Introduction

- There are greater than 40,000 new head and neck squamous cell carcinoma (SCC) cases and more than 10,000 deaths annually in the United States.
- Despite advances in therapy, locoregional recurrence may occur in up to 60% of patients.
- Cancer immunotherapy is a method of modulating the innate immune system to treat malignant tumors.
- Recent advances in immunotherapy using gene transfer have shown promising results in several forms of cancer.
- We studied the effects of gene transfer of interleukin 12 (IL-12) and granulocyte macrophage-colony stimulating factor (GM-CSF) via intratumoral injections of adenoviral vectors with and without the use of systemic Ig-4-1BB Ligand (L) in an orthotopic murine floor of mouth (FOM) SCC model.

Methods

- Adenoviral vectors were constructed as previously reported by Chen et al.
- In vitro, the effects of the viral vectors were tested on human SCC lines FaDu and SCC 09, and murine SCC VII.
- Cells were treated with various multiplicities of infection (MOI) of the respective virus or phosphate-buffered saline (PBS) control.
- After 24 and 48 hours mL-12 and mGM-CSF levels were quantified using ELISA.
- After 24 and 48 hours mIL-12 and mIL-12+ Ig-4-1BBL had a cure rate of almost 1/3 animals with FOM SCC.
- Our data provides support for future clinical development of the double therapy regiment for the treatment of FOM SCC, with potential development of an advIL-12/GM-CSF agent in combination with Ig-4-1BBL pending further investigation.

Results

- In vitro, the advCMV-IL-12/GM-CSF had a greater than 10-fold increase in expression of IL-12 along all cell line (p<0.001 vs. advRSV-IL-12).
- In vivo, advIL-12/GM-CSF + Ig-4-1BBL and advIL-12 + Ig-4-1BBL demonstrated a statistically significant survival over PBS (p<0.0001;p<0.006 respectively vs. PBS).
- In vivo, advIL-12/GM-CSF + advIL-12 + Ig-4-1BBL demonstrated a statistically significant survival over PBS (p<0.0001;p<0.006 respectively vs. PBS).

Conclusions

- The data suggests, in vitro, the adenoviral vector is more effective for IL-12 expression than the cytomegaloviral vector.
- There is a survival advantage of the double therapy, advIL-12 + Ig-4-1BBL, in FOM SCC in a murine model.
- Triple therapy, advIL-12/GM-CSF + Ig-4-1BBL had a cure rate of almost 1/3 animals with FOM SCC.
- Our data provides support for future clinical development of the double therapy regiment for the treatment of FOM SCC, with potential development of an advIL-12/GM-CSF agent in combination with Ig-4-1BBL pending further investigation.

References