A Novel Modular Polymer Platform for the Treatment of Head and Neck Squamous Cell Carcinoma

Ontario D. Lau, MD1, Sherven Sharma, PhD2, Ben Wu, PhD3, Steven M. Dubinett, MD2, Maia A. St. John, MD PhD1

Division of Head and Neck Surgery1, Division of Pulmonary and Critical Care2, Department of Bioengineering3, UCLA & VA Medical Centers

Abstract

Educational Objective: At the conclusion of this presentation, the participants should be able to understand the design and clinical benefits of a novel biocompatible modular polymer platform for patients with advanced or recurrent Head and Neck Squamous Cell Carcinoma (HNSCC).

Objectives: We are developing a novel biocompatible modular polymer platform which will improve the outcome for patients with advanced or recurrent Head and Neck Squamous Cell Carcinoma (HNSCC). The ability to decrease mortality, and improve survival for these patients has been a longstanding goal for cancer researchers.

Study Design: We are developing a polymer wrap that has the following characteristics: is biocompatible; is slowly degradable; can provide an initial mechanical barrier to metastasis and angiogenesis; and can serve as a platform to deliver immunomodulators and radiosensitizers so as to most effectively kill tumor cells in the proximity of the polymer application. This polymer wrap is designed to be applied intraoperatively to the surgical bed after removing or debulking the tumor, thus allowing for enhanced post-operative radiation treatment, and also functioning as a mechanical barrier to the spread of disease.

Methods: The safety and efficacy of the polymer platform will be tested in vitro, and subsequently in vivo in a mouse model system.

Results: Once the polymer platform is optimized in an in vivo model, we will plan for the ultimate validation in the context of a prospective trial in patients with unsuitable advanced or recurrent HNSCC.

Conclusions: A novel biocompatible modular polymer platform for the treatment of HNSCC is being developed and tested. Our study will provide the crucial platform to identify a promising intervention that warrants larger scale research efforts or multi-site clinical trials.

Background

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer in the world, and affects 60,000 Americans annually. Patients with HNSCC are at considerable risk of mortality, with more than 300,000 deaths attributable to the disease in 20001. During the past 30 years, the 3-to 5-year survival rate of patients with advanced T3 and T4 HNSCC has remained poor (20-30%) despite considerable advances in surgical techniques and irradiation and improvement in chemotherapeutic strategies. Unfortunately, many advanced head and neck cancers are unsuitable for surgical resection due to proximity to vital structures such as the carotid artery or the skull base. Although palliation by chemotherapy is often attempted, systemic toxicity and its impact on the quality of life of patients prevents its wider clinical application.2

Preliminary Results

Fabrication of porous foams. Foams for tissue engineering scaffolds was fabricated using the salt leaching technique. Figure 2 shows an example of a macroporous foam made from PLGA. Several highly complex scaffolds have been created by Wu et al.1 Figure 3 below shows an example of an open foam matrix that has been infused with gelatin5.

Methods

Fabrication of the Modular Polymer Platform

The proposed modular device consists of two major layers (Figure 1). The first layer is the Impermeable Backing Layer, a 1.5 mm thick, non-porous polymer film constructed from a slowly degradable polymer (PL-PLGA) that, even under the influence of ionizing radiation, will remain impermeable during the initial 4-6 weeks. After 4-6 weeks this film will breakdown to the point that impermeability will be lost, while the release of immunomodulators (CCL21) will increase to accompany the invasion of host immune cells. The Impermeable Backing Film is connected to a second layer that is comprised of two interpenetrating, porous materials (macroporous and microporous) which degrade at different rates and deliver different bioactive materials at different times. The Intermediate Release layer is a 3 mm thick macroporous polymer (PLGA) that will, under the influence of ionizing radiation, degrade and release the radiosensitizer cisplatin during the initial 4-6 weeks. The pore of the macroporous matrix are filled by a microporous gel matrix (gelatin) that will provide the rapid immediate release of a polymer.

Methods

Degradation and Release Kinetics of Bioactive Materials

Candidate materials were individually immersed into vials of different solutions at 37°C. 10 specimens were removed every 2 days during the first week, and then every week for the next 7 weeks (8 weeks total). Mass loss and water up-take of the sample was determined on 5 samples from each material at each time point by thermogravimetric analysis, in which the mass of the sample was measured continuously at a given temperature was increased at a constant rate. Release kinetics of bioactive materials over this experimental time course was determined by HPLC (Waters, Milford, MA) with corresponding HPLC protocols for each respective material.

Conclusions & Future Directions

A novel biocompatible modular polymer platform for the treatment of HNSCC is being developed and tested. In a three-stage study, the polymer will be developed; its safety and efficacy will continue to be tested in vitro, and subsequently in vivo in a mouse model system. Once the device parameters are optimized in animal models, we will plan for the ultimate validation in the context of a prospective trial in patients with unsuitable advanced or recurrent HNSCC.

References


