Impact of radio(chemo)therapy on immune cell composition and function in cervical cancer patients

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INTRODUCTION

New combination treatment paradigms in oncology that are currently actively explored, consist of standard treatments and immunotherapy including so called checkpoint blockers

AIM

Combination treatments require profound understanding of immune modulatory properties of standard treatments. The aim of this study was to evaluate the impact of radio (chemo) therapy (RCT) on the immune system of cervical cancer patients.

METHODS

- 30 patients with cervical cancer, treated with radiotherapy with of without concurrent cisplatin
- Serial blood sampling
- Profiling immune cells including different lymphocyte and myeloid cell populations and the expression of co-stimulatory molecules
- Proliferation assays to determine T-cell and antigen presenting capacity
- Response to *in vitro* blocking of programmed cell death-1 (PD-1).

RESULTS

- Radio(chemo) therapy significantly decreased the absolute number of circulating white blood cells (fig.1)
- Treatment increased circulating monocytes and myeloid-derived suppressor cells (MDSCs) and decreased $CD4^+$ and $CD8^+$ T-cells
- Impaired responsiveness to anti- or mitogenic stimulation of remaining T-cells
- Impaired capacity of APCs to stimulate allogeneic T-cells
- Increased expression PD-1 $CD4^+$ T-cells (fig.2).
- *In vitro* blocking of PD-1 fully restored T-cell reactivity in pre-treatment samples, but only partially in post-treatment samples (fig.3).

CONCLUSIONS

- Conventional RCT in cervical cancer patients profoundly suppresses the immune system
- Combination of conventional RCT with immunotherapy unlikely to be synergistic
- Further research on the immunological effects of bone marrow sparing radiotherapy warranted to explore if this treatment modality could synergistically improve immune responses and outcomes

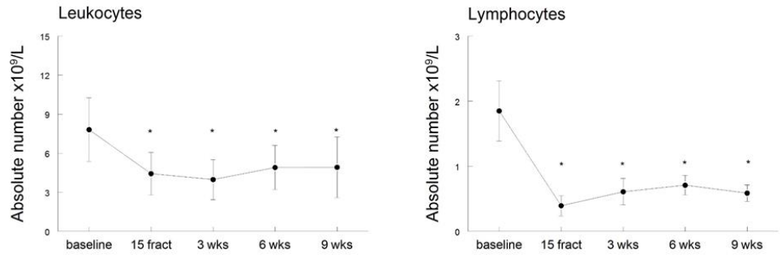

*Figure 1: Time course changes in leukocytes and lymphocytes before (baseline), during (15 fract) and after radio(chemo)therapy (3, 6 and 9 wks after completion). *p<0.05*

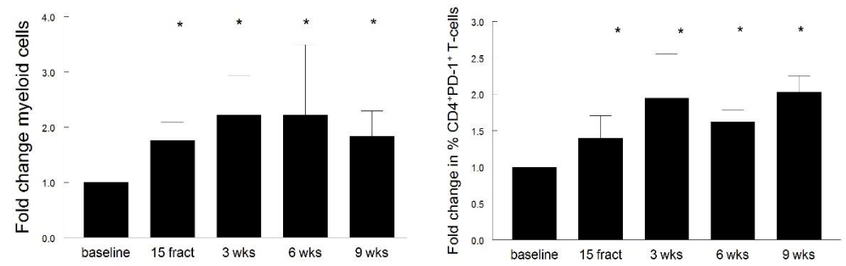

*Figure 2: Fold changes in the percentage of $CD3^-CD19^-$ myeloid cells of viable cells (left) and of $PD\text{-}1^+$ expressing $CD4^+$ T-cells (right). *p<0.05*

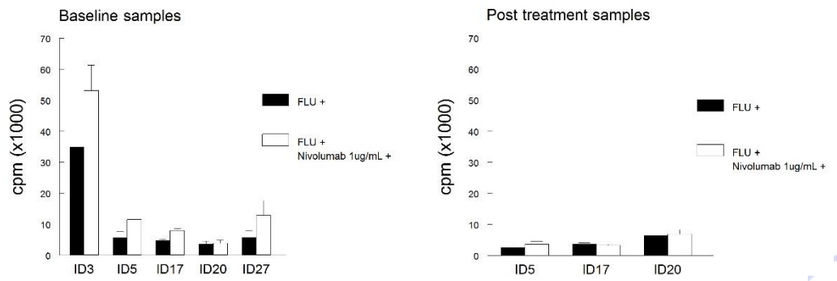

Figure 3: Stimulation of baseline (left) and post-treatment (right) samples and with FLU in vitro in the presence of absence ofrPD-1 blocking

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