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Anti-angiogenic effect of bortezomib in multiple myeloma is associated with lower NF-kB expression

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ABSTRACT

THE AIM OF STUDY: in the present pilot study the effects of the first-in class proteasome inhibitor-bortezomib on expression of NF-kB and angiogenesis were examined using immunohistochemical analysis of bone marrow biopsies (BMB) in patients before and after treatment

PATIENTS AND METHODS: thirty newly diagnosed multiple myeloma patients at the Department of Hematology, Clinical Hospital Center Rijeka, with paraffin-embedded BMB tissue available before and after 6-8 cycles of bortezomib-based regimens, who achieved response to therapy, were evaluated

- the immunoreactivity of NF-kB was evaluated on the basis of percentage of positive plasma cells
- computer assisted image analysis was used for more objective and accurate determination of average quantity of microvessels per 1 mm^2 (microvessel density – MVD)
- the association of NF-κB and MVD with overall survival was also evaluated

RESULTS

The comparison of the analyzed parameters showed significantly lower percentages of NF-κB in plasma cells (p=0.0006) and MVD (p=0.0092) in the post-treatment BMB samples

- significant positive correlation of NF-kB and MVD was detected in pre-treatment bone marrow biopsy samples, (p=0.002) but there was no correlation in post-treatment BMB samples
- the overall survival rates were significantly shorter in patients with higher MVD in posttreatment BMB samples (p=0.025)

CONCLUSION

Our results support a hypothesis that bortezomib inhibits the NF-kB signal pathway in MM and reduced angiogenesis in post-treatment bone marrow samples which can influence survival of myeloma patients.

REFERENCES

1. Roccaro AM, Hideshima T, Raje N, Kumar S, Ishitsuka K, Yasui H, et al. Bortezomib mediates antiangiogenesis in multiple myeloma via direct and indirect effects on endothelial cells. Cancer Res. 2006;66(1):184-91. 2. Ntellas P, Perivoliotis K, Dadouli K, Koukoulis GK, Ioannou M. Microvessel Density as a Surrogate Prognostic Marker in Patients with Multiple Myeloma: A Meta-Analysis. Acta Haematol. 2017;138(2):77-84. 3. Lee N, Lee H, Moon SY, Sohn JY, Hwang SM, Yoon OJ, et al. Adverse prognostic impact of bone marrow microvessel density in multiple myeloma. Ann Lab Med. 2015;35(6):563-9. 4. Annunziata CM, Davis RE, Demchenko Y, Bellamy W, Gabrea A, Zhan F, et al. Frequent engagement of the classical and alternative NF-kappaB pathways by diverse genetic abnormalities in multiple myeloma. Cancer Cell. 2007;12(2):115-30. 5. Keats JJ, Fonseca R, Chesi M, Schop R, Baker A, Chng WJ, et al. Promiscuous mutations activate the noncanonical NF-kappaB pathway in multiple myeloma. Cancer Cell.2007;12(2):131-44.

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