**PB1953 ASSESSMENT OF THE EFFICACY OF BORTEZOMIB-CONTAINING THERAPY REGIMENS DEPENDING ON MAGE-C1 GENE EXPRESSION IN MULTIPLE MYELOMA PATIENTS.**

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

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**Background:**

The treatment of multiple myeloma (MM) has undergone significant changes over the past decade due to the emergence of new therapeutic agents and the development of personalized approaches. The search for factors to predict the course of the disease remains relevant. MAGE-C1 gene expression is considered as a possible marker of refractoriness to bortezomib-containing therapy regimens.

**Aims:**

Determine MAGE-C1 gene expression by real-time polymerase chain reaction (RT-PCR). Evaluate the effectiveness of bortezomib-containing regimens in MM patients depending on MAGE-C1 gene expression.

**Methods:**

The prospective study from February 2019 to November 2021 included 81 MM patients (37 men, 44 women), aged 35 to 82 years (Me 59). The level of MAGE-C1 gene expression by RT-PCR in bone marrow samples, enriched with CD138+ cells, was determined in all patients. The diagnosis of MM was made according to the IMWG (2014). The ISS stage was determined as I in 24 (20%) patients, II in 21 (67%), III in 36 (13%). Plasma cell content ranged according to myelogram from 1 to 89% (Me 26%), paraprotein secretion was 0.1 to 85 g/L, Bens-Jones protein in urine (from trace values to 12.54 g/day) was determined in 54 patients. Bone plasmacytomas were documented in 42 patients, myeloma nephropathy in 19 cases, high risk cytogenetic in 25. Induction of remission was carried out by three-component regimens including bortezomib, 30 patients required two or more lines of therapy with lenalidomide or daratumumab. The number of courses was 4 to 10 (median 7). The anti-tumor response after 2-6 courses of therapy with bortezomib-containing regimens was evaluated in 68 patients according to the IMWG (2016). Anti-tumor ≥partial response (PR) was achieved in 52, refractory to bortezomib MM was found in 16 patients. As a control, similar bone marrow cells of 7 healthy donors were investigated.

**Results:**

The maximum value of MAGE-C1 gene expression in donors was 0.06 (2ΔCt). The MAGE-C1 gene expression value >0.06 (2ΔCt) in patients was accepted as increased. The group with normal MAGE-C1 gene expression (0.003 to 0.05, 2ΔCt) consisted of 25 patients and the group with increased expression (0.07 to 14.12, 2ΔCt) consisted of 56 patients.

The probability of achieving ≥PR in patients with normal MAGE-C1 gene expression was 87.8% and in patients with increased expression- 72.8%. The median time to achieve ≥PR in patients with an expression value ≤0.06 (2ΔCt) was 1.77 months, and in patients with an expression >0.06 (2ΔCt) was 3.06 months, p=0.03 (Fig. 1). In addition, we were able to determine that the expression values of the studied gene were significantly lower in patients with ≥PR compared to patients who were refractory to bortezomib: median 0.15 vs 0.27 (2ΔCt), p=0.05.

**Image:**

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Summary/Conclusion: In a single-factor analysis, we were able to determine that patients with normal MAGE-C1 gene expression were significantly more likely to achieve an overall response (≥PR) compared to patients whose MAGE-C1 gene expression was increased. Achievement of ≥PR on bortezomib-containing therapy regimens was documented twice as fast in patients with normal expression of the investigated gene. Further study of the MAGE-C1 gene may allow to determine the tactics of induction therapy already at the diagnostic stage.