Individualized Therapeutic Vaccine in Second Line Recurrent/Metastatic HNSCC

Abstract

Biomechanochemical deviation of fibroblasts (HSP) is associated with multiple augmenting therapies and anatomic changes, but the HSP 1 molecular repertoire in disease states is not well understood. To study tumor antigen chaperoned on HSP, we collected biopsy samples from patients with recurrent/metastatic HNSCC at baseline, and tumour lysates were harvested. The HSP were collected by isoelectric focusing and the individualized vaccine candidate, with additional chaperones of the endogenous or exogenous HSP, was tested in an in vitro model of the fibroblast microenvironment. The results provide rationale for further evaluation of this vaccine in this and other HNSCC populations.

METHODS:

Baseline and 8 weeks tumor biopsy samples were collected from ten subjects with recurrent/metastatic HNSCC and visible tumors. All subjects were also treated with BAG in circulation, each wave of activated non-memory allo-specific and tumor-specific Th1/CTL along with resident M1 macrophages mediates non-specific tumor lysis. The priming injection of BAG cells causes waves of activated non-memory allo-specific Th1/CTL and allo-specific Th1/CTL which in turn cause extravasation of allo-specific and tumor-specific Th1/CTL along with resident M1 macrophages mediate non-specific tumor lysis. The priming phase was repeated and each wave of activated Th1/CTL results in the development of a sustained immune response. Activated memory allo-specific and tumor-specific Th1/CTL, which in turn cause extravasation of allo-specific and tumor-specific Th1/CTL along with resident M1 macrophages mediate non-specific tumor lysis. The priming phase was repeated and each wave of activated Th1/CTL results in the development of a sustained immune response.

RESULTS:

The individualized vaccine phase was tested in an in vitro model of the fibroblast microenvironment. The results provide rationale for further evaluation of this vaccine in this and other HNSCC populations.

SUBJECTS

SUBJECT A

SUBJECT B

SUBJECT C

SUBJECT D

SUBJECT E

SUBJECT F

SUBJECT G

SUBJECT H

SUBJECT I

SUBJECT J

Introduction

This is a Phase I clinical trial that evaluating whether individually processed tumor antigen-chaperoned on HSP could be included in a clinical trial setting. The study is designed to assess the safety, feasibility, and immunogenicity of the vaccine candidate.

Vaccination Phase

In the priming phase, the cells are injected intradermally in order to elicit high-titer of all specific Th1/CTL in circulation. These activated/cytotoxic T-cells are non-specifically activated on HSP, DCs and macrophages and are recruited in the skin surface or by endoscopy. The BAG cells in circulation produce a cytokine storm which activates the circulating monocytes and monocytes/macrophages to release endogenous DAMPs. The DAMPs activate circulating Th1/CTL which in turn activate these circulating memory allo-specific and tumor-specific Th1/CTL along with resident M1 macrophages mediate non-specific tumor lysis. The priming phase was repeated and each wave of activated Th1/CTL results in the development of a sustained immune response.

Amplification

In order to amplify the anti-tumor effects of priming and accelerate the development of anti-tumor immunity, the tumor tissue is processed into a homogenate and the homogenate is injected intradermally. The BAG cells in circulation serve as naïve T-cells and the tumor tissue serves as an anti-alloantigen vaccine. The iDC engulf and process the alloantigens to the injection site. These cells reject the BAG, which causes the release of endogenous DAMP and HSP chaperones of the tumor. The endogenous HSP and DAMP chaperones of the tumor are processed in the skin, allowed to extravasate, and the skin surface or by endoscopy. The BAG cells in circulation produce a cytokine storm which activates the circulating monocytes and monocytes/macrophages to release endogenous DAMPs. The DAMPs activate circulating Th1/CTL which in turn activate these circulating memory allo-specific and tumor-specific Th1/CTL along with resident M1 macrophages mediate non-specific tumor lysis. The priming phase was repeated and each wave of activated Th1/CTL results in the development of a sustained immune response.

Activation and Booster

The priming and the second phase are repeated and each wave of activated non-memory allo-specific and tumor-specific Th1/CTL along with resident M1 macrophages mediates non-specific tumor lysis. The BAG cells in circulation serve as naïve T-cells and the tumor tissue serves as an anti-alloantigen vaccine. The iDC engulf and process the alloantigens to the injection site. These cells reject the BAG, which causes the release of endogenous DAMP and HSP chaperones of the tumor. The endogenous HSP and DAMP chaperones of the tumor are processed in the skin, allowed to extravasate, and the skin surface or by endoscopy. The BAG cells in circulation produce a cytokine storm which activates the circulating monocytes and monocytes/macrophages to release endogenous DAMPs. The DAMPs activate circulating Th1/CTL which in turn activate these circulating memory allo-specific and tumor-specific Th1/CTL along with resident M1 macrophages mediate non-specific tumor lysis. The priming phase was repeated and each wave of activated Th1/CTL results in the development of a sustained immune response.

In the event of normalization of the immune system, resulting in immune-mediated toxicity, the patient may be treated with the dendrocyte treatment option or activated Th1/CTL may serve as a “tumor agent.”

RESULTS

The results show that the vaccine candidate is safe and feasible in the clinical trial setting. The immune response is sustained and the tumor-specific immunity is developed. The vaccine candidate is broadly applicable and may be used as a treatment for recurrent/metastatic HNSCC.