ROLE OF ESTROGEN REPLACEMENT THERAPY IN THE CONTROL OF IMMUNE SYSTEM IN POSTMENOPAUSAL OSTEOPOROSIS

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INTRODUCTION

Menopause is the main factor responsible for the loss of bone mass in women [1].
It is now clear that the antiresorptive activity of estrogen is the result of genomic and non-genomic effects on bone marrow and bone cells, resulting in a reduction of osteoclasts (OC) formation, in an increase of OC apoptosis and in a decreased ability of mature OC to resorb bone [2].
It is also known that the increase of bone resorption secondary to estrogen deficiency is primarily due to increased OC formation stimulated by several cytokines. The important role of TNF in the molecular mechanisms through which estrogen deficiency causes bone loss has been demonstrated in animal models and also in humans [3,4].
In our recent work we have shown that estrogen deficiency increases osteoclastogenesis through increased production of pro-inflammatory cytokines such as TNF-alpha and RANKL, and that T cells play a key role in postmenopausal bone loss and in osteoclastogenesis induction in humans [4].

The aim of this study is to investigate the influence of estrogen replacement therapy (HRT) in the control of the immune system and osteoclastogenesis.

The authors have no conflict of interest in this study

METHODS

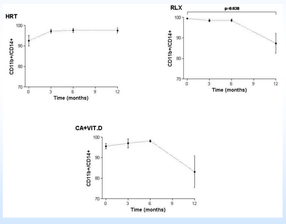
✓ We enrolled in the study **38 female patients** affected by postmenopausal osteoporosis. Patients were randomized to receive **HRT** plus Calcium and Vitamin D (11), **RLX** plus Calcium and Vitamin D (12) and **Calcium and Vitamin D** alone (15).

✓ In all the subjects we measured **osteoclast precursors** (OCP) and **T cells subsets** in peripheral blood mononuclear cells (PBMC) by flow cytometry, at baseline and after 3, 6 and 12 months of therapy.

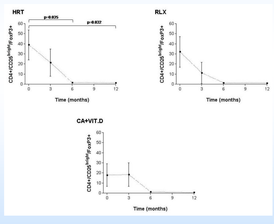
✓ We evaluated by ELISA technique **cytokines levels** in sera and in cell cultures supernatants from all patients, at baseline and after 3, 6 and 12 months of therapy.

RESULTS

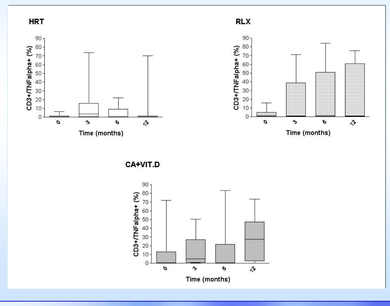
OCP WERE SIGNIFICANTLY REDUCED BY THE SOLE RLX



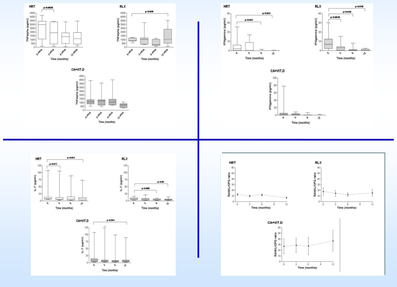
Tregs WERE REDUCED BY HRT, AND NOT BY OTHER THERAPIES



HRT AMELIORATES T CELLS IMMUNE RESPONSE



TNF-ALPHA, IL-7, IFN-GAMMA AND RANKL/OPG RATIO WERE SIGNIFICANTLY REDUCED BY HRT



CONCLUSIONS

Here we demonstrate that estrogens have an immunomodulatory effect on T cells, reduce Tregs and ameliorate T cells response to immune stimulation.
HRT reduces the production of pro-inflammatory cytokines as TNF-alpha, IL-7 and IFN-gamma. These cytokines are also responsible for increased osteoclastogenesis.
HRT reduces the RANKL/OPG which is the main driver of osteoclast formation and activity, whereas it has no direct effect on OCP number.

In conclusion our data suggest that the effect of estrogen on bone turnover is mainly mediated by T cells.

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