Update on Aspyrian Trial: Study of RM-1929 and Photoimmunotherapy in Patients with Recurrent Head and Neck Cancer

John Gleysteen, MD[1]; Joseph Curry, MD[1]; Adam Luginbuhl, MD[1]; Jennifer Johnson, MD, PhD[1]; Ralph Zinner, MD[1]; Merrill Biel, MD, PhD[2]; David Cognetti, MD[1]

[1]Thomas Jefferson University, Philadelphia, PA [2]Aspyrian Therapeutics, San Diego, CA

Abstract

Background: This is an update of an ongoing Phase 1 multicenter combination trial of targeted photoimmunotherapy for patients with recurrent head and neck squamous cell carcinoma (HNSCC) that cannot be satisfactorily treated with surgery, radiation or platinum chemotherapy.

Methods: Seven patients with recurrent head and neck SCC who had failed previous definitive treatment were enrolled and underwent treatment with RM-1929, a conjugate of cetuximab and IR700. Infusion of RM-1929 was performed 24 hours prior to light treatment. In the operating room, high intensity visible light (690 nm) was applied to the tumors either on the surface for mucosal/skin disease, or within the tumor via needle-catheter placed fiberoptic light diffuser fibers for submucosal and nodal disease. The treatment time was 4-6 minutes for each lesion treated. Subsequent treatments were performed for persistent lesions where deemed appropriate.

Results: Six of the 7 patients tolerated the treatment well with less than 24-hour post-treatment in-hospital observation required. All patients showed some evidence of tumor necrosis at the treatment site. Four out of 7 (57%) patients had regression of tumor with no progression at 3 months. The 3 other patients had progression at the periphery of tumor margin. Four patients underwent subsequent light treatments within 4-6 weeks after the first treatment, and 1 underwent surgical resection after partial response to 4 treatments. One patient was transitioned to hospice, and 1 underwent treatment with palliative chemotherapy. One patient had tumor surrounding her carotid artery; when the tumor shrunk the carotid became exposed and she died from bleeding.

Conclusion: At this early stage in a phase 1 multicenter clinical trial, targeted photoimmunotherapy with RM-1929 appears to be a well-tolerated option for patients with recurrent head and neck squamous cell carcinoma who have not responded to other treatments. Four out of 7 (57%) patients have demonstrated durable clinical response to the treatment. No skin photosensitivity or normal tissue toxicity was noted.

Introduction

- Photoimmunotherapy with RM-1929 is a novel targeted anticancer light-activated treatment for the locoregional management of epidermal growth factor receptor (EGFR)-expressing tumors
- This Phase 1 clinical trial seeks to determine the safety and efficacy of the tumor-specific antibody-drug conjugate (cetuximab + IR700) and interstitial light activation to induce death of cells overexpressing the antigen

Methods

Primary Objective: Determine optimum light fluence to achieve clinical response with acceptable safety profile over up to 4 treatments

Inclusion Criteria: Recurrent HNSCC who cannot be satisfactorily treated with surgery, radiation, or chemotherapy. Must have received prior systemic platinum-based chemotherapy.

Pre-Treatment and Drug Treatment (Day 1)
- Pretreat with antihistamine and steroid
- Challenge dose 100mg of Erbitux IV over 30 minutes
- If adverse reaction >/= 3 to Erbitux, supportive care and removal
- After challenge dose, RM-1929 infusion over 120 minutes
- Whole blood sample for blood PK and immunologic assays

Light Treatment (Day 2)
- One light application performed 24 hours post drug administration

Follow Up Period
- Examine at 1 week, 2 weeks, 1 month after drug infusion
- Follow every three months for 2 years

Results

Age	Tumor site	Treatments	Comments
78M	oropharynx, hypopharynx	2	Clinical and radiologic improvement, no evidence of disease currently
67M	retropharyngeal nodes, bilateral neck nodes	4	Moderate rash of scalp and back from drug initially, continued clinical and radiologic improvement of tumor noted
59F	right and left neck, peristomal area	3	Strong tumor response leaving right carotid artery exposed, developed pharyngocutaneous fistula; died of carotid bleed after exposure
66M	left neck mass	4	Partial response of tumor to treatments, underwent resection after completion
65M	neopharynx	1	Progression of disease posteriorly into spine, palliative chemotherapy, died due to disease
86M	left face and neck	1	Extensive tumor necrosis debrided, wound granulating with NED. Noted increased appetite, weight gain, and activity
75M	right face and neck	1	Partial response on right (treated) side but progression on left, transitioned to hospice, died due to disease

Conclusion

- Targeted photoimmunotherapy using a conjugate of cetuximab and IR700 dye is safe and well tolerated and led to evidence of tumor necrosis at the treatment site in 7/7 (100%) patients. No skin photosensitivity or normal tissue toxicity noted.
- Four out of 7 (57%) patients had durable clinical response to the treatment without progression of disease

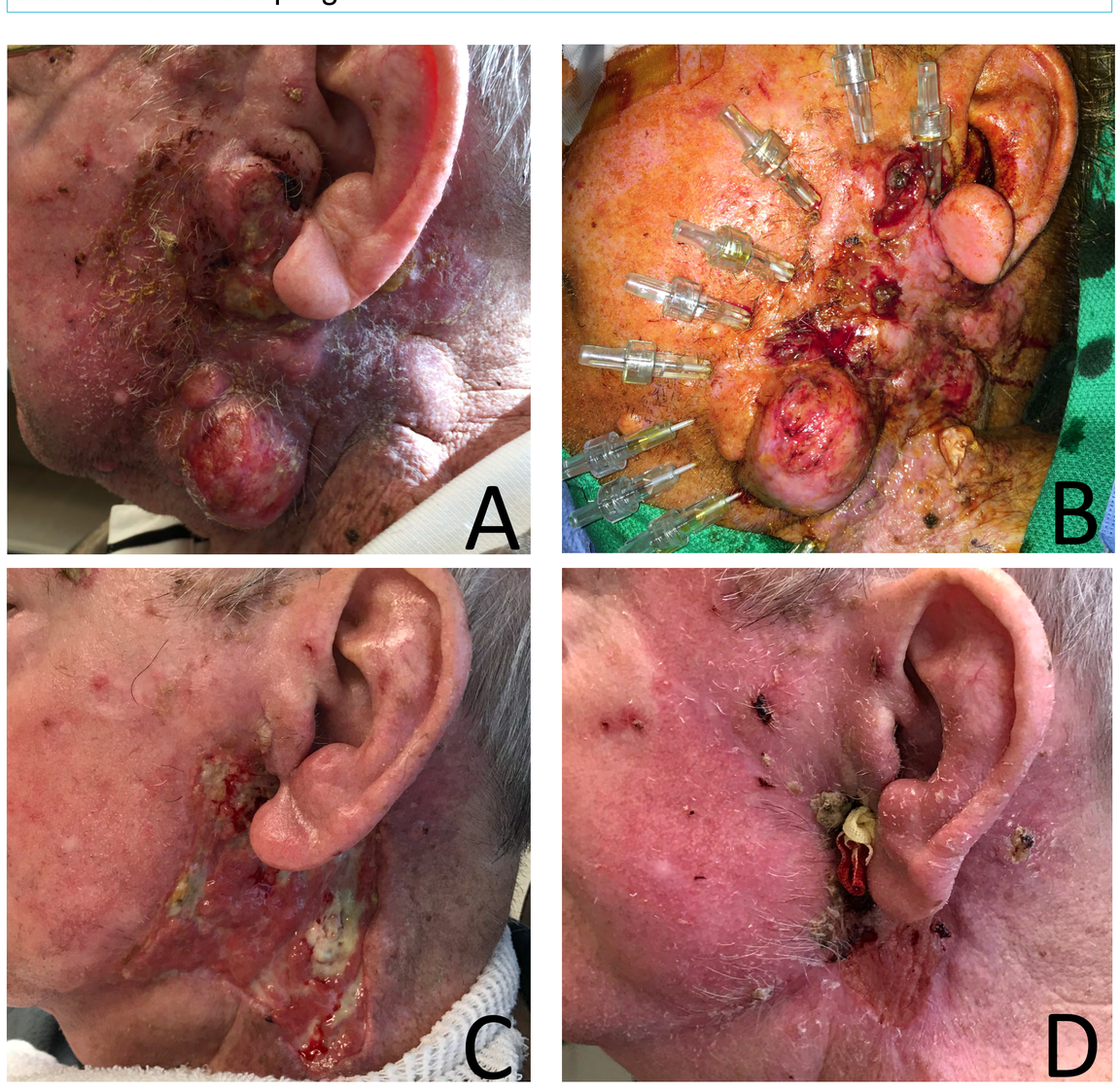

Fig 1: 86 YOM patient with left parotid squamous cell carcinoma, treated initially with surgery followed by radiation and systemic therapy, who then recurred. He enrolled in the Aspyrian trial and underwent treatment. Photographs show (A) pre-operative appearance, (B) intra-operative appearance, (C) 1 month post-treatment, (D) 3 months post-treatment.

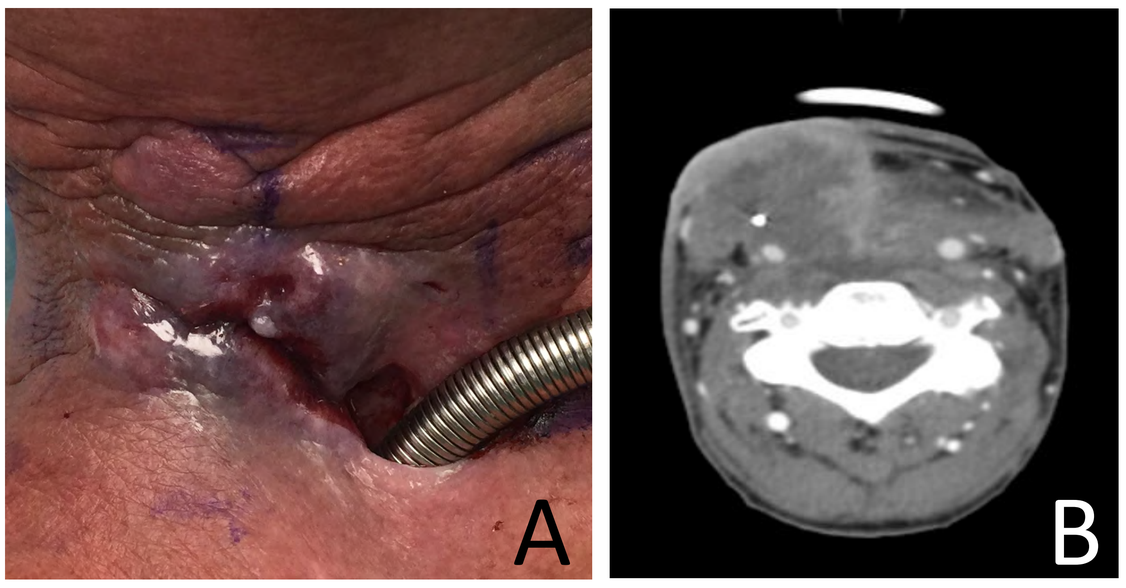

Fig 2: 59 YOF patient with history of salvage laryngectomy for recurrent squamous cell carcinoma who developed peristomal recurrence then enrolled in the Aspyrian trial. Photographs show (A) pre-treatment appearance of stoma and (B) pre-treatment CT scan, (C) 6 weeks post-treatment appearance of stoma and (D) 6 week post-treatment CT scan.

Contact

John Gleysteen, MD
John.gleysteen@jefferson.edu

References

1. Mitsunaga M, Ogawa M, Kosaka N et al. Cancer cell-selective in vivo near infrared photoimmunotherapy targeting specific membrane molecules. Nat Med. 2011 Nov 6; 17 (12): 1685-91.