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652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Association of p16, a Biomarker of Cellular Senescence, with Receipt of Therapy for Plasma Cell Disorders

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Introduction

Multiple myeloma (MM) and immunoglobulin light chain (AL) amyloidosis are clonal plasma cell disorders (PCDs) of aging, with median ages at diagnosis of 69 and 76 years, respectively. The care of adults with these disorders is often challenging due to the higher prevalence of vulnerabilities with advancing age. We examined patterns of senescence biomarkers and associations with therapy receipt among adults treated for plasma cell disorders.

Methods

Adults undergoing treatment for PCDs were recruited to a longitudinal observational study (NCT03717844) from 2018 to 2020. Study participants provided blood samples and completed study assessments at pre-specified intervals.

Cellular senescence was quantified by measuring mRNA expression of p16 in peripheral blood T lymphocytes. Expression of p16 is reported as log2 arbitrary units. A linear regression formula previously derived from p16 expression in 633 subjects was utilized to translate p16 expression levels into an age equivalent. These values were used to calculate the p16AgeGap, a difference between an individual's p16 expression and their chronological age. Subjects with p16 levels below the age-appropriate population mean have a negative p16AgeGap, and those with p16 above the population mean have a positive p16AgeGap.

Exposures included both treatment receipt and duration of therapy. Treatment was assessed via categorical classification of treatment intensity, and treatment duration was quantified from diagnosis to time of p16 blood draw.

Descriptive statistics were calculated for baseline demographic and disease characteristic variables. The p16 and p16AgeGap variables were summarized in terms of means and 95% confidence intervals (CI). The significance of associations between p16/p16AgeGap and categorical variables was assessed via Kruskal-Wallis or Wilcoxon rank-sum tests. Associations between continuous variables were assessed via calculation of Pearson correlation coefficients.

Results

The cohort consisted of 109 individuals (88 with multiple myeloma and 21 with other plasma cell disorders). Mean age was 68 years (range 39-91). The sample was predominantly male (56.9%) and White (70.6%). Samples for p16 were drawn prior to any treatment in 20 subjects. The remainder had received prior therapy and 36 had relapsed/refractory disease.

There was a significant association between the treatment receipt and p16 as well as between the treatment receipt and p16AgeGap (Figure 1). We observed a significant modest positive correlation between the duration of treatment and p16 (correlation coefficient 0.27, p=0.007) and p16AgeGap (0.22, p=0.03). Among those who had undergone transplant, we observed higher mean p16 (mean 12.84 [95% CI 12.46-13.23] vs 11.81 [11.51-12.11] for non-recipients, p=0.0001) and p16AgeGap (mean 50.6 [39.6-61.6] vs 16.9 [8.4-25.4], p <0.0001). There was a significant association between receipt of bortezomib-containing regimens with both p16 levels p16AgeGap, with higher mean p16 & mean p16AgeGap for those who did not receive bortezomib.

For the subset of patients with transplant date before the p16 collection date (N=38), there was no significant association between time since transplant and either p16 level or p16AgeGap.

Conclusion

This study elucidates the relationship between markers of cellular senescence, specifically p16 levels and the p16AgeGap, and the impact of treatment receipt and duration in a cohort of patients undergoing treatment for plasma cell disorders.

There was a clear significant association between the receipt of treatment and both markers of senescence, along with a modest positive correlation between the duration of treatment and these markers. Further analyses involving this cohort will evaluate the relationship between these biomarkers and patient-centered endpoints, including disease-related symptoms and functional outcomes.

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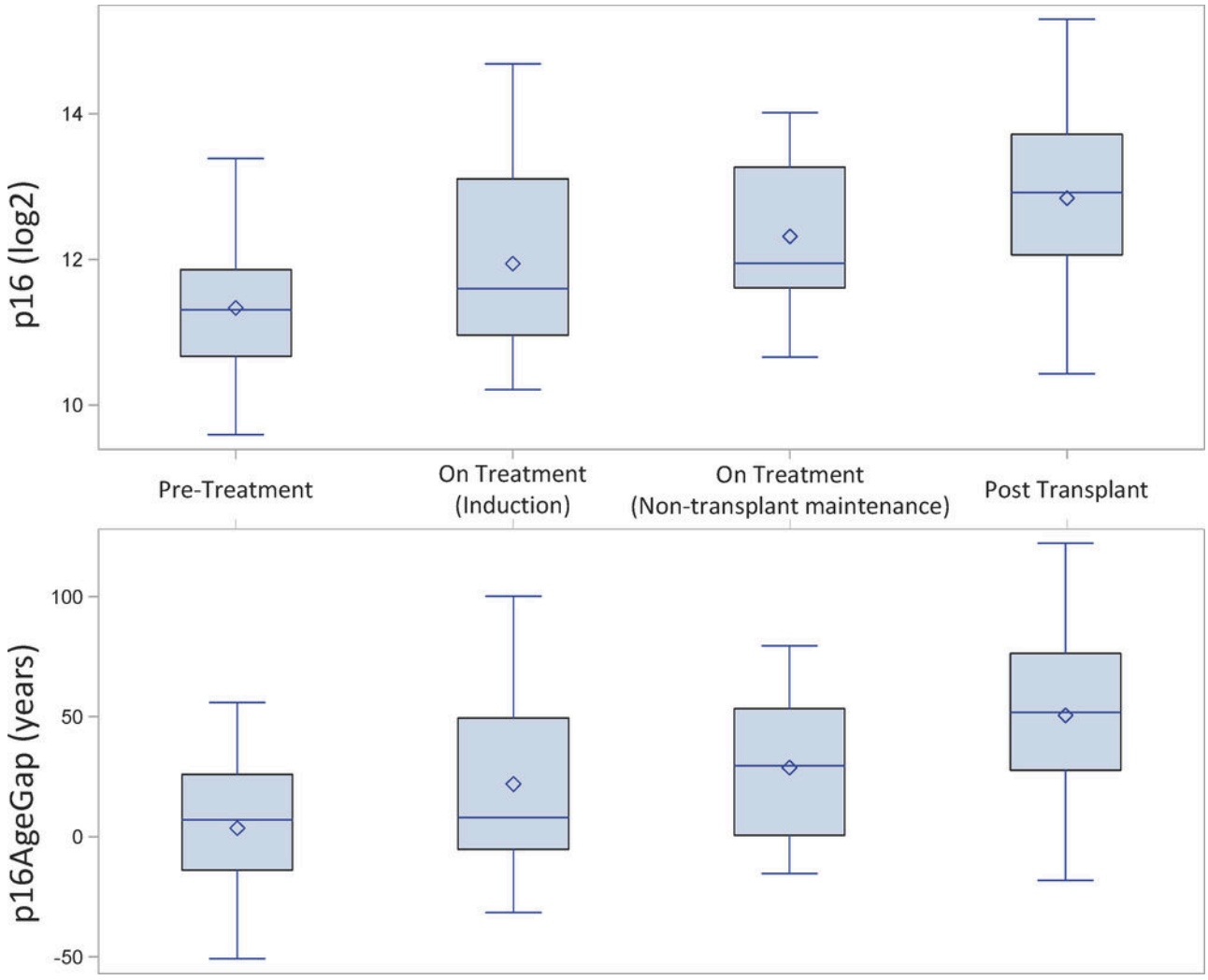

Figure 1

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