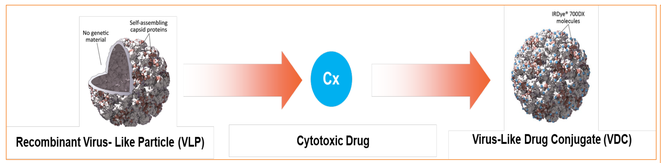
Ocular distribution and exposure of AU-011 after suprachoroidal or intravitreal administration in an orthotopic rabbit model of human uveal melanoma

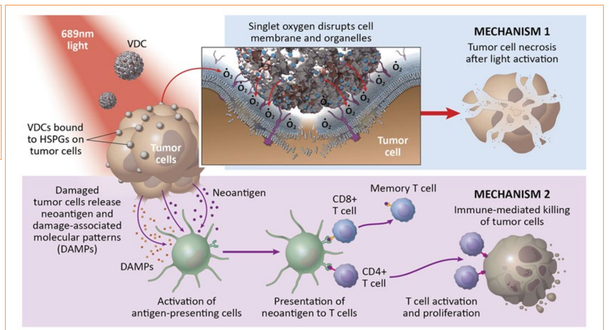
Savinainen, Anneli[1], Grossniklaus, Hans[2]; Kang, Shin[2]; Wicks Joan[3]; Rich, Cadmus[1]
[1] Aura Biosciences, Cambridge , Massachusetts, [2] Emory Eye Care Center, GA, Atlanta, Georgia, [3] Stage Bio, Mt Jackson, VA, United States

Introduction

This study compared the ocular distribution and exposure, after suprachoroidal (SC) and intravitreal (IVT) administration of AU-011 in an orthotopic rabbit model of uveal melanoma. AU-011 (belzupacap sarotalocan) is designed as a first in class targeted investigational therapy for the primary treatment of uveal melanoma that once activated with infrared light has shown an ability to cause acute cellular necrosis of tumor cells with a pro-immunogenic cell death, that triggers a T-cell response that it is believed to potentially elicit long-term anti-tumor immunity. AU-011 has shown promising preliminary results in a Phase 1b/2 clinical trial in primary choroidal melanoma delivered by IVT administration. A Phase 2 clinical trial is ongoing to evaluate SC administration, which may be a more targeted route of administration to the posterior segment of the eye.

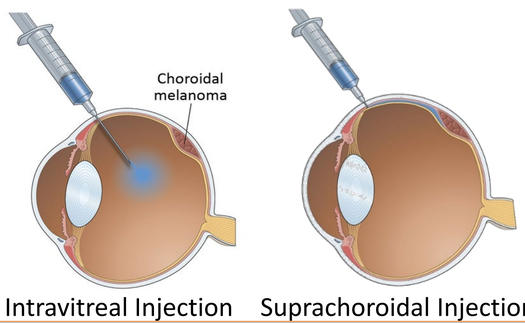
AU-011: A Novel Approach to Target Tumors with Dual Mechanism





AU-011 is an investigational Virus-Like Drug Conjugate (VDC) consisting of a recombinant Virus-Like Particle (VLP) that targets the tumor cell surface and a cytotoxic drug payload that is activated with infrared light

Suprachoroidal vs Intravitreal Injection



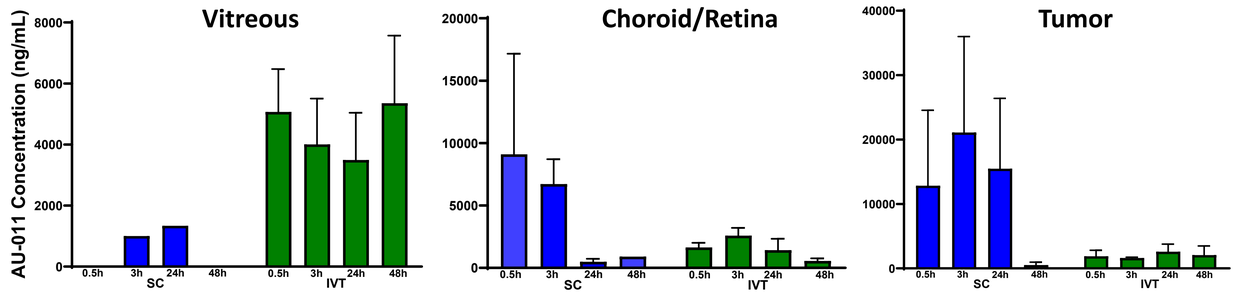
Delivery to the suprachoroidal may optimize AU-011's therapeutic index based on:

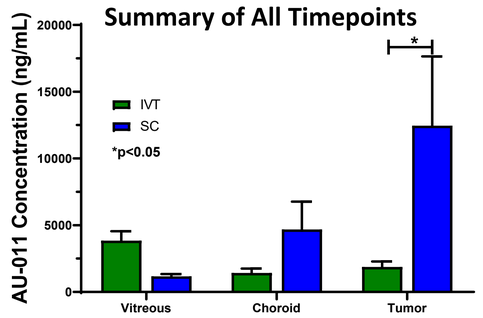
- **Higher tumor drug exposure**
- **Lower vitreous exposure which may lower risk of vitreous inflammation**
- **Optimized treatment parameters (shorten the time between injection and laser)**

Methods

Human uveal melanoma 92.1 cells were implanted in the choroid of immunosuppressed (Cyclosporine, 10-15 mg/kg/day subcutaneously) female New Zealand White (NZW) rabbits (N=3 animals/group/timepoint). Once tumors reached ~5 mm in basal diameter, AU-011 was administered by SC or IVT injection. Ocular tissues including vitreous, choroid and tumor samples were collected at multiple time points up to 48 hours post injection. AU-011 exposure levels in vitreous, choroid/retina and tumor was determined using an electrochemiluminescence immunoassay. Distribution of AU-011 in the tumor was evaluated by immunohistochemical staining using a monoclonal rat antibody against the VLP component of AU-011.

Superior Tumor Exposure After Suprachoroidal Injection

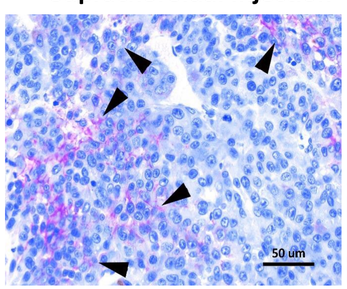




- **After SC injection there was negligible exposure of AU-011 in the vitreous and high exposure in the tumor and choroid/retina**
- **SC injection of AU-011 resulted in higher tumor and choroid exposure (~6x) compared to IVT injection with mean concentrations of 12459 +/- 5190 and 1996 +/- 421 ng/mL, respectively**
- **IVT injection resulted in relatively high exposure in the vitreous**

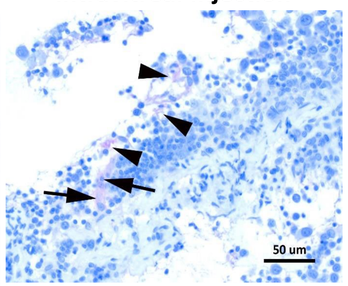
Ocular Distribution After Suprachoroidal or Intravitreal Injection

Suprachoroidal Injection



IHC staining of AU-011 (pink) 3 hours post SC Injection of AU-011. AU-011 positive staining (extracellular) infiltrating within tumor (arrowheads)

Intravitreal Injection



IHC staining of AU-011 (pink) 3 hours post IVT Injection of AU-011. Small amount of extracellular (arrowheads) and possible intracellular (arrows) AU-011 positive staining in vitreal surface of tumor

- **IHC staining supports that AU-011 was present in the tumor after both SC and IVT injections**
- **AU-011 staining was observed penetrating throughout the tumor in the SC injected eyes**
- **AU-011 staining in the IVT injected eyes demonstrated that AU-011 was mostly localized on the apex or vitreal surface of the tumor**

Conclusion

- **Data suggest that suprachoroidal administration is superior to intravitreal administration, which may support an optimized therapeutic index for AU-011:**
  - **Higher tumor bioavailability with improved tumor exposure and distribution**
  - **Reduced exposure in the vitreous and other key ocular structures, which may result in an improved safety profile**

ARVO, May 1-7, 2021

Disclosures: Anneli Savinainen and Cadmus Rich, Aura Biosciences Code E (Employment)