**Background and previous work**

- New York esophageal squamous cell carcinoma-1 (NY-ESO-1)–specific T cells are a unique subset of human T cells that are capable of recognizing NY-ESO-1–specific TAA epitopes. A separate study using engineered T cells targeting NY-ESO-1 have shown a partial response in a patient with advanced lung adenocarcinoma. Decitabine (DAC) is a hypomethylating agent and an inhibitor of TAA expression in TAA-low-expressing tumor cell lines to enhance T-cell sensitivity.

**Aims**

- The aim of this study was to assess enhancement of combination therapy with lete-cel in vivo in a NSCLC model.

**Methods**

- The in vitro use of DAC to selectively modulate TAA expression in TAA low-expressing cell lines following DAC treatment to combined levels to induce specific responses by lete-cel. Highlighting the additive effect of NY-ESO-1 and LAGE-1a in their contribution to the triggering of a T-cell response.

- Treatment of solid tumors remains challenging. Possibly due to the immunosuppressive tumor microenvironment (TME), heterogeneity of antigen expression and uncontrolled metastatic conditions.

**Results**

- Lete-cel in combination with DAC significantly enhanced anti-tumor efficacy in a NSCLC model in vivo, compared with lete-cel monotherapy (Figure 2). 

- Expression of the antigens NY-ESO-1 and LAGE-1a can be enhanced independently of one another in in vitro tumor cell lines following DAC treatment to combined levels to induce specific responses by lete-cel. Highlighting the additive effect of NY-ESO-1 and LAGE-1a in their contribution to the triggering of a T-cell response.

- The presented data show no significant differences in tumor volumes were noted between the combination and other treatment groups with no significant difference between decitabine and untreated.

- Consistent with our previous in vitro studies, DAC treatment in vivo resulted in induction of LAGE-1a (RT-PCR) in the NSCLC (NCI-H1703) tumor model. Endogenous expression of NY-ESO-1 was high in the NSCLC (NCI-H1703) and no further increase was observed following DAC treatment (Figure 3).

- Anti-tumor responses in late-stage monotherapy and combination groups was confirmed in a clinically relevant model, mimicking developed NSCLC.

- Anti-tumor efficacy was associated with increased IFN-γ secretion at early timepoints (Day 7 post T-cell infusion; Figure 4). Results at the later timepoints Day 21 post T-cell infusion were confounded by onset of graft versus host disease.

**Conclusions**

- Pre-treatment of NCI-H1703 with DAC resulted in increase in expression of LAGE-1a in vivo. This was associated with a reduction in tumor burden and a nominal increase in IFN-γ in late-stage in combination with DAC compared with treatment with lete-cel alone.

- DAC is currently enrolling a Phase IIb, multicenter, open-label study (NCT03971566) of lete-cel as a monotherapy or in combination with pembrolizumab in patients for the use of DAC in combination with pembrolizumab to improve the efficacy of NY-ESO-1–specific T cells, by increasing levels of target antigens and anti-tumor effect in NSCLC.

**References**


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