Angiogenic markers in plasma cell myeloma patients treated with novel agents

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Angiogenesis plays an important role in pathogenesis and progression of plasma cell myeloma (PCM). Novel agents such as thalidomide, lenalidomide and bortezomib, have in part antiangiogenic mechanisms of action. In this study, we examined angiogenic markers in patients with PCM and correlated these markers to treatment response to novel agents.; We included 93 patients newly diagnosed with PCM treated with novel agents thalidomide or lenalidomide (immunomodulatory drugs; IMiDs), bortezomib, or a combination of IMiD and bortezomib. A panel of serum angiogenic markers was assessed by a quantitative sandwich enzyme-linked immunosorbent assay (ELISA) before and in the course of the therapy. The response evaluation was performed after three cycles of therapy. The patients were divided into responders [(stringent complete remission (sCR), complete remission (CR), very good partial response (VGPR)] and non-responders [(partial response (PR) stable disease (SD), progressive disease (PD)].; The CR-plus-VGPR rate was 45% in the IMiD-based group (13/29), 52% in the bortezomib-based group (16/30) and 58% in the combination group (20/34). Baseline levels of vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), tumor necrosis factor-α (TNFα), and angiopoietin-2 (ANG2) correlated positively with advanced disease stage (p>0.005 in each case). Regarding all 93 patients, levels of VEGF, soluble VEGF receptor-2 (sVEGFR-2), basic fibroblast growth factor (bFGF), placental-derived growth factor (PGF), ANG2, HGF and neuropilin-1 (NRP1) were significantly different in responders compared to non-responders. The levels of these angiogenic factors were significantly different in the IMiD-based group and the combination group after therapy but not in the bortezomib group.; The mode of action of IMiDs possibly leads them to have a greater antiangiogenic effect than bortezomib and thus the levels of angiogenic markers was more influenced by IMiD-based therapies in PCM. This study contributes in the understanding of the mode of action of novel agents in the treatment of PCM.
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