860 *IN VIVO* EFFECTIVENESS OF TUMOR TREATING FIELDS (TTFIELDS) CONCOMITANT WITH IMMUNE CHECKPOINT INHIBITORS IN NON-SMALL CELL LUNG CANCER (NSCLC)

Yiftah Barsheshet*, Tali Voloshin, Boris Brant, Gadi Cohen, Lilach Avigdor, Roni Blatt, Shay Cahal, Tharwat Haj Khalil, Efrat Zemer-Tov, Rom Paz, Anat Klein-Goldberg, Catherine Tempel-Brami, Sara Jacobovitch, Alexandra Volodin, Tal Kan, Bella Koltun, Cfir David, Adi Haber, Moshe Giladi, Uri Weinberg, Yoram Palti. *Novocure Ltd, Haifa, Israel*

Background Tumor Treating Fields (TTFields) are electric fields that disrupt cellular processes critical for cancer cell division and tumor progression. Recently, cancer cell death following delivery of TTFields has been shown to stimulate anti-tumor immunity and promote maturation of dendritic cells. The efficacy of TTFields concomitant with anti-PD-1 was previously shown *in vivo*, and is currently under clinical investigation. Here, we investigated whether concomitant treatment with TTFields and the anti-PD-1 and anti-CTLA-4 combination can improve therapeutic efficacy.

Methods Lung tumor-bearing mice were treated with TTFields (150 kHz, continuously for 10 days), with the anti-PD-1 and anti-CTLA-4 combination (3 i.p. injections, one every 72 h), or with the two modalities together. At the end of treatment, tumor volume was measured, tumor single-cell suspensions were generated, and tumor-infiltrating lymphocytes (TILs) were characterized by flow cytometry using fluorochrome-conjugated anti-mouse antibodies for lineage defining factors. Furthermore, TILs were isolated using mouse pan T magnetic beads, and IFN-γ levels were examined. Blood and spleen were examined for changes in effector memory cells.

Results The combined treatment of TTFields and anti-PD-1/anti-CTLA-4 led to a significant decrease in tumor volume as compared to untreated control mice, as well as relative to mice treated with only one of the modalities. In addition, a significant increase in the number of tumor infiltrating immune cells, specifically cytotoxic T-cells, was observed in the TTFields plus anti-PD-1/anti-CTLA-4 group. Correspondingly, cytotoxic T-cells isolated from these tumors have shown higher levels of IFN-γ production relative to untreated mice. The levels of splenic and blood effector memory cytotoxic T-cells were elevated following TTFields with anti-PD-1/anti-CTLA-4 relative to control and TTFields alone, and were similar to those induced by anti-PD-1/anti-CTLA-4 alone.

Conclusions Our results suggest that combining TTFields with the immune checkpoint inhibitors combination anti-PD-1/anti-CTLA-4 may enhance antitumor immunity relative to each modality alone.

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