Abstract Submission

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ALTERED MICRORNA EXPRESSION PROFILE IN THE PERIPHERAL LYMPHOMONOCYTES OF MULTIPLE MYELOMA PATIENTS WITH BISPHOSPHONATE-INDUCED OSTEONECROSIS OF THE JAW.

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Background: Bisphosphonates are formidable inhibitors of osteoclast-mediated bone resorption employed for therapy of multiple myeloma (MM) subjects with osteolytic lesions. Osteonecrosis of the jaw (ONJ) is an uncommon drug-induced adverse event of these agents. MicroRNAs (miRNAs) are a group of small, noncoding RNAs nucleotides, which are essential post-transcriptional controllers of gene expression. They have a central role in the normal bone development.

Aims: The goal of our study was to investigate 18 miRNAs, whose targets were previously validated and described in MM subjects without ONJ, in peripheral lymphomonocytes of MM subjects with bisphosphonate-induced ONJ.

Methods: Utilizing reverse transcription quantitative polymerase chain reaction we evaluated miRNAs in five healthy subjects and in five MM patients with ONJ.

Results: Our experimental data revealed that a diverse miRNA signature for ONJ subjects emerged respect to control subjects. Using the filter for *in silico* analysis, among 18 miRNAs we recognized 14 dysregulated miRNAs. All of these miRNAs were significantly over-expressed in patients vs controls (MIR-16-1, MIR-21, MIR-23A, MIR-28, MIR-101-1, MIR-124-1, MIR-129, MIR-139, MIR-145, MIR-149, MIR-202, MIR-221, MIR-424, MIR-520). Among them, six were strongly up-regulated (4-fold up-regulated and more). These miRNAs target numerous pathways and genes implicated in calcium ion binding, bone resorption, mineralization of bone matrix, differentiation and maintenance of bone tissue.

Summary/Conclusion: A modified microRNA expression profile after zoledronate therapy could participate to the onset of ONJ. Targeting these miRNAs could provide a new treatment for the prevention or treatment of ONJ.

Keywords: Bisphosphonate, Genetic modifiers, Multiple myeloma, Osteonecrosis