.25%) *vs* 22.9% (P<0.001)
  - 1q21 gains = 9 pts (18.8%) *vs* 41.7% (P=0.001)
- Different cytogenetic abnormalities require different treatment plans, so the authors described two cases for which the more accurate diagnosis from microfluidic enrichment was able to positively influence the treatment decision

Patient 1:

- A 60-year old male was diagnosed with type IgG, λ MM, ISS stage III

- No cytogenetic abnormalities were found using the classic methods; pt was classified as low-risk
- MF-CD45-TACs enrichment led to detection of del(17p) & del(13q14), and reclassification as high-risk
- Treatment was switched from VTD (bortezomib, thalidomide, and dexamethasone) to VRD (bortezomib, lenalidomide, dexamethasone) induction therapy leading to very good partial remission (VGPR)
- After four courses of autologous stem cell transplantation (ASCT), pt achieved complete remission (CR)
- Another five courses of VRD consolidation therapy were given; pt now remains stable in CR, with RD maintenance therapy

Patient 2:

- A 41-year old male, diagnosed with IgG, λ type MM, ISS stage III
- FISH analysis revealed del(13q14) and IgH rearrangement; pt was classified as intermediate-risk
- MF-CD45$^-$TAC enrichment detected del(17p), leading to a high-risk classification
- Treatment with 4 cycles of VTD led to very good partial remission (VGPR)
- Pt underwent a transplant with familial donated allogeneic hematopoietic stem cells
- Achieved a stringent CR with thalidomide maintenance therapy

This microfluidic method (MF-CD45$^-$TACs) was able to enrich malignant PCs and significantly increased the detection rate for genetic abnormalities in MM patients. This overcomes the problem of false negatives due to 'the unpredictable distribution and rarity of MM cells'. Of note, the authors were able to use two case studies to illustrate the detection of abnormalities that went undetected with the use of classic methods. As a consequence, the treatment plans for the two patients were amended accordingly and led to improved outcomes.

References

1. Gao L. *et al.* Microfluidic enrichment of plasma cells improves treatment of multiple myeloma. Mol Oncol. 2018 Apr 11. DOI: 10.1002/1878-0261.12201.