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POSTER ABSTRACTS

731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL

Patterns of Change in Multiple Myeloma (MM) Clone Size with Autologous Hematopoietic Stem Cell Transplantation (ASCT) Assessed By Next Generation Sequencing (NGS) in Patients (pts) Receiving Modern Therapy

Tylan Magnusson, MD[1], *Luciano Costa, MDPhD*[2], *Smith Giri, MDMS*[3], *Gayathri Ravi, MD*[3], *Kelly Godby, MD*[3], *Binod Dhakal, MBBS*[4], *Bhagirathbhai Dholaria, MBBS*[5], *Eva Medvedova, MD*[6], *Natalie S. Callander, MD*[7], *JoAnn Steele*[3], *Kathy Langley*[3], *Baylie Mullinax, BSN, RN, OCN*[3], *Melissa Sentell*[3], *Stephen Horn*[3], *Candace Hill*[3], *Megan Boullion*[3], *Susan Bal, MD*[3]

[1] University of Alabama at Birmingham, GARDENDALE, AL
[2] The University of Alabama at Birmingham, Vestavia, AL
[3] University of Alabama at Birmingham, Birmingham, AL
[4] BMT and Cellular Therapy Program, Department of Medicine, Medical College of Wisconsin, Milwaukee, WI
[5] Division of Hematology/Oncology, Vanderbilt University Medical Center, Nashville, TN
[6] Knight Cancer Institute, Oregon Health & Science University, Portland, OR
[7] University of Wisconsin Carbone Cancer Center, Madison

Background

Measurable residual disease (MRD) is a quantitative, dynamic prognostic marker of progression free and overall survival in MM. With modern triplet and quadruplet induction strategies deep responses are the norm and the incremental effect of ASCT impact may vary substantially among pts and be influenced by disease and treatment features. However, the accurate characterization of the impact of ASCT is diluted by measuring a disease surrogate (paraprotein) instead of clone size. We examine the quantitative impact of ASCT on MM clone size by serial NGS testing before and after ASCT and evaluate disease and induction treatment features that modulate this impact.

Methods

We included pts with newly diagnosed MM from five US centers, who received modern triplet and quadruplet induction followed by single melphalan ASCT between 3/2018 and 5/2023 with MRD testing (ClonoSEQ®) pre and post ASCT. ClonoSEQ® platform utilizes NGS to quantify unique immunoglobulin genes rearrangements associated with MM clone, therefore directly capturing clone size. We excluded pts with clone size $<10^{-5}$ prior to ASCT. We explored patient-, disease-, and treatment features influencing clone size reduction with AHCT by 1 $\log_{10}$. We used binary logistic regression to identify factors associated with $\geq$1 $\log_{10}$ clone reduction (60-100 days post ASCT).

Results

One hundred and forty-nine pts with NDMM had pre and post ASCT results and pre ASCT MRD $\geq 10^{-5}$ and met the inclusion criteria. The median age was 63 years (35-79), 37 pts (25%) $\geq$70 years, 62% male, 27% Black, 23% ISS3 and 16% RISS3. Seventy-three pts (49%) had high risk chromosomal abnormalities [HRCA, gain/amp(1q), t(4;14), t(14;16), t(14;20) or del(17p)]]; 72 pts (48%) had 0 HRCA, 50 (34%) had 1 HRCA, and 23 (15%) had 2+ HRCA. AntiCD38 monoclonal antibody (mAb) was part of induction in 125 (84%) pts [68 pts quadruplet containing carfilzomib; 53 pts quadruplet containing bortezomib], 28 pts received triplets. Eighty-seven pts (58%) had >1$\log_{10}$ reduction in MRD burden with ASCT. The median log reduction in MRD burden was 1.15 (IQR 0.65-1.75). For pts with 0, 1 and 2+ HRCA, 47% (34/72), 68% (34/50), 74% (17/23) had a >1 $\log_{10}$ reduction in clone size and the median reduction was 0.96 $\log_{10}$ (IQR 0.47-1.66), 1.24 $\log_{10}$ (IQR 0.89-1.91) and 1.5 $\log_{10}$ (IQR 0.89-2.20), respectively (Figure). Among pts without HRCA, those with hyperdiploid MM had a trend towards less frequent $\geq$1 $\log_{10}$ clone size reduction with ASCT (38% vs. 57%, p=0.18). Overall, we saw reduction $\geq$1 $\log_{10}$ in clone size in 61% of pts receiving anti-CD38 mAb in induction (N=125) vs. 46% among those who did not (N=24, p= 0.18). Among pts treated with melphalan 200 mg/m^2 (N=113) compared to those who received 140 mg/m^2 (N=36), $\geq$1 $\log_{10}$ reduction in clone size was noted in 61% vs. 50% (p=0.25), respectively. In multivariable analysis that included stage, antiCD38 mAb in induction, use of carfilzomib in induction, HRCA and melphalan dose, the presence of HRCA was the only factor associated with greater than 1 $\log_{10}$ reduction in MRD burden with ASCT [1 HRCA, OR 2.34 (1.07-5.14); $\geq$2 HRCA, OR 2.71 (0.91-8.03); p=0.049].

Conclusions

The impact of high dose melphalan and AHCT on MM clone size is heterogeneous, of greater magnitude in pts with one or more high-risk chromosome abnormalities, and less pronounced in pts with standard risk disease, particularly hyperdiploid MM. The use of antiCD38 mAb in induction regimens or dose of melphalan does not impact the effect of ASCT on MM clone size, likely owing to the distinct mechanism of action of melphalan. This dataset provides context to explore risk- and response-adapted use of ASCT and use of new cellular and non-cellular immunotherapies as post-induction consolidative strategies.

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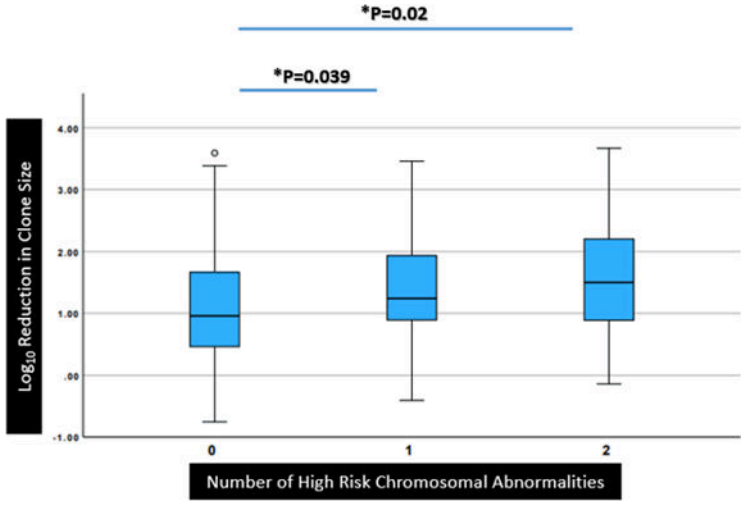

Figure 1

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