

## Abstracts

expression with myeloma stage, response rate post-treatment, and progression-free survival (PFS) were compared using bivariate and multivariate statistics. **Results:** 762 patients were included in the analysis. The median age at diagnosis was 63 (range 27-93) and 50% were male. Mean LAT1 expression was 3.00 logs ( $\pm$  0.95); 30% were considered to have high LAT1 expression. High LAT1 was observed in 40% of patients with Stage III disease, compared to 27% of those with Stage I or II disease ( $p < .001$ ) 296 patients underwent ASCT during first-line treatment with 39% having a complete response (CR). 49% of those with high LAT1 obtained a CR compared to 35% of those without ( $p = .030$ ). 16% of the 466 patients who did not undergo ASCT also obtained a CR. 21% of those with high LAT1 obtained a CR compared to 14% of those without, which was not statistically significant. Overall, high LAT1 expression was associated with a 34% increase risk for PFS (aHR 1.34; 95% CI 1.07-1.69;  $p = .012$ ) after controlling for ASCT, CR, and ISS stage. However, the risk was mitigated in patients undergoing ASCT. For those with high LAT1, receiving an ASCT resulted in a 47% decrease in risk (aHR 0.53; 95% CI 0.37-0.74;  $p < .001$ ) and PFS was similar to those with normal LAT1 expression. **Discussion:** Melphalan-based ASCT may mitigate the higher risk associated with high LAT1 expression at diagnosis of multiple myeloma. While ASCT is generally recommended for all eligible patients with multiple myeloma, those with high LAT1 may receive an even larger benefit.

**Keywords:**

autologous stem cell transplant  
gene expression  
High risk

**Tracks:**

Multiple Myeloma Genomics

**FP-015**

### Next-generation optical mapping reveals numerous previously unrecognized structural variants in multiple myeloma

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Multiple myeloma (MM) is characterized by high genetic heterogeneity, which in turn affects not only the development of the disease but also the therapeutic response. To further characterise the genetic heterogeneity in MM, we applied a novel approach of next-generation optical mapping to study a genomic architecture of MM cells. We analysed samples of bone marrow from two patients with newly diagnosed MM using optical mapping together with standard

Methods (karyotype, FISH, and arrayCGH) and compared the Results of these approaches. For optical mapping, high-molecular weight DNA was isolated from sorted MM cells, labelled by DLS chemistry and visualised on Saphyr system (BioNano Genomics). The optical genome maps (480 Gbp, coverage 124X) were aligned to a human reference genome (GRCh38) and the detected structural variants (SVs) were compared against the database of healthy controls; only rare de novo variants were analysed. In Patient 1 (male, 77 years, MM IgG kappa, stage IIIA (Durie-Salmon, DS), International Staging System (ISS) 2, revised ISS (R-ISS) 2) numerous genetic aberrations were detected by both optical mapping and arrayCGH (trisomy 4, 11, 18, 19, 21, monosomy 13 and tetrasomy 15). Optical mapping revealed additional 47 deletions, 16 insertions, 14 inversions, 4 duplications and 4 translocations. All translocations were within unusual chromosomes 3 and 6. We also identified 587 bp insertion in 17p13 chromosome and 8.1 kbp deletion in 18q21 chromosome, both regions affecting the activation of cancer genes tumor suppressors and oncogenes. Additionally, several large SVs were located on chromosome 3, including duplication, inversion, intra- and inter-chromosomal translocations t(3;6). In Patient 2 (male, 74 years, MM IgA kappa, st. IIIA (DS), ISS 2, R-ISS 2), both optical mapping and arrayCGH detected trisomy 3, 5, 9, 11, 15, 18, 19 and tetrasomy 21. Optical mapping revealed additional 35 deletions, 22 insertions, 11 inversions, 2 duplications and 8 intrachromosomal translocations affecting chromosomes 3, 4, 14, and 18. Although no IGH locus rearrangements were detected by standard methods, monosomy on chromosome 14 and 20.5 kbp deletion were found within IGH locus by optical mapping. As conclusion, a large number of additional novel genomic rearrangements was detected in MM using next-generation mapping technology, showing a high potential of optical maps for refinement of genomic variability in MM. The study on larger patient cohort and longer follow-up of patients may identify structural variants associated with the clinical course and therapy response. Support: research grant Celgene, MZ ČR VES16-32339A, NV18-03-00500, MZ ČR – RVO (FNOI, 00098892).

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genomic architecture  
optical mapping

**Tracks:**

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### Fusion gene detection across a large cohort of multiple myeloma patients

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Gene fusions are an important class of genetic variation relevant across cancer types. We detected gene fusion events from a cohort of 742 patients from the Multiple Myeloma Research Foundation CoMMpass Dataset, combining sequencing data from RNA and DNA with clinical information to form a landscape of fusion events.