Tumor Treating Fields (TTFields) Concomitantly with Anti-PD-1 and Cisplatin in a Mouse Model of Non-Small Cell Lung Cancer

Poster 1748

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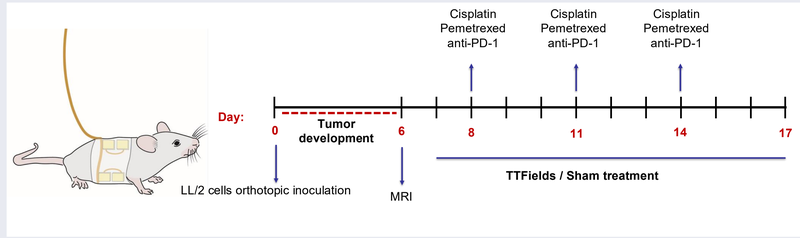
Introduction

- Tumor Treating Fields (TTFields) are low-intensity electric fields that disrupt cellular processes critical for cancer cell division and tumor progression.[1,2]
- TTFields have been shown to induce immunogenic cell death (ICD) in cancer cells and elicit a systemic anti-cancer immune response. [3-4]
- TTFields are approved for treatment of glioblastoma and pleural mesothelioma together with standard chemotherapy, and for treatment of metastatic non-small cell lung cancer (NSCLC) together with immune checkpoint inhibitors or docetaxel after progression on platinum-based therapy.[1,2,5]
- The ongoing LUNAR-2 clinical trial (NCT06216301) is evaluating first-line TTFields administered concomitantly with pembrolizumab and platinum-based chemotherapy in metastatic NSCLC.
- The current study aimed to investigate TTFields concomitant with anti-PD-1, cisplatin, and pemetrexed (PCP) in NSCLC preclinical models.

Methods

- C57BL/6 mice were orthotopically implanted with LL/2 lung carcinoma cells. After 7 days, after confirming tumor localization by MRI, the mice were randomized into 4 groups: control, TTFields, anti-PD-1/cisplatin/pemetrexed (PCP), and TTFields together with PCP. Treatment consisted of TTFields (150 kHz) or sham (heat) continuously for 10 days, and vehicle or anti-PD-1 (10 mg/kg), cisplatin (1 mg/kg), and pemetrexed (6 mg/kg), administered via intraperitoneal injection every 72 hours (three doses total), 24 hours after treatment initiation. At study end, tumors were examined with MRI, weighed and measured with calipers. Tumors were processed into single cell suspensions and peripheral blood was collected for spectral flow cytometry-based immunophenotyping.

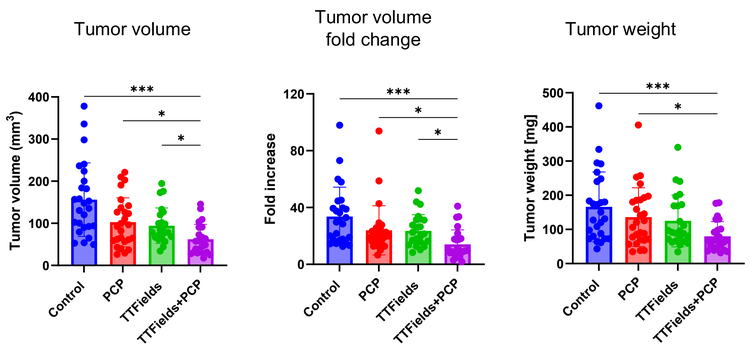


- Tumor single cell suspensions and peripheral blood were stained with Zombie NIR and for the following immune-markers: CD45, CD11b, CD3e, CD4, CD8a, CD11c, CD44, CD62L, F480. Tumor cells were further stained for Granzyme-B expression by intracellular staining.
- For the detection of cells pre-expressing IFNγ, the single cell suspensions were re-stimulated using PMA/Ionomycin for 2 hours, followed by intracellular staining of IFNγ.

Results

FIGURE 1.

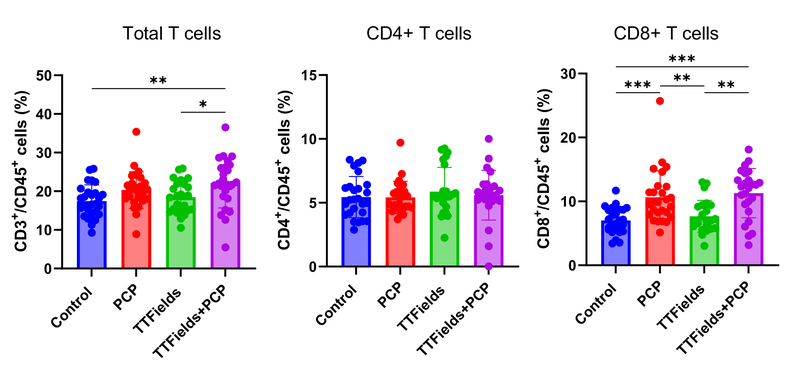
TTFields and PCP each inhibit tumor growth, with greater efficacy observed when administered concurrently



Kruskal-Wallis test with Dunn's multiple comparisons; *p < 0.05, **p < 0.01, ***p < 0.001

FIGURE 2.

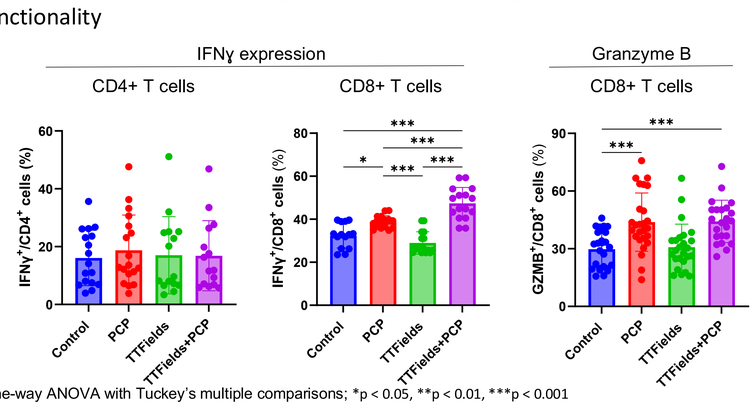
PCP alone and in conjunction with TTFields promote tumor infiltration of CD3+ T cells, with a notable increase in CD8+ T cells



One-way ANOVA with Tuckey's multiple comparisons; *p < 0.05, **p < 0.01, ***p < 0.001

FIGURE 3.

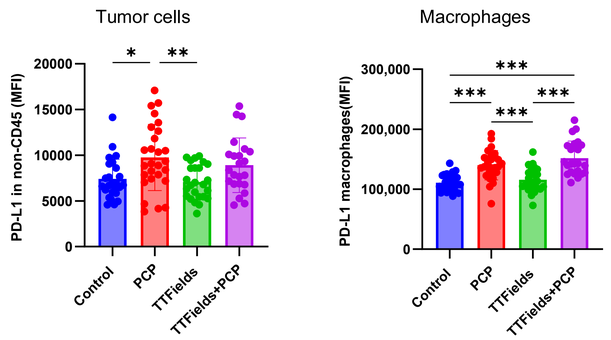
TTFields concurrent with PCP enhance IFNγ production and granzyme B expression by tumor-infiltrating CD8+ T cells, indicating improved cytotoxic functionality



One-way ANOVA with Tuckey's multiple comparisons; *p < 0.05, **p < 0.01, ***p < 0.001

FIGURE 4.

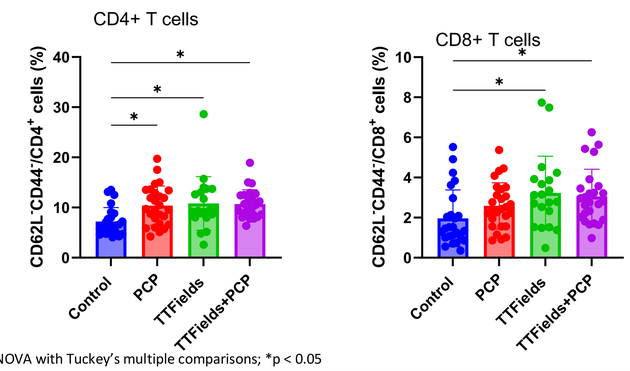
PCP alone and together with TTFields increase tumor PD-L1 expression, a marker of inflammatory response



One-way ANOVA with Tuckey's multiple comparisons; *p < 0.05, **p < 0.01, ***p < 0.001

FIGURE 5.

TTFields, PCP, and their concurrent administration increase the frequency of pre-effector CD4+ and CD8+ T cells in peripheral blood



One-way ANOVA with Tuckey's multiple comparisons; *p < 0.05

Conclusions

TTFields administered concurrently with standard immunochemotherapy improved tumor control and amplified the cytotoxic immune response in a mouse model of NSCLC

References: 1. Moser, J. C., et al. (2022). *Cancer Res* 82(20): 3650-3658. **2.** Karanam, N. K. and M. D. Story (2021). *Int JRadiat Biol* 97(8): 1044-1054. **3.** Voloshin, T., et al. (2020). *Cancer Immunol Immunother* 69(7): 1191-1204. **4.** Barsheshet, Y., et al. (2022). *Int J Molec Sci* 23(22): 14073. **5.** Leal, T., et al. (2023). *The Lancet Oncology* 24(9): 1002-1017.