Tumor Treating Fields (TTFields) concomitant with antiangiogenic therapy in non-small cell lung cancer in vivo model

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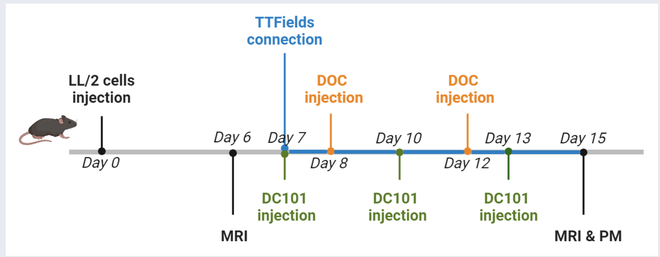
Introduction

- Angiogenesis is a hallmark of disease progression and poor prognosis in non-small cell lung cancer (NSCLC)[1]
- Ramucirumab, an antiangiogenic antibody that binds the vascular endothelial growth factor receptor (VEGFR), is approved as second line treatment for metastatic NSCLC, in combination with docetaxel[1]
- Angiogenic inhibitors function by normalizing tumor vasculature, hence improving drug delivery and immune cell infiltration to the tumor[2]
- Tumor Treating Fields (TTFields) are electric fields that disrupt cellular processes critical for cancer cell viability and tumor progression[3-4]
- TTFields therapy, together with immune checkpoint inhibitors or docetaxel, is approved for treatment of metastatic NSCLC following progression on or after platinum-based therapy[5]
- In the current study, we examined the effects of TTFields concomitant with docetaxel and anti-VEGFR treatment in an orthotopic NSCLC mouse model

Methods

C57Bl/6 mice were injected orthotopically with LL/2 lung carcinoma cells, and tumors were allowed to grow for 7 days. The mice were then treated with TTFields (150 kHz) or sham (heat) continuously for 8 days. Vehicle or the murine anti-VEGFR DC101 (10mg/kg) were intraperitoneally administered on days 1, 4, and 7 of treatment. Vehicle or docetaxel (DOC, 3mg/kg) were intraperitoneally administered on days 2, and 6 of treatment. Overall, there were 6 study groups: control, DOC alone, DOC plus DC101, TTFields alone, TTFields plus DOC, and TTFields plus DOC plus DC101. At treatment end, tumors were weighed and analyzed by immunohistochemistry, with anti-CD31 for vessel staining and additional functional markers. Tumor volume was measured by MRI before and after treatment, and fold change was calculated.

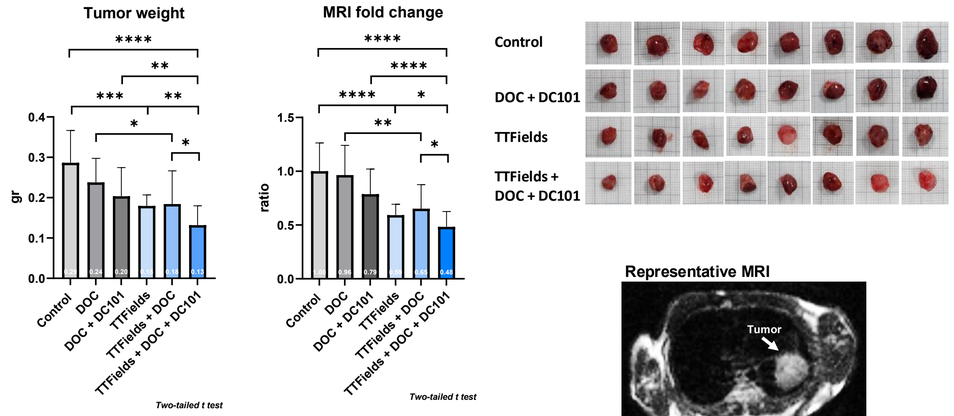


Conclusions

TTFields application alongside docetaxel and an anti-VEGFR antibody increased treatment efficacy via normalization of tumor blood vessels, which allowed for increased tumor immune cell infiltration

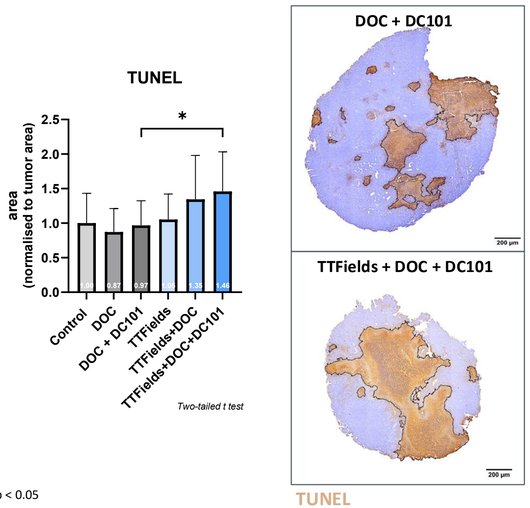
Results

FIGURE 1. TTFields concomitant with docetaxel and DC101 decreased tumor growth as compared to the monotherapies and the dual therapies



*p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001

FIGURE 2. TTFields concomitant with docetaxel and DC101 elevated tumor cell death



*p < 0.05

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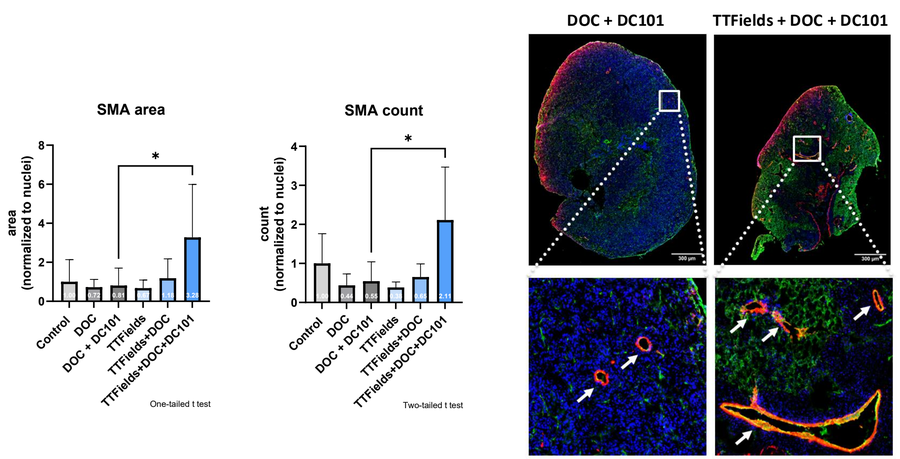
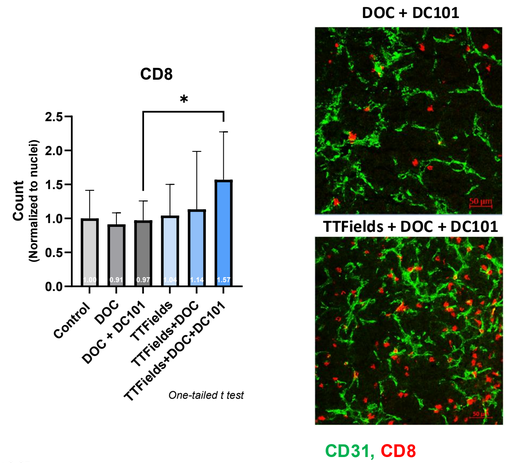
FIGURE 3. TTFields concomitant with docetaxel and DC101 enhanced vessel maturity



*p < 0.05

FIGURE 4. TTFields concomitant with docetaxel and DC101 treatment increased tumor CD8 infiltration



*p < 0.05

References: 1. Maione P, et al. (2017). *Curr Med Chem.* 24(1): 3-13. 2. Magnussen, A.L., Mills, I.G. (2021) *Br J Cancer.* 125, 324–336. 3. Karanam NK, Story MD (2021). *Int J Radiat Biol.* 97(8): 1044-1054. 4. Moser JC, et al. (2022). *Cancer Res.* 82(20): 3650-3658. 5. Leal, T., et al. (2023). *The Lancet Oncology.* 24(9): 1002-1017.

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