**BACKGROUND**

- Relapsed pediatric sarcomas have a poor prognosis with no available curative options.
- Alpha-Tocopheryloxyacetic acid (a-TEA) is a redox-silent analog of alpha-tocopherol that induces apoptotic and immunogenic cell death of tumor cells.
- In a first-in-human clinical trial, a-TEA was well tolerated in adults with advanced solid tumors (NCT02192346) but has not yet been studied in pediatric sarcoma.
- We used a murine model of rhabdomyosarcoma (M3-9-M RMS) to assess the in vivo and in vitro anti-tumor effects of a-TEA.

**METHODS**

- Mice were randomized to a control diet or a TEA enriched diet for 3 weeks. Spleens were then randomized to receive a control diet or an a-TEA enriched diet for 3 weeks. Spleens were analyzed at the end of treatment.
- Increased levels of Arg1+ PD-L1+ myeloid cells were also seen.
- RNA-seq analysis of tumors from treated and control groups showed gene expression changes in EP300, c-Jun, and CXCR4.

**RESULTS**

- a-TEA, Alpha-Tocopheryloxyacetic acid (a-TEA), is a redox-silent analog of alpha-tocopherol that induces apoptotic and immunogenic cell death of tumor cells.
- a-TEA mediates apoptosis of RMS in vitro and suppresses in vivo tumor growth, leading to prolonged survival.
- Spleens from a-TEA treated mice showed increased levels of IFN-gamma+, CD4+ T cells, and decreased levels of Arg1+ and PD-L1+ myeloid cells.

**CONCLUSIONS**

- a-TEA mediates apoptosis of RMS in vitro and suppresses in vivo tumor growth, leading to prolonged survival.
- Potential mechanisms may include direct apoptosis of RMS versus enhanced activation of adaptive immunity through IFN-gamma+ production by CD4+ T cells and/or suppression of Arg1+ PD-L1+ myeloid cells.
- a-TEA may have direct effects on tumor cell proliferation through EP300 and c-Jun as well as indirect effects by immune cell recruitment through CXCR4 expression.

**ADDITIONAL KEY INFORMATION**

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