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PB1967 ROLE OF CYTOKINES IN MULTIPLE MYELOMA: IL-1RN AND IL-4 VNTR POLYMORPHISMS

Topic: 13. Myeloma and other monoclonal gammopathies - Biology & Translational Research

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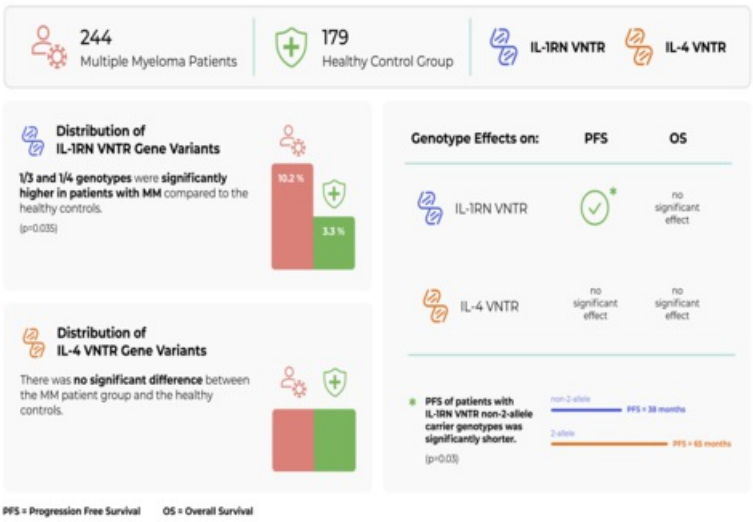
Background: Cytokines have important effects on immune regulation and oncogenesis. IL-1 is a cytokine with important physiological roles in cytokine regulation, vascular permeability and sepsis in autoimmune diseases. The IL-1 receptor antagonist (IL-1Ra or IL-1RN) is a member of the IL-1 superfamily that functions as a competitive antagonist of the cell surface IL-1 receptor, thereby regulating various immune and inflammatory responses related to IL-1. IL-1 induces tumor growth and metastasis, while IL-1RN inhibits the secretion of IL-1α and IL-6 in cancer cells. Interleukin-4 (IL-4) is a potent anti-inflammatory cytokine, and its gene is located on the long arm of chromosome 5 (q23-31) along with other cytokine genes. IL-4 can be secreted by many types of immune cells, including basophils, eosinophils, myeloid lineage cells, mast cells, and activated T cells.

Aims: In this study, it was aimed to reveal the effects of IL-1RN and IL-4 VNTR polymorphisms on disease development and survival in patients with MM.

Methods: In this study, 244 patients diagnosed with MM in hematology clinic between January 2010 and January 2021, and 179 healthy individuals were included. The control group did not have any kind of cancers and consisted of a unrelative population permanently residing in Turkey. ASCT was performed for 73% of the patients after 4 courses of VCD (bortezomib, cyclophosphamide, and dexamethasone) with at least a partial remission and then LD (lenalidomide and dexamethasone) was used as a maintenance therapy for the following follow-up period. The 1/1, 1/2, 1/3, 1/4, 2/2, 2/3 and 2/4 genotypes of the IL-1RN VNTR polymorphism were statistically compared before treatment between patients having undergone ASCT and healthy controls, as were the 1/1, 1/2 and 2/2 genotypes of IL-4 VNTR polymorphism. Additionally, the statistically significant effects of these genotypes on survival were examined.

Results: The median age of 244 patients included in the study was 58 old years (range: 29-81). The 5-year and 10-year OS were 76% and 53%. The 5-year and 10-year PFS were 42% and 21%, respectively. The median PFS was 42,3 months. The median follow-up period was 27 months (4,4-155 months). In the statistical analysis of the distribution of IL-1RN VNTR gene variants, 1/3 and 1/4 genotypes were found to be significantly higher in patients with MM compared to the healthy controls (p=0,035). In the statistical analysis of the distribution of IL-4 VNTR gene variants, there was no significant difference between the MM patient group and the healthy controls in terms of genotype distribution (p>0.05, for all). IL-4 VNTR genotype distribution did not have a significant effect on PFS and OS. PFS of patients with IL-1RN VNTR non-2-allele carrier genotypes was significantly shorter, but no significant effect was found on OS (p=0,03, p=0,786, respectively. Patients with IL-1RN VNTR non-2-allele carrier genotypes had 1,718-fold increased risk of shorter PFS.

Image:



Summary/Conclusion:

In conclusion, with this study, the effects of IL-1RN VNTR and IL-4 VNTR polymorphisms on MM were evaluated for the first time in the literature. The IL-1RN 1/3 and 1/4 genotypes were significantly more common in patients with MM compared to healthy controls. Patients with IL-1RN VNTR non-2-allele carrier genotypes had 1,718-fold increased risk of shorter PFS, but no significant effect on OS was demonstrated. IL-4 polymorphism, on the other hand, did not have a significant effect on MM development or survival. This study will shed light on ones on cytokine-MM relationship and epigenetic mechanisms.