MEDICAL THERAPIES AND PHARMACOLOGY

THE EVALUATION OF THE EFFECTIVENESS OF ANTI PD-1 MONOCLONAL ANTIBODY AND INTRATUMORAL BACILLE CALMETTE-GUERIN VACCINE MALIGN MELANOMA IN RAT MODEL.

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Background: Immunotherapy obtains significant advantages in the treatment of melanoma, but only a subset of patients exhibit durable responses with single-agent strategies.

Objectives In this study, we planned to increase the antitumoral efficacy by combining intratumoral BCG and programmed cell death protein 1 (PD-1) monoclonal antibodies.

Material and Methods: Murine B16 melanom model was performed with C57bl mice and study arms (sham, intratumoral BCG, anti PD1 therapy and intratumoral BCG+ anti-PD1 therapy) were formed. Tumour volume was screened twice a week and mices were sacrified after 15 days of therapy. Anti-mouse CD4, CD8, PDL-2, CD28, IL-2, TNF-à, IFN-ɣ, Tim3, LAG3, CTLA-4 were used for immunohistochemistry. The blood and tissue flowcytometric experiments were performed with anti-mouse CD90, CD4, CD8, CD29 and cytokin experiments were performed with RT PCR for IL-2, TNF-à and IFN-ɣ.

Results: CD29, CD8, CD28, CTLA-4, Tim3, PDL-2, IL-2, TNF-à and IFN-ɣ expressions in the tumoral tissues were increased according to the sham group, but the combined therapy group showed the most significant levels. While there was a homogenous cytokine expression in the other treatment groups, TNF-à expression in the combined grup was significantly elevated which was correlated with necrosis and CD90 decrease in the tumour. Clinically, both BCG granuloma and tumour mass were under control in this group.

Conclusions: İmmun checkpoint inhibitors activates nonspesific immun response, but the inflammatory response against tumour is not sufficient owing to the activation of other self tolerence mechanisms. Immunotherapy success is increased with intratumoural prokaryotic BCG antigens which strengthen immun response.